Helicobacter Test *INFAI*®

^{13}C-UBT for *H. pylori* detection

Helicobacter pylori infection:
A worldwide problem

Helicobacter Test *INFAI*®

Facts

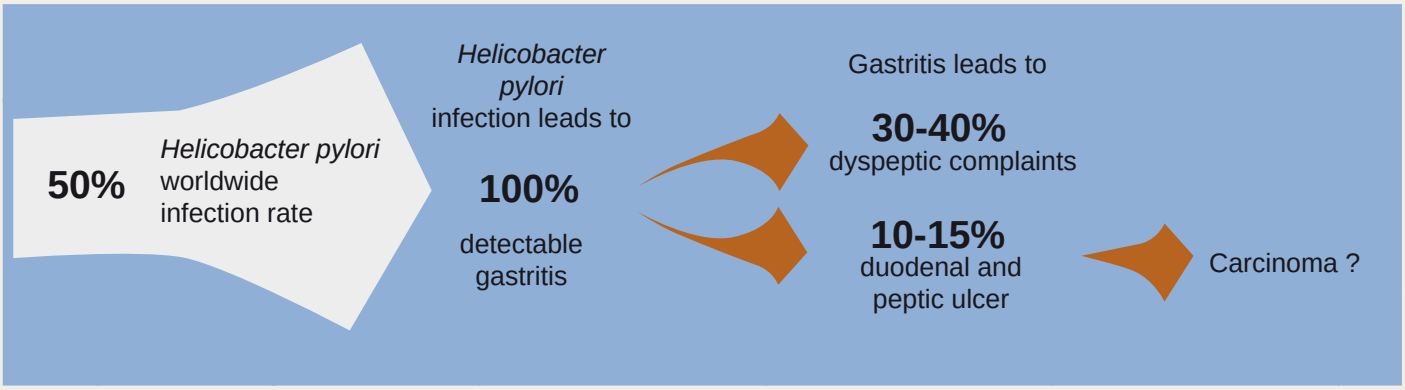
Helicobacter pylori infection

A worldwide problem

On average, 50 % of the World's population are already infected with *Helicobacter pylori*.

Infection rates in Europe range from 35 - 40 %.

Helicobacter pylori infection places the affected person under considerable physical and emotional strain. High economic costs lead to the necessity for eradication of the bacterium.



The most used ^{13}C-urea breath test worldwide

- Internationally approved medicinal product subject to medical prescription
- Gold standard for the diagnosis of *Helicobacter pylori* (Maastricht III)
- Suitable for diagnosis and control after eradication treatment of an infection with *Helicobacter pylori*
- Registered in 34 countries worldwide
- Easy handling
- Analysis via mass spectrometry or infrared spectroscopy
- Reimbursement by health insurance in most European Countries
- Cost-effective and non-invasive
- New *INFAI* test meal (Refex®) for patients with dyspepsia taking PPI
- New: CLINIPAC for 50 patients for GP, laboratory and hospital use
- New: Only approved special test for children from the age of 3 - 11

References

- Comparison of non-invasive tests to detect Helicobacter pylori infection in children and adolescents: Results of a multicenter European study.
  (Mégraud, F. et al.: The Journal of Pediatrics 2005, 146(2): 198)
- Randomised trial of endoscopy with testing for Helicobacter pylori compared with non-invasive H. pylori testing alone in the management of dyspepsia
  (McColl K. et al.; BMJ 2002, 324: 999)
- Utility and acceptability of INFAI ^{13}C-urea breath test
  (Alberti H.; BMJ 2002, 324: 485)
- Recommendation of ^{13}C-urea breath test after eradication therapy.
  (Current concepts in the Management of Helicobacter pylori infection. The Maastricht III-2005 Consensus Report.)
- BSG Dyspepsia Management Guidelines
  (British Society of Gastroenterology, Guidelines in Gastroenterology (1996) with revisions in 2005)
- NICE Guidance on the use of proton pump inhibitors in the treatment of dyspepsia
  (National Institute for Clinical Excellence (2000); Technology Appraisal Guidance No. 7)
- SIGN Helicobacter pylori - Eradication Therapy in Dyspeptic Disease
  (Scottish Intercollegiate Guidelines Network; Guidelines: Helicobacter pylori, No. 7,1996)

Helicobacter Test *INFAI*®

Performance of the test

Sampling of the 00-minute value t_0

Before performing the test, the patient should have fasted 4-6 hours, preferably overnight. The test starts with the collection of the baseline breath samples (t_0). The breath is collected either in a sampling tube (MS-version) or in a breath bag (IR-version) by gently blowing through a straw.

