

## GASTROPANEL- and ACETIUM INNOVATIONS:

The GastroPanel blood examination reveals in symptomatic and asymptomatic subjects, *Helicobacter pylori* infection and atrophic gastritis, both being associated with an increased risk of gastric cancer. Acetium capsule binds carcinogenic acetaldehyde in the stomach and may decrease the risk of gastric and esophageal cancer (<http://www.biohithealthcare.com/scientific>: State of the art GastroPanel and Acetium innovations for the unmet need, <http://www.gastropanel.com/>; <http://www.acetium.com/>)

**GastroPanel®**, the unique *Helicobacter pylori* test can detect the following conditions:

1) *Helicobacter pylori* (HP) infection (and chronic gastritis) which is an independent risk factor of both gastric cancer and gastric- and duodenal ulcer.

2) HP infection-induced atrophic gastritis (AG), which in most cases is asymptomatic, as well as the topographic site of AG either in the corpus or in antrum. Apart from HP infection, AG in the corpus can also develop through an autoimmune disease.

2.1) AG of the corpus results in low acid output and eventually into an acid-free stomach. This increases the risk of gastric or esophageal cancer. AG may also cause malabsorption of vitamin-B12, calcium, magnesium and zinc. In addition, absorption of some medicines is impaired as a result of acid-free stomach. Calcium deficiency can cause osteoporosis, and vitamin-B12 deficiency can contribute to development of Alzheimer's disease, dementia, depression or peripheral neuropathies.

2.2) AG of the antrum increases the risk of peptic ulcer and gastric cancer. Co-existent AG of the corpus and antrum (pangastritis) increases the risk of gastric cancer up to 90-fold.

3) HP infection also in subjects with AG, MALT-lymphoma or bleeding peptic ulcer, and in those taking PPI medication or antibiotics. In these cases, <sup>13</sup>C-urea breath test (UBT) or stool HP antigen test (SAT) frequently give false negative results. UBT may also give false positive results in subjects with acid-free stomach. These two tests fail to detect AG due to HP-infection or autoimmune disease (<http://www.biohithealthcare.com/limitations-of-helicobacter-pylori-diagnostics>).

4) High acid output of the stomach mucosa, which predisposes to esophageal reflux disease with potential complications such as ulcerative esophagitis, Barrett's esophagus or lower esophageal cancer.

**GastroPanel-detected i) symptomatic HP infection after eradication, ii) atrophic gastritis (AG) or iii) symptomatic high acid output are all indications for gastroscopy and biopsy examination.**

The GastroPanel innovation is based on follow-up studies on gastritis patients conducted in Finland and Estonia (1) as well as on the discovery of the role of *Helicobacter pylori* in pathogenesis of gastritis and peptic ulcer disease, which led to Nobel Prize in 2005 (2). In addition to Biohit's R&D, GastroPanel innovation was made possible by the microplate immunoassay analyzers based on the invention of the vertical light beam measurement principle (3,4).

1. Sipponen P, Maaros HI. Chronic gastritis, Scand J Gastroenterol. 2015 Jun 3; 50(6): 657-667.

2. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet.

1984;323:1311-15.

<http://nobelprize.org/medicine/laureates/2005/press.html>

3. [www.biohithealthcare.com/Scientific/Literature/](http://www.biohithealthcare.com/Scientific/Literature/) Suovaniemi O. Automated Instrumentation for Clinical and Research Laboratories. Innovations and development of vertical light beam photometers and electronic pipettes. University of Helsinki 1994; Academic dissertation.

4. <http://www.biohithealthcare.com/about-us/history> Suovaniemi O. Aggressive innovation and patenting

strategy.

**The GASTROPANEL- and ACETIUM innovations encompass a unique combination that can help prevent gastric and oesophageal cancers.**

GastroPanel detects AG caused by *Helicobacter* infection or autoimmune disease, with increased risk to develop gastric and esophageal cancer. Detection of this risk condition and its adequate follow-up are the key to successful prevention of gastric cancer. AG of the corpus is an irreversible condition that leads to permanent achlorhydria. In an acid-free stomach, microbes from the mouth can survive and produce acetaldehyde from alcohol and sugars derived from foodstuffs. In 2009, WHO classified acetaldehyde present in alcoholic beverages or endogenously derived from it, as Group 1 human carcinogen. Acetaldehyde exposure is associated with a number of globally important malignancies, including cancers of the upper respiratory and digestive tract, as well as those of colon and lung. Biohit Oyj has developed Acetium products designed to reduce the exposure to acetaldehyde derived from ethanol or cigarette smoke ([www.acetium.com](http://www.acetium.com); [www.biohithealthcare.com/scientific/study-protocols](http://www.biohithealthcare.com/scientific/study-protocols)).

