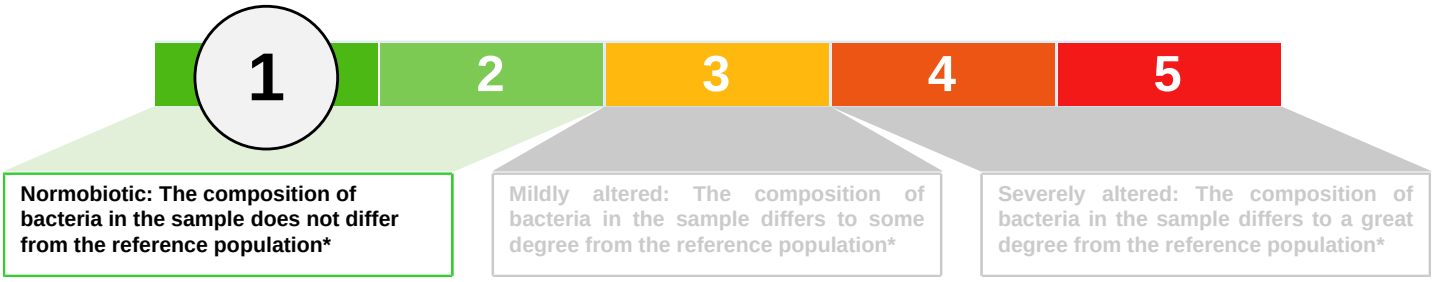
TEST RESULTS

SAMPLE ID: CPnone-DI1	Collection Date:	Date Received:	Report Date: 2024-01-16

RECOMMENDED BY		TEST SUBJECT	
Clinic		Name	
Name		Date of Birth	

DYSBIOSIS INDEX

Dysbiosis is defined as a permanent or transient imbalance in the gut microbiota composition. This imbalance could be due to an increase in potentially harmful bacteria and/or a decrease in commensal bacteria. The dysbiosis index (DI) is reported on a scale from 1 to 5. See explanation of the scale and results below.



Result: The microbiota is normobiotic

DIVERSITY

Diversity of the gut microbiota is defined as the number of different bacterial species in the gut and their abundance. Diversity is reported as "lower than expected", "slightly lower than expected" or "as expected", and is calculated based on Shannon diversity index.

Result: The bacterial diversity is as expected

*Reference population: A clinically validated group of healthy adults (age 18-70) with no gastrointestinal symptoms and no history of gastrointestinal diseases [1].

BACTERIA ABUNDANCE TABLE

The relative abundance of 48 preselected bacteria markers are presented below. The bacteria markers are placed in categories and groups based on their functional properties. Note that a single bacterial marker may belong to multiple categories/groups. The bacteria were grouped to facilitate the interpretation of the results, placing markers in the categories that most closely relate to human health within the context of host - gut microbiota interactions.

Category A. Broad commensals

Group	No.	Bacteria	Reduced -3	-2	-1	Normal*	Elevated 1	2	3	Group result
A1. Prominent gut microbes	300	Various Bacillota				●				✓
	206	Various Bacteroidota				●				
A2. Diverse gut bacterial communities	100	Various Actinomycetota			●					!
	302	Various Bacilli				●				
	305	Various Clostridia & Negativicutes					●			
	331	Various Bacillales & Lachnospirales				●				

A1. **Prominent gut microbes** represent the two most abundant bacteria phyla in the gut: Bacillota (Firmicutes) and Bacteroidota (Bacteroidetes). Increased Bacillota-to-Bacteroidota ratio has been associated with obesity and metabolic syndrome, while decreased Bacillota with IBD [2]. **Result: expected abundance of these bacteria.**

A2. **Diverse gut bacterial communities** cover a broad range of gut commensals within the indicated taxa. Imbalanced levels of any of these taxa indicate changes in the variety and composition of microbes in the gut relative to those typically found in a healthy population, often associated with lower species richness (internal observation). **Result: slightly deviating abundance of these bacteria.**

Category B. Enriched on animal-based diet

Group	No.	Bacteria	Reduced -3	-2	-1	Normal*	Elevated 1	2	3	Group result
B1. Enriched on animal-based diet	201	*Alistipes* spp.				●				✓
	202	*Alistipes onderdonkii*				●				

B1. *Alistipes* are bile-resistant bacteria, highly **enriched on animal-based diets** [3]. They can metabolize tryptophan into indole derivatives. While moderate levels are beneficial, excessive indole production may come at the expense of serotonin levels, which are essential for regulating mood and cognition [4]. For this reason, elevated *Alistipes* levels are often linked to depression [4]. Increased abundance of *A. onderdonkii* may also serve as a marker of high body fat and total cholesterol [5]. On the other hand, decreased levels of these species are associated with increased inflammation in conditions like non-alcoholic fatty liver disease (NAFLD) and Crohn's disease [4, 6]. **Result: expected abundance of these bacteria.**

*Reference population: A clinically validated group of healthy adults (age 18-70) with no gastrointestinal symptoms and no history of gastrointestinal diseases [1].