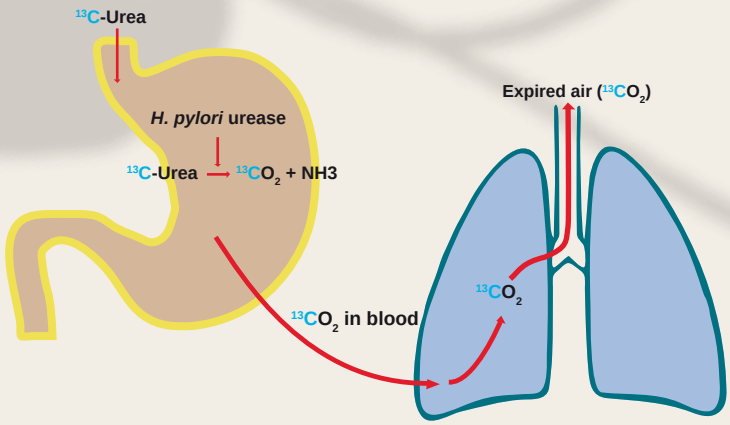
Administration of ^{13}C-urea (test solution)

After drinking 200 ml of orange juice (100 ml of pure orange juice for children) or a solution of 1 g citric acid diluted in 200 ml of water to delay gastric emptying, the test solution is prepared. The enclosed ^{13}C-urea (45 mg for children or 75 mg for adults and adolescents) is dissolved in 30 ml of water and taken immediately.

Sampling of the 30-minute value t_{30}

30 minutes after administration of the test solution, the second breath samples are collected (t_{30}). Barcoded labels are provided to ensure safe and distinctive identification during analysis. Breath samples should be dispatched to INFAI or other qualified laboratories in the box provided.

Basic principle



To establish an infection with Helicobacter pylori, ^{13}C-labelled urea is administered which is then split up into ^{13}C-labelled carbon dioxide and ammonia in the presence of the bacteria.

Quality criteria

Specifity of 98.5 % and sensitivity of 97.9 % of the Helicobacter Test *INFAI*® surpass all other diagnostic methods.

Helicobacter Test *INFAI*®

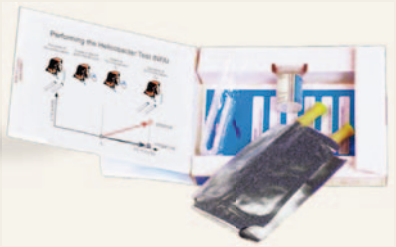
Analysis

Analys of the breath test

Helicobacter Test *INFAI*® is safe, reliable, cost-saving, and the test can be performed easily and fast.
The analysis of the breath samples can be carried out either by means of Isotope Ratio Mass Spectrometry (IRMS) or Non-Dispersive Infrared Spectroscopy (NDIR). For both analytical methods, the European Agency for the Evaluation of Medicinal Products (EMEA) has defined and approved minimum specifications.

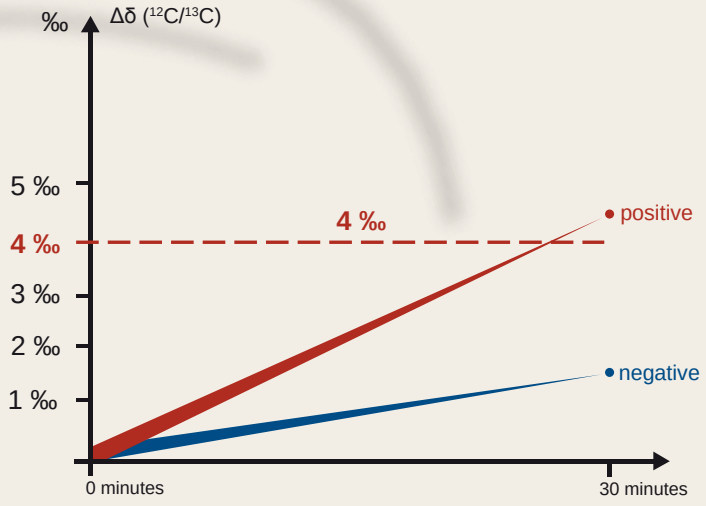
Test kit for Mass Spectrometry

or



Test kit for Infrared Spectroscopy

Evaluation



An infection with *Helicobacter pylori* is regarded as proven if the difference in $^{13}C/^{12}C$ of 00-minute-value (t_0) and 30-minute-value (t_{30}) exceeds 4‰.