**Acetium capsule** binds carcinogenic acetaldehyde in the stomach in individuals suffering from an acid-free stomach due to any of the following reasons: 1) atrophic gastritis, 2) PPI medication, 3) stomach resection, 4) subjects with ALDH2 gene mutation with deficient acetaldehyde metabolism, or 5) chronic *Helicobacter pylori* infection. Acetium capsules might also prevent migraine headache episodes (ongoing clinical trials; [www.biohithealthcare.com/scientific/study-protocols](http://www.biohithealthcare.com/scientific/study-protocols))

**Acetium lozenge effectively binds (up to 90%) acetaldehyde dissolved in saliva during alcohol drinking and from cigarette smoke and by that doing promotes oral health. Used concomitantly with each cigarette, Acetium lozenge helps quit smoking (1).**

- Acetaldehyde is the most important carcinogen in cigarette smoke.
- Alcohol and tobacco together with poor oral hygiene explain 80% of the oral-, pharyngeal- and esophageal cancers. In addition, cigarette smoking is an independent risk factor of gastric cancer, similar as HP infection and AG (acid-free stomach).

1.Syrjänen, K., Eronen, K., Hendolin, P., Paloheimo, L., Eklund, C., Bäckström, A. and Suovaniemi, O. Slow-release L-cysteine (Acetium ) lozenge is an effective new method in smoking cessation. A randomized, double-blind, placebo-controlled intervention. *Anticancer Res.* 2017;37:3639-3648.

**The state-of-the-art GastroPanel examination is not hampered by the following serious medical problems:**

In diagnosis of dyspepsia and HP-infection, the <sup>13</sup>C urea breath test (UBT), stool antigen test (SAT) and HP-antibody tests do not detect AG caused by *H. pylori* infection or an autoimmune disease. An early diagnosis of AG is important because of its potentially serious risks including the unnecessary deaths due to gastric and esophageal cancer.

In addition to the risks of gastric and esophageal cancer, acid-free stomach may cause malabsorption of vitamin B12, iron, magnesium, calcium and some drugs. Calcium deficiency causes osteoporosis, and

vitamin B12 deficiency can cause Alzheimer's disease, dementia, depression and peripheral neuropathy. Vitamin B12 deficiency also leads to increased homocysteine levels in the body, which is considered as an independent risk factor for atherosclerosis, heart attacks and strokes (10). The absorption of dipyridamole, some iron products and antifungals (fluconazole, itraconazole), thyroxine and atazanavir is considerably impaired in an acid-free stomach. Particularly in elderly people, reduced acid output in the stomach can increase the risk of serious infections in the gastrointestinal- and respiratory tract, including giardiasis, malaria, *Clostridium difficile*, *E. coli* EHEC and pneumonia.

None of the above-listed three *H. pylori* tests (UBT, SAT, HP-Ab test) provides any information on increased gastric acid output, which is diagnosed by GastroPanel, and which in patients with gastro-esophageal reflux disease may cause asymptomatic complications in the esophagus. Such complications include ulcerative esophagitis and Barrett's esophagus, which may lead to esophageal cancer. In addition, the UBT and SAT tests may give up to 40% false negative results if the patient has a) AG, b) MALT lymphoma, c) bleeding peptic ulcer disease, or d) if the patient is under PPI or antibiotic treatment. UBT can also give false positive results when the stomach is acid-free and colonized by urease-positive bacterial species.

**The sensitivity of <sup>13</sup>C urea breath test was erroneously reported to be 98% and its specificity almost 100%. Furthermore, this particular review neglected to mention that the UBT does not disclose AG caused by *Helicobacter pylori* infection or autoimmune disease (Färkkilä M. Miten dyspepsia tulisi hoitaa? Duodecim 2004;120:2537-2542).**

**Diagnosis of the upper abdominal complaints (dyspepsia) and *H. pylori* infection is still hampered by the shortcomings of the currently used USB and SAT tests that, at worst, can lead to maltreatment and progression of severe diseases beyond reach of a curative treatment.**

**Before entry of the GastroPanel innovation in the market in the early 2000's, HP-induced or autoimmune AG as well as HP infection itself remained undiagnosed. The eventually resulting gastric cancer has been detected in most cases only after appearance of alarming signs or as an incidental finding on gastroscopy and biopsies.**