Category C. Essential cross-feeders

Group	No.	Bacteria	Reduced -3	-2	-1	Normal*	1	Elevated 2	3	Group result
C1. Complex carbohydrate degraders	205	*Bacteroides xylanisolvens*				●				✓
	207	*Bacteroides stercoris*				●				
	208	*Bacteroides zoogleoformans*				●				
	209	*Parabacteroides johnsonii*				●				
	210	*Parabacteroides* spp.				●				
	306	*[Clostridium] methylpentosum*						●		
	316	*[Eubacterium] siraeum*				●				
	323	*Ruminococcus bromii*				●				
	332	*[Bacteroides] pectinophilus*				●				
C2. Lactic acid bacteria and probiotics	103	*Bifidobacteriaceae*				●				✓
	319	*Pediococcus* & *Ligilactobacillus ruminis*				●				
	320	*Lactobacillaceae*				●				
	321	*Lactobacillus acidophilus* & *L. acetotolerans*				●				
	325	*Streptococcus agalactiae* & *Blautia wexlerae*				●				
	326	*Streptococcus thermophilus, S. gordonii* & S. sanguinis					●			
	327	*Streptococcus salivarius* group & *S. mutans*				●				

C1. **<u>Complex carbohydrate degraders</u>** thrive on various types of dietary fiber and prebiotics, such as inulin, resistant starch, and pectin, which are abundantly found in foods like oats, bananas, apples, garlic and onions (high FODMAP foods). By breaking down complex carbohydrates, they support the production of short-chain fatty acids (SCFA) and other beneficial metabolites that are important for cross-feeding among microbial species [5, 7]. Notably, many bacteria in this group contribute to the build-up of intestinal gas, so an increase in their abundance may be linked to bloating and abdominal pain [8]. **Result: expected abundance of these bacteria.**

C2. **<u>Lactic acid bacteria and probiotics</u>** produce lactic acid and other antimicrobial substances that help control pathogen growth, support the gut barrier, modulate the immune system, and aid in the fermentation of dietary fibers. These functions are essential for preventing infections, reducing inflammation, supporting nutrient synthesis (notably as major producers of vitamins B and K), and maintaining overall gut health [9]. Many of these bacteria are also marketed as probiotics and are naturally found in fermented food such as yogurt. Of note, proton pump-inhibitor use may increase the abundance of *Streptococcus* and *Lactobacillus* species [10]. Overgrowth of lactate producers in the gut can promote sulphide formation by sulphate-reducing bacteria, potentially harming gut health and contributing to conditions like colitis [11]. **Result: expected abundance of these bacteria.**

*Reference population: A clinically validated group of healthy adults (age 18-70) with no gastrointestinal symptoms and no history of gastrointestinal diseases [1].

Category D. Anti-inflammatory bacteria

Group	No.	Bacteria	Reduced -3	-2	-1	Normal*	1	Elevated 2	3	Group result
D1. Gut epithelial integrity marker	701	*Akkermansia muciniphila*			●					!
D2. Major SCFA producers	304	*Catenibacterium mitsuokai*				●				✓
	307	*Clostridium* sp. L2-50				●				
	308	*Coprobacillus cateniformis*				●				
	310	*Dialister* spp.				●				
	312	*Dorea* spp., *Blautia faecicola* & *Mediterraneibacter massiliensis*					●			
	313	*Holdemanella biformis*				●				
	314	*Anaerobutyricum hallii* & *A. soehngenii*						●		
	315	*Agathobacter rectalis*				●				
	317	*Faecalibacterium prausnitzii*					●			
	318	Various *Lachnospiraceae* & *Clostridiaceae*					●			
	330	Various Veillonellales, Lachnospirales & Eubacteriales				●				
	322	*Phascolarctobacterium faecium*				●				