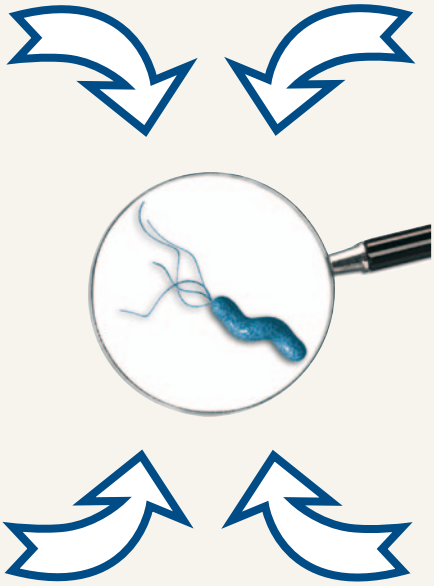
Helicobacter Test *INFAI*®

Products

Products

Helicobacter Test *INFAI*® for children age 3-11 (mass spectrometry)
EU/1/97/045/003

Helicobacter Test *INFAI*® for adults and adolescents (infrared spectroscopy)
EU/1/97/045/002



Helicobacter Test *INFAI*® for adults and adolescents (mass spectrometry)
EU/1/97/045/001

Helicobacter Test *INFAI*® Clinipac 50 for 50 tests
EU/1/97/045/004

Helicobacter Test *INFAI*® for adolescents and adults (for mass spectrometry, for infrared spectroscopy), Clinipac 50 for 50 tests, EU 01/97/045 001, 002, 004

See Summary of Product Charactestics before prescribing

PHARMACEUTICAL FORM: Powder for oral solution.
CLINICAL PARTICULARS: Therapeutic indications: Helicobacter Test *INFAI*® may be used for in vivo diagnosis of gastroduodenal Helicobacter pylori infection in adults and adolescents, who are likely to have peptic ulcer disease.
POSOLOGY AND METHOD OF ADMINISTRATION: This medicinal product should be administered by a healthcare professional and under appropriate medical supervision. Helicobacter Test *INFAI*® is a breath test for single administration. Patients from the age of 12 must take the content of 1 jar with 75 mg. For performance of the test, 200 ml 100 % orange juice or 1 g citric acid in 200 ml water for patients from the age of 12 and older (as a pre-administered test meal), as well as tap water (for dissolving the ^{13}C-urea powder) are necessary. The patient must have fasted for over 6 hours, preferably overnight. The test procedure takes approximately 40 minutes. In case it is necessary to repeat the test procedure, this should not be done until the following day. The suppression of Helicobacter pylori might give false negative results. Therefore the test shall be used after at least four weeks without systemic antibacterial therapy and two weeks after last dose of acid antisecretory agents. Both might interfere with the Helicobacter pylori status. This is especially important after Helicobacter eradication therapy. It is important to follow the instructions for use adequately, otherwise the reliability of the outcome will become questionable. **CONTRAINDICATIONS**: The test must not be used in patients with documented or suspected gastric infection or atrophic gastritis, which might interfere with the urea breath test. **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**: A positive test alone does not constitute indication for eradication therapy. Differential diagnosis with invasive endoscopic methods might be indicated in order to examine the presence of any other complicating conditions, e.g. ulcer, autoimmune gastritis and malignancies. There is insufficient data on the diagnostic liability of the Helicobacter Test *INFAI*® to recommend its use in patients with gastrectomy. In individual cases of A-gastritis (atrophic gastritis) the breath test may have false positive results; other tests may be required to confirm the Helicobacter pylori status. If the patient vomits during the test procedure, necessitating the repetition of the test, this should be done in fasted condition and not before the following day. **INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION**: Helicobacter Test *INFAI*® will be affected by all treatments interfering with Helicobacter pylori status or urease activity. **PREGNANCY AND LACTATION**: It is not expected that the test procedure may be harmful during pregnancy or lactation. It is recommended to take notice of the product information of eradication therapy products for their use during pregnancy and lactation. **EFFECTS ON ABILITY TO DRIVE AND USE MACHINES**: Helicobacter Test *INFAI*® has no influence on the ability to drive and use machines. **UNDESIRABLE EFFECTS**: None known. **OVERDOSE**: Due to the fact that only 75 mg of ^{13}C-urea is delivered, an overdose is not expected. **LIST OF EXCIPIENTS**: None. **INCOMPATIBILITIES**: Not applicable. **SHELF-LIFE**: 3 years. **SPECIAL PRECAUTIONS FOR STORAGE**: Do not store above +25°C.