**There are only estimates how many people since the early 2000's have remained undiagnosed and thus suffered from an asymptomatic acid-free stomach, and as a result, have contracted gastric or esophageal cancer or vitamin-B12 deficiency with clinical sequels, when their "dyspeptic symptoms" and "HP-infections" have been diagnosed with UBT test, as recommended in the above cited article.**

**In addition to providing erroneous information, that particular article also fails to mention the use of GastroPanel in diagnosis of dyspepsia and *Helicobacter pylori*. The purpose of the author might have been to promote the marketing of the UBT test in Finland by the company for which he himself is a consultant (<http://www.biohithealthcare.com/limitations-of-helicobacter-pylori-diagnostics>).**

**Early diagnosis of *Helicobacter pylori* infection and atrophic gastritis can reduce gastric cancer deaths**

GastroPanel detects *Helicobacter* infection and gastric mucosal atrophy (AG). The test also gives information on disturbance of the gastric acid output, which, similar as AG, remains undetected by the

conventional HP-tests (UBT, SAT, and HP-Ab tests). **In addition, these tests fail to recognize that even a successful HP-eradication does not cure atrophic gastritis!**

To increase the patient safety and to achieve savings in health care costs, GastroPanel should be included in the diagnostic repertoire of all dyspeptic patients as well as an integral part of the health control of elderly people (1). The national state-of-art management guidelines for dyspepsia derived from 2013 still instruct the physicians to use, instead of GastroPanel, the UBT and SAT tests. This inevitably obsolete Finnish management guidelines fail to emphasize that the conventional HP-tests do not detect AG or even *Helicobacter* infection accurately enough.

In this respect, a progress has been made that contributes to an increased patient safety, once Huslab announced that its sub-contractor, Gastroenterology Department of HUCS, has stopped providing <sup>13</sup>C-urea breath test, and UBT has been subsequently deleted from the list of Huslab laboratory tests (May 8<sup>th</sup>, 2017).

GastroPanel biomarkers are included in the Huslab test repertoire, and the physicians can request GastroPanel-examination (fP-Mahalaukun biomerkkiainetutkimus, [www.biohit.fi/gastropanel-lahete](http://www.biohit.fi/gastropanel-lahete); <http://www.gastropanel.com/>).

**Indications of GastroPanel-examination – use of GastroPanel by general practitioners- a major unmet need ([www.gastropanel.fi](http://www.gastropanel.fi); [www.biohit.fi/gastropanel-lahete](http://www.biohit.fi/gastropanel-lahete); [www.biohit.fi/Tutkimus](http://www.biohit.fi/Tutkimus)) State of the art GastroPanel and Acetium innovations for the unmet need)**

- GastroPanel is the first-line diagnostic test for dyspepsia (prevalence 20-40%) and *H. pylori* infection (5-80% of the world population, depending on the age)
- GastroPanel should be used to rule out or confirm the high acid output of reflux patients instead of the trial and error use of PPIs. This treatment can alleviate the symptoms and thus delay the diagnosis. The long-term use of PPIs might increase the risk of stomach and esophageal cancer as well as that of osteoporosis and dementia.
- GastroPanel biomarkers Pepsinogen I (PGI), Pepsinogen II (PGII), Gastrin-17 (G-17) and *H.pylori* antibodies reveal:
  - Subjects at increased risk for stomach- and esophageal cancer, i.e., those with AG. Similarly, the subjects with a low risk of cancer; *H.pylori* infection with no AG in the antrum or corpus.
  - Early and reliable diagnosis of *H.pylori* infection and AG saves costs and may prevent many unnecessary deaths due to stomach and esophageal cancer.
- GastroPanel is also suitable for examination of special groups of patients, particularly those with autoimmune diseases (usually more than one at the same time), including, e.g.:
  - patients with autoimmune thyroid disease (AITD) who may have autoimmune atrophic gastritis (AAG, 18% of AITD patients) in the corpus
  - patients with type 1 diabetes who may have AAG and B-12 vitamin deficiency (12% of type 1 diabetes patients)
  - patients with celiac disease with possible AAG, and
  - patients with rheumatoid arthritis who may have AAG
- In patients with AG or AAG, absorption of vitamin-B12 is impaired (10).
  - B12 vitamin deficiency increases the risk of Alzheimer's disease, dementia, depression

and polyneuropathy. Consequently, all patients should be examined by GastroPanel to rule out or confirm AG or AAG