D1. **Gut epithelial integrity marker**: *A. muciniphila* regulates mucus production in the intestinal lining, supporting metabolic health and reducing inflammation [12]. Diminished levels of this bacterium have been associated with metabolic disorders and cardiovascular disease [12, 13]. Polyphenols and prebiotic fibers, which are abundant in foods like red berries, cocoa powder, seeds and nuts, support healthy levels of *A. muciniphila* [14]. Increased levels of this species are also expected in patients treated with metformin [15]. **Result: slightly deviating abundance of these bacteria.**

D2. **Major SCFA producers** are critical for producing acetate, propionate, and butyrate through the fermentation of resistant starches and dietary fibers. These short-chain fatty acids (SCFAs) maintain gut barrier integrity, regulate gut acidity, reduce inflammation, and facilitate gut-brain communication [16]. Butyrate, in particular, serves as a primary energy source for colonocytes and plays a pivotal role in maintaining intestinal barrier function. Decreased levels of butyrate-producing bacteria, such as *F. prausnitzii*, are linked to inflammatory and functional gastrointestinal disorders, including irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) [17]. Reduced levels are also associated with mental health conditions like anxiety and depression, likely due to impaired gut-brain signalling [18]. Of note, while SCFA producers provide critical benefits, overgrowth of bacteria in this group can lead to excess gas production, potentially causing bloating and abdominal discomfort [8]. **Result: expected abundance of these bacteria.**

*Reference population: A clinically validated group of healthy adults (age 18-70) with no gastrointestinal symptoms and no history of gastrointestinal diseases [1].

Category E. Pro-inflammatory & opportunistic pathogens

Group	No.	Bacteria	Reduced -3	-2	-1	Normal*	Elevated 1	2	3	Group result
E1. Inflammation indicator	324	*Ruminococcus gnavus*				●				✓
E2. Potentially virulent	203	*Bacteroides fragilis*				●				✓
E3. Facultative anaerobes	500	Various Pseudomonadota				●				
	502	*Enterobacter, Cronobacter, Citrobacter* & *Salmonella*				●				✓
	504	*Escherichia, Shigella, Citrobacter koseri*				●				
E4. Predominantly oral bacteria	101	Various *Actinomycetaceae* & *Corynebacteriaceae*			●					
	311	*Dialister invisus* & *Megasphaera micronuciformis*				●				✓
	328	*Streptococcus mitis* group				●				
	329	*Streptococcus viridans* group				●				
E5. Genital, respiratory, and skin bacteria	501	*Acinetobacter junii*				●				
	601	*Metamycoplasma* spp.				●				✓

E1. *R. gnavus*, recently reclassified as *Mediterraneibacter gnavus*, is a common marker of inflammation-associated diseases and serves as an **inflammation indicator**. It produces pro-inflammatory molecules during mucin degradation, which can compromise the gut mucosal barrier, leaving the underlying mucus layer vulnerable to opportunistic pathogens and toxins [19]. **Result: expected abundance of these bacteria.**

E2. **Potentially virulent**: Some *B. fragilis* strains produce a virulence factor known as the *Bacteroides fragilis* toxin (BFT), which can disrupt epithelial cell tight junctions, increase intestinal permeability, and trigger inflammation [20]. IBS patients with increased abundance of this marker may respond better to low FODMAP diet [21]. **Result: expected abundance of these bacteria.**

E3. **Facultative anaerobes** represent bacteria tolerating and thriving in oxygenated environments. A healthy human colon is strictly anaerobic. An increase in the abundance of these microbes, coupled with a decrease in other markers, may indicate an oxygenated gut environment, which could suggest inflammation and occult intestinal bleeding [22]. **Result: expected abundance of these bacteria.**

E4. **Predominantly oral bacteria** are microbes that typically thrive in the oral environment. An increased relative abundance of these bacteria in fecal samples may indicate diminished gut microbiota or potential colonization of the gut by oral bacteria, which could be linked to oral diseases or disruptions in oral-gut microbial balance [23]. **Result: expected abundance of these bacteria.**

E5. **Genital, respiratory, and skin bacteria** are linked to hospital-acquired infection, typical in immunocompromised individuals. They are often linked to urinary tract infection [24, 25]. **Result: expected abundance of these bacteria.**

S9-016-A1-9.0

*Reference population: A clinically validated group of healthy adults (age 18-70) with no gastrointestinal symptoms and no history of gastrointestinal diseases [1].

REPORT FORM EXPLANATION

The results in this report were generated using the GA-map® Dysbiosis Test Lx v2 reagent kit (part no 1001, Genetic Analysis AS, Norway).