- Because of vitamin B12 deficiency, homocysteine may accumulate in the body that may be related to:
  - Atherosclerosis – these patients should be examined by GastroPanel to rule out or confirm AG or AAG
  - Heart attacks – also these patients should be examined by GastroPanel
  - Strokes – also for these patients GastroPanel is indicated
- In patients with AG or AAG of the corpus, absorption of Ca, Fe, Mg and Zn is impaired. GastroPanel is indicated in patients with osteoporosis and anemia
- The risk of pneumonia and particularly in senior citizens, also the risk of fatal intestinal infections (such as giardiasis, malaria, *Clostridium difficile* and *E. coli* EHEC) may increase significantly due to acid-free stomach. Patients with such infections should be examined by GastroPanel to rule out AG and AAG.
- **Subjects diagnosed with i) AG and AAG, ii) high acid output or iii) symptomatic *H. pylori* infection in the GastroPanel examination must be referred for gastroscopy and biopsies.**

### **GastroPanel - expertise**

In 2012, group of 16 of the leading gastroenterologist from 12 different countries released a joint statement that the atrophic gastritis screening and detection by GastroPanel biomarkers is a clearly justified (1). The same conclusion was reached by the widespread Maastrich IV/V recommendation, according to which the biomarker tests are recommended as part of the diagnosis and management strategy of *Helicobacter pylori* infection and atrophic gastritis (2).

In addition, a recent international conference held in Kyoto published recommendations that the use biomarkers included in GastroPanel is a highly suitable method to replace the often unnecessary endoscopies, (of which 80% are unnecessary) for the diagnosis and screening of stomach diseases (3).

Furthermore in 2012, 63 experts from 24 countries found that gastric mucosal atrophy (atrophic gastritis) may result in, among other things, gastric cancer, and therefore should be monitored at regular intervals (4).

Early detection of the gastric cancer risks and patient management improves the prognosis significantly. Finding atrophic gastritis requires gastric endoscopy and regular monitoring. In current practice, gastric cancers are in most cases diagnosed too late, because the current practice used in the diagnosis of *Helicobacter pylori* infection (UBT, SAT) do not reliably find *Helicobacter pylori* infection and completely miss AG.

Among dyspeptic patients, GastroPanel helps detecting those, for whom gastroscopy is mandatory to disclose e.g. the increased risks of gastric cancer (Syrjänen K. Serologinen testi dyspepsia-potilaiden diagnostiikkaan ja mahasyövän riskiryhmien seulontaan. BestPractice Gastroenterologia 2015;1:2-7, [www.biohit.fi/tutkimus](http://www.biohit.fi/tutkimus)).

### **GastroPanel increases the patient safety and saves the costs**

GastroPanel blood test has been shown to increase the patient safety and save health care costs. According to cost-efficiency model developed by Nordic Healthcare Group, organized GastroPanel screening for the gastric cancer risks of e.g. 10 age groups (65-74-year-old), would save over EUR 800 million in the life-time health care costs in Finland. Reaching these savings necessitates, however, a nationwide implementation of GastroPanel <https://www.gastropanel.com/decision-makers/screening-model>.

GastroPanel biomarkers are capable of diagnosing atrophic gastritis affecting either the corpus or antrum or both. As compared with gastroscopy, accurate diagnosis of atrophic gastritis is not always possible in a few small biopsy specimens representing only a minimal sample (possibly a few pro mils at most) of the whole area of the adult gastric mucosa. The diagnosis of AG (particularly the mild grade) made by the pathologist is always subjective, with substantial inter-observer variation. Similarly, the accuracy of gastroscopy depends on the experience of the endoscopist.

GastroPanel biomarkers are devoid of these shortcomings, because they are automated laboratory immunoassays. In fact, endoscopic biopsy histology is not a reliable gold standard (5), albeit currently used as such. As compared with biomarkers, its limitations in diagnostic accuracy should be kept in mind (6,7).

When performed by skillful gastroenterologists and pathologists, the agreement between GastroPanel and gastric biopsy histology is very good, exceeding 0.8 (the limit of almost perfect) by weighted kappa test (8). The diagnosis of AG on the basis of only gastroscopy with no biopsies is highly subjective and unreliable (9, [www.biohit.fi/Tutkimus](http://www.biohit.fi/Tutkimus); State of the art GastroPanel and Acetium innovations for the unmet need).

### **ColonView-FIT innovation**

When GastroPanel biomarkers indicate that gastric mucosa is healthy, the clinical symptoms are often caused by functional disturbance without an organic disease in the gastric mucosa. As much as 50% of dyspepsia symptoms may originate from the colon, especially in the elderly population. Consequently, Biohit GastroPanel- and ColonView-innovations together provide plenty of valuable information in the diagnosis of gastrointestinal diseases.

Biohit's ColonView Hb and Hb/Hp Fecal Occult Blood Test is an immunochromatographic quick test for the detection of human hemoglobin (Hb) and hemoglobin/haptoglobin complex (Hb/Hp) in stool samples. This test is based on the pioneering invention of Labsystems Oyj (predecessor of Biohit Oyj) dating back to the 1980's (1,2).

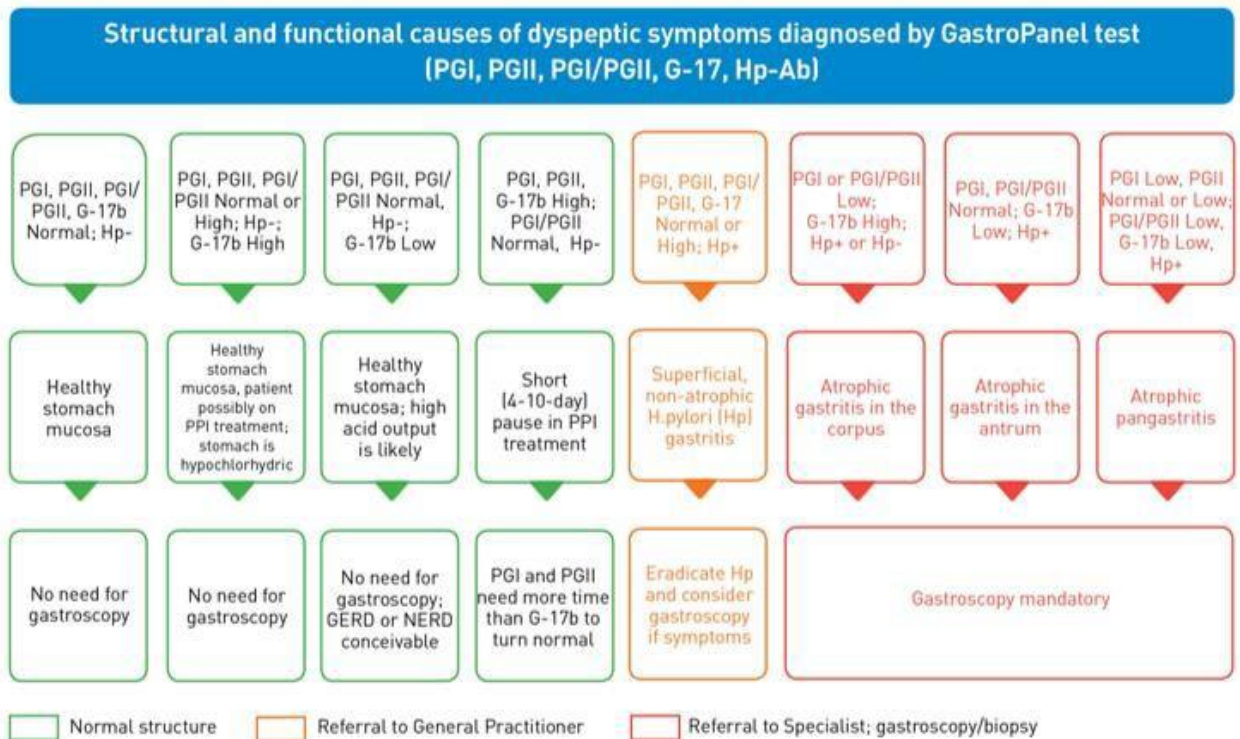
ColonView Hb and Hb/Hp Fecal Occult Blood Test was designed to aid the diagnosis of lower GI pathologies, such as colorectal cancers and large bleeding adenomas. In 2012, colorectal cancer was the third most common cancer in men (746,000 cases) and the second in women (614,000 cases), with more than 690,000 annual deaths worldwide. Screening for colorectal cancer reduces disease-specific mortality by detecting the cancer precursors and increasing the cancer detection at its early stages (3).

1. Immunoassay for fecal human hemoglobin; <https://patents.google.com/patent/US4427769>

2. <http://www.biohithealthcare.com/about-us/history>: Suovaniemi O. Aggressive innovation and patenting strategy

3. Vasilyev S, Smirnova E, Popov D, Semenov A, Eklund C, Hendolin P, Paloheimo L, Syrjänen K. A new-generation fecal immunochemical test (FIT) is superior to guaiac-based test in detecting colorectal neoplasia among colonoscopy referral patients. *Anticancer Res* 2015;35:2873-2880.