The GA-map® Dysbiosis Test is used as a fecal gut microbiota DNA analysis tool to identify and characterize dysbiosis in adults. Clinical studies report that among a healthy population 16% of individuals have a mild dysbiosis (DI 3) [1]. In patients with irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD), about 20-30% have a microbiota profile within the normal range (DI 1-2), while about 70-80% have a microbiota profile that falls outside of the normal range (DI > 2) [1]. IBD patients tend to have a more severe dysbiosis than IBS patients (DI 4-5) [1].

(These test results are not intended to be used as a sole means for clinical diagnosis or patient management decisions)

THE ABUNDANCE TABLE OF PRESELECTED BACTERIA MARKERS

The results are presented in an easy-to-read abundance table of 48 preselected bacteria markers. Some bacteria markers are specific for one bacterial species (e.g. *Akkermansia muciniphila*), while others cover groups of bacteria (e.g. phylum, Pseudomonadota). The selected bacteria have proven to be of high importance and clinically relevant for gut health and disorders in the literature and in laboratory testing.

The group results are reported as **(Expected)**, **(Slightly deviating)** or **(Deviating)**. The group results indicate how closely the patient's microbiota resembles the GA-map® healthy reference.

Category D. Anti-inflammatory bacteria

Group	No.	Bacteria	Reduced -3	-2	-1	Normal*	Elevated 1	2	3	Group result
D1. Gut epithelial integrity marker	701	*Akkermansia muciniphila*				●				✓

Colormap in bacteria abundance table:

- Association to normobiosis
- Little association to increased DI score
- Moderate association to increased DI score
- High association to increased DI score

- The black dot indicates the abundance of the bacteria marker
- Each bacteria marker is assigned a unique identification number (e.g. GA ID: 701 - *Akkermansia muciniphila*)
- Bacteria signal levels are reported on a scale from -3 (strongly reduced abundance of the bacteria) to +3 (strongly elevated abundance of the bacteria)
- The dark green center field indicates the reference relative abundance of bacteria based on a healthy reference population*
- The possible detection range for each bacterium is given as the green to red shaded boxes
- Boxes with no color indicate levels outside the detection range for each bacterium

COMMON HUMAN GUT BACTERIA TARGETED BY BROAD MARKERS ("Various")

No.	Bacteria	Targeted bacteria genera per marker
300	Various Bacillota	*Oscillibacter, Dysosmobacter, Phascolarctobacterium, Lawsonibacter, Coprobacillus, Flintibacter, Acidaminococcus, Intestinimonas, Enterococcus, Mitsuokella, Negativibacillus, Allisonella, Longicatena,* etc.
206	Various Bacteroidota	*Bacteroides, Phocaeicola, Prevotella, Mediterranea,* etc.
100	Various Actinomycetota	*Bifidobacterium, Actinomyces, Arcanobacterium, Winkia, Alloscardovia, Gardnerella, Kocuria, Rothia, Microbacterium,* etc.
302	Various Bacilli	*Streptococcus, Enterococcus, Lactococcus, Lactobacillus, Staphylococcus, Latilactobacillus, Bacillus, Granulicatella, Ligilactobacillus, Paenibacillus, Psychrobacillus, Cytobacillus,* etc.
305	Various Clostridia & Negativicutes	*Clostridium, Anaerotignum, Intestinibacter, Romboutsia, Megasphaera, Monoglobus, Mitsuokella, Veillonella, Frisingicoccus, Negativicoccus, Colibacter, Paeniclostridium*
331	Various Bacillales & Lachnospirales	*Lachnospira, Staphylococcus, Christensenella, Eubacterium, Bacillus, Alkalihalobacillus, Psychrobacillus, Anaerostipes, Cytobacillus, Peribacillus, Priestia, Rossellomorea, Virgibacillus,* etc.
318	Various Lachnospiraceae & Clostridiaceae	*Blautia, Fusicatenibacter, Roseburia, Coprococcus, Anaerobutyricum, Butyrivibrio, Tyzzerella, Butyribacter, Pararoseburia, Lachnoclostridium, Enterocloster, Hungatella, Anaerostipes,* etc.
330	Various Veillonellales, Lachnospirales & Eubacteriales	*Roseburia, Dialister, Veillonella, Megasphaera,* etc.
500	Various Pseudomonadota	*Shigella, Escherichia, Salmonella, Enterobacter, Bilophila, Haemophilus, Klebsiella, Citrobacter, Desulfovibrio, Pantoea, Leclercia, Lelliottia, Proteus,* etc.

*Reference population: A clinically validated group of healthy adults (age 18-70) with no gastrointestinal symptoms and no history of gastrointestinal diseases [1].

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