## GastroPanel® – interpretation guide snapshot



“Healthy stomach mucosa” in GastroPanel report indicates that there is no *Helicobacter* infection or AG, and also the stomach function (acid output) is normal ([www.gastropanel.fi](http://www.gastropanel.fi); [www.biohit.fi/gastropanel-lahete](http://www.biohit.fi/gastropanel-lahete); [www.biohit.fi/Tutkimus](http://www.biohit.fi/Tutkimus); State of the art GastroPanel and Acetium innovations for the unmet need).

### References:

- 1) Agréus L, Kuipers EJ, Kupcinskas L, Malfertheiner P, Di Mario F, Leja M, Mahachai V, Yaron N, van Oijen M, Perez Perez G, Rugge M, Ronkainen J, Salaspuro M, Sipponen P, Sugano K and Sung J: Rationale in diagnosis and screening of atrophic gastritis with stomach-specific plasma biomarkers. *Scand J Gastroenterol* 47:136–147, 2012. <https://www.ncbi.nlm.nih.gov/pubmed/22242613>
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- 3) Sato K et al. 2014 Serological tests (Pepsinogen I and II and anti-*H.pylori* antibody) are useful for selecting subjects at high risk for gastric cancer. The Kyoto Global Consensus Meeting on *H. pylori* Gastritis. Time for a change. January 30th – February 1st, 2014. Kyoto, Japan. (lähetyt julkaistavaksi) <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4552923/>
- 4) Dinis-Ribeiro M et al. 2012 Management of precancerous conditions and lesions in the stomach (MAPS): guideline from the European Society of Gastrointestinal Endoscopy (ESGE), European *Helicobacter* Study Group (EHSg), European Society of Pathology (ESP), and the Sociedade Portuguesa de Endoscopia Digestiva (SPED). *Endoscopy* 2012;44:74-94. <https://www.ncbi.nlm.nih.gov/pubmed/22198778>
- 5) Iijima K, Abe Y, Kikuchi R, Koike T, Ohara S, Sipponen P, Shimosegawa T. Serum biomarker tests are useful in delineating between patients with gastric atrophy and a normal, healthy stomach. *World J Gastroenterol* 2009;15:853-859. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2653386/>
- 6) Storskrubb T, Aro P, Ronkainen J, Sipponen P, Nyhlin H and Talley NJ: Serum biomarkers provide an accurate method for diagnosis of atrophic gastritis in a general population: the Kalixanda study. *Scand J Gastroenterol* 2008;43:448-1455. <https://www.ncbi.nlm.nih.gov/pubmed/18663663>

- 7) Ren JS, Kamangar F, Qiao YL, Taylor P, Liang H, Dawsey S, Liu B, Fan JH, Abnet C. Serum pepsinogens and risk of gastric and oesophageal cancers in the General Population Nutrition Intervention Trial cohort. *Gut* 2009;58:636–42. doi:10.1136/gut.2008.168641. <https://www.ncbi.nlm.nih.gov/pubmed/19136509>
- 8) Väänänen H, Vauhkonen M, Helske T, et al. Non-endoscopic diagnosis of atrophic gastritis with a blood test. Correlation between gastric histology and serum levels of gastrin-17 and pepsinogen I: a multicenter study. *Eur J Gastroenterol Hepatol* 2003;15:885–891. <https://www.ncbi.nlm.nih.gov/pubmed/?term=Non-endoscopic+diagnosis+of+atrophic+gastritis+with+a+blood+test.+Correlation+between+gastric+histology+and+serum+levels+of+gastrin-17+and+pepsinogen+I>
- 9) Yanaoka K, Oka M, Yoshimura N, Mukoubayashi C, Enomoto S, Iguchi M, Magari H, Utsunomiya H, Tamai H, Arai K, Yamamichi N, Fujishiro M, Takeshita T, Mohara O, Ichinose M. Risk of gastric cancer in asymptomatic, middle-aged Japanese subjects based on serum pepsinogen and Helicobacter pylori levels. *Int J Cancer* 2008;123:917–926. <https://www.ncbi.nlm.nih.gov/pubmed/?term=Risk+of+gastric+cancer+in+asymptomatic%2C+middle-aged+Japanese+subjects+based+on+serum+pepsinogen+and+Helicobacter+pylori+levels>
- 10) [www.biohithealthcare.com/](http://www.biohithealthcare.com/) Investors/Annual Report: 2000, page 23 Figure.



## APPENDIX

### BIOHIT Oyj's INFORMATION FOR HEALTH CARE PROFESSIONALS AND -USERS

The purpose of this information is to draw the attention of the health care professionals and health care users to the significant benefits obtainable in the Finnish healthcare by implementing the diagnostic tests and other products of Biohit Oyj. We hope you would find time to read this information and **give us feedback** e.g. by describing us the situations, where you have experienced that the diagnostic procedures and/or management strategies have not succeeded in the most optimal way.

#### Gastric- and esophageal cancer

Gastric cancer decreases in Finland but identification of the risk factors is even more challenging, because the incidence of gastric cancer has steadily decreased since the 1960's. Nevertheless, the risk factors remain the same. The two most important ones are ***Helicobacter Pylori (HP)*** and **atrophic gastritis** (atrophy of the stomach mucosa). In 2014, 650 patients developed gastric cancer and 430 died of it. The corresponding figures for esophageal cancer were 307 and 257 persons.

The diagnosis for gastric cancer is still made too often in a stage when alarming symptoms, e.g., loss of weight and hematemesis, have already appeared and the prognosis is poor. One of the possible reasons might be that in our country, the clearly outdated <sup>13</sup>C-urea breath test (UBT) and stool antigen test (SAT) are still used for HP diagnostic in patients suffering from upper abdominal complaints, despite the fact that these two tests might give false negative results. UBT might also give false positive results. In addition, these two tests, similar as HP-Ab tests, fail to diagnose AG with the associated increased risk of gastric- and esophageal cancer ([above-mentioned limitations](#), [research information](#)).

#### From GastroPanel – blood test for the screening of gastric- and esophageal cancer risks

In patients suffering from dyspeptic symptoms as well as from asymptomatic subjects, GastroPanel detects, in addition to possible HP, also AG caused by HP or an autoimmune disease. GastroPanel is also suitable for screening of gastric- and esophageal cancer risk groups (HP and AG). GastroPanel-examination also gives valuable additional diagnostic information for disease prevention and treatment ([additional information](#), [cost savings](#)).

If GastroPanel detects 1) a symptomatic HP-infection after eradication therapy; 2) usually asymptomatic AG, or 3) symptomatic high acid output, it is recommended that a gastroenterologist performs gastroscopy with directed biopsies, which can detect even other diseases. In the primary- and occupational healthcare, GastroPanel should be an integral part of the diagnostic algorithm of all patients suffering from upper abdominal complaints. Also among asymptomatic subjects, [GastroPanel](#) detects the risk patients who should be referred for gastroscopy and biopsies.

Worldwide, approximately 1.4 million people each year develop gastric- and esophageal cancer. Because the symptoms of these cancers are non-specific and the pivotal risk factors, HP-infection and AG, are asymptomatic in most cases, the diagnosis is usually delayed. Only 15% of gastric cancer patients are alive after 5 years.

As explained before, an authoritative [international group of experts](#) recommended in 2012 that GastroPanel biomarkers should be used as the first-line diagnostic test for all patients suffering from

dyspeptic symptoms. According to a [domestic](#) and [an Italian](#) meta-analysis published recently, the accuracy of GastroPanel test in diagnosis of the gastric cancer risk conditions (AG) is very high. GastroPanel is also highly suitable for population-based screening of the risk groups, because its biomarkers have an excellent [longitudinal predictive value](#) for gastric cancer.

One should also keep in mind that in association with many relatively [common autoimmune diseases](#), such as type 1 diabetes, thyroiditis or rheumatoid arthritis, an asymptomatic autoimmune AG (AAG) can develop, an early diagnosis of which is important due to the same reasons as diagnosis of AG.

### **ColonView-FIT for screening of colorectal cancer**

ColonView-FIT, an immunochromatographic test specific and sensitive for human blood, is designed for [early diagnosis and screening](#) of colorectal cancer and its precursors. Particularly among elderly people, the cause of upper abdominal complaints can often be of colon origin. Thus, using GastroPanel and ColonView-FIT tests together in diagnosis of all patients suffering from such complaints contributes to i) reaching the correct diagnosis, ii) increasing the patient safety and iii) cost savings.

Implementation of the national colorectal cancer screening program should be speeded up because over 3000 patients develop and over 1200 dies of colorectal cancer in Finland each year. Because of this, colorectal cancer screening with the modern FIT test should be included in the national screening program. Screening of colorectal cancer would be the first national cancer screening, in which also the men can participate.

### **Biologically active vitamin-B12**

The most important cause for vitamin-B12 deficiency is AG, which still often remains undiagnosed in an early stage as explained before. When GastroPanel detects AG (acid-free stomach) caused by HP or autoimmune disease, the possibility of B12 deficiency should always be considered, caused by malabsorption due to AG. Vitamin-B12 deficiency is [very common](#) especially among elderly people, being present in approximately one out of ten subjects over 65-years of age in Finland. A delayed diagnosis can be accompanied by permanent neurological damage, depression and dementia. When AG has been detected in an asymptomatic subject, the eventual vitamin-B12 deficiency is easy to confirm with another Biohit test, which measures the level of [active vitamin-B12](#) from a blood sample.

### **Acetium capsule and Acetium lozenge**

Acetium capsules bind carcinogenic [acetaldehyde](#) in an acid-free stomach binding it into a harmless MTCA-compound. As a result of a long-term PPI-medication, acid-free stomach develops, sharing the risk factors in common with AG. Because of this, it is recommended that persons on protracted PPI-medication should start using Acetium-capsules to reduce the risk of gastric and esophageal cancer.

It is estimated that 10% of the western population is using occasionally or continuously PPI-medication, which by eliminating the symptoms, might delay the diagnosis of gastric cancer beyond reach of a curative treatment. Because of this, it is always advisable that before starting PPI-medication, GastroPanel-examination is performed to confirm that the patient does not already have an acid-free stomach.

Acetium capsule is the only product on the market, which significantly helps reduce the exposure of carcinogenic acetaldehyde in the stomach and esophageal mucosa thus potentially preventing the development of these cancers. Globally, approximately 500 million people are estimated to suffer from an [atrophic gastritis](#).

### **New indications of use for Acetium capsule and lozenge**

The currently ongoing clinical trials are examining new potential indications of use for Acetium capsules. Preliminary evidence suggests e.g. that regularly used Acetium capsules can help prevent migraine headache episodes ([teaser](#); [Study Protocols](#)).

Acetium lozenge might also provide an effective means in [smoking intervention](#). This type of evidence was provided by two separate studies, during which the likelihood to stop smoking was 51% higher among the Acetium- than in the placebo arm. In addition, Acetium lozenge promotes oral health by its xylitol content as well as by binding carcinogenic acetaldehyde dissolved into the saliva from cigarette smoke and alcohol.

Because smoking and alcohol are the most important risk factors of oral cancer, Acetium lozenge might also provide protection against oral cancers. Although Acetium lozenge clearly reduces the harmful effects of smoking, Biohit primarily recommends giving up smoking.

### **Possibilities for improving treatment practices**

It is possible to improve the diagnostic and management practices in Finland by new domestic innovations (GastroPanel, ColonView-FIT and Acetium) designed for diagnosis and prevention, both increasing the patient safety and contributing to [cost savings](#) in healthcare.

As a representative example of these obsolete management and treatment practices, the current management guidelines for dyspeptic patients published in 2013 still instruct using UBT and SAT tests instead of GastroPanel. These same guidelines fail to report that these HP-tests do not find AG and [not accurately even Helicobacter](#) infection.

In this respect, positive development has taken place when Huslab announced that its sub-contractor (Department of Gastroenterology, HUCS) has stopped providing UBT test, which was subsequently removed from the Huslab test catalogue (May 8<sup>th</sup>, 2017). Biohit GastroPanel biomarkers are included in the Huslab test portfolio, where the physicians can request GastroPanel-examination (fP-Mahalaukun biomerkkiainetutkimus, <http://www.gastropanel.com>; <http://www.biohit.fi/gastropanel-lahete>).

Given the above, in practice, the patient safety and costs also depend on the information that the health care users do receive and/or are capable of demanding from their service providers. We would be pleased by your feedback that you can submit to [info@biohit.fi](mailto:info@biohit.fi).

Anybody suffering from dyspeptic complaints or those who want to monitor their health, can request GastroPanel, ColonView-FIT and other Biohit tests on private clinics and public health centers or from their occupational healthcare providers. It is also possible to book an appointment for the tests without doctor's referral by calling +358 400 603 222, on weekdays 9-15. Acetium products can be purchased at pharmacies, prescription-free (<http://www.biohitshop.fi/>).

**Additional information from [info@biohit.fi](mailto:info@biohit.fi)**