MARKETING AUTHORISATION HOLDER: INFAI Institut für biomedizinische Analytik und NMR-Imaging GmbH, Universitätsstraße 142, D-44799 Bochum, Germany.
MARKETING AUTHORISATION NUMBER: EU/1/97/045/001, EU 1/97/045/002, EU 1/97/045/004.
DATE OF REVISION OF THE TEXT: March 4, 2008

Helicobacter Test *INFAI*® for children aged 3 to 11 years EU 01/97/045 003

See Summary of Product Charactestics before prescribing

PHARMACEUTICAL FORM: Powder for oral solution.
CLINICAL PARTICULARS: Therapeutic indications: Helicobacter Test *INFAI*® for children aged 3 to 11 years may be used for in vivo diagnosis of gastroduodenal Helicobacter pylori infection in children aged 3 to 11 years, who are likely to have peptic ulcer disease.
POSOLOGY AND METHOD OF ADMINISTRATION: This medicinal product should be administered by a healthcare professional and under appropriate medical supervision. Helicobacter Test *INFAI*® for children aged 3 to 11 years is a breath test for single administration. Children from the aged of 3 to 11 years must take the content of 1 jar with 45 mg. For performance of the test, 100 ml 100 % orange juice for patients from the age of 3 to 11 (as a pre-administered test meal), as well as tap water (for dissolving the ^{13}C-urea powder) are necessary. The patient must have fasted for over 6 hours, preferably overnight. The test procedure takes approximately 40 minutes. In case it is necessary to repeat the test procedure, this should not be done until the following day. The suppression of Helicobacter pylori might give false negative results. Therefore the test shall be used after at least four weeks without systemic antibacterial therapy and two weeks after last dose of acid antisecretory agents. Both might interfere with the Helicobacter pylori status. This is especially important after Helicobacter eradication therapy. It is important to follow the instructions for use adequately, otherwise the reliability of the outcome will become questionable. **CONTRAINDICATIONS**: The test must not be used in patients with documented or suspected gastric infection or atrophic gastritis, which might interfere with the urea breath test. **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**: A positive test alone does not constitute indication for eradication therapy. Differential diagnosis with invasive endoscopic methods might be indicated in order to examine the presence of any other complicating conditions, e.g. ulcer, autoimmune gastritis and malignancies. There is insufficient data on the diagnostic liability of the Helicobacter Test *INFAI*® to recommend its use in patients with gastrectomy. In individual cases of A-gastritis (atrophic gastritis) the breath test may have false positive results; other tests may be required to confirm the Helicobacter pylori status. If the patient vomits during the test procedure, necessitating the repetition of the test, this should be done in fasted condition and not before the following day. **INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION**: Helicobacter Test *INFAI*® for children aged 3 to 11 years will be affected by all treatments interfering with Helicobacter pylori status or urease activity. **PREGNANCY AND LACTATION**: Not applicable. **EFFECTS ON ABILITY TO DRIVE AND USE MACHINES**: Helicobacter Test *INFAI*® has no influence on the ability to drive and use machines. **UNDESIRABLE EFFECTS**: None known. **OVERDOSE**: Due to the fact that only 45 mg of ^{13}C-urea is delivered, an overdose is not expected. **LIST OF EXCIPIENTS**: None. **INCOMPATIBILITIES**: Not applicable. **SHELF-LIFE**: 3 years. **SPECIAL PRECAUTIONS FOR STORAGE**: Do not store above +25°C.

MARKETING AUTHORISATION HOLDER: INFAI Institut für biomedizinische Analytik und NMR-Imaging GmbH, Universitätsstraße 142, D-44799 Bochum, Germany.
MARKETING AUTHORISATION NUMBER: EU/1/97/045/003.
DATE OF REVISION OF THE TEXT: March 4, 2008

Helicobacter Test *INFAI*®

The Company

INFAI is represented in several countries throughout Europe:

INFAI UK Ltd
Innovation Centre,
University Science Park
University Road, Heslington
YORK YO1 5DG, UK
Phone: ++44 1904 435 228
Fax: ++44 1904 435 229

Infai Contract Research
Universitätsstr. 142
D-44799 Bochum, Germany
Phone: ++49 234 97 113-0
Fax: ++49 234 97 113-25

INFAI FRANCE SARL
Eurocentre Tertiaire
50, Avenue d'Alsace
F-68025 Colmar, Cedex
Phone: ++33 3 8920 4382
Fax: ++33 3 8920 4379

INFAI CH
Bahnhofstrasse 29
CH-9470 Buchs, Switzerland
Phone: ++41 81 755 6380
Fax: ++41 81 755 6365

INFAI Italia Srl
Via Borgogna
I-20112 Milano
Phone: ++39 0481 79 03 50
Fax: ++39 0481 79 03 50

INFAI TR GmbH
Irfan Bastuğ Caddesi Nr. 5/18
Diskapi / Ankara
Phone: ++90 312 311 11 46
Fax: ++90 312 311 11 46

INFAI España
C/Balmes 297, 1r2a
E-08006 Barcelona
Phone: ++34 93 362 05 39
Fax: ++34 93 240 05 45

Development and production of non-invasive methods for gastro-intestinal *in vivo* diagnosis

INFAI is a company of the researching pharmaceutical industry and offers new, innovative methods in the field of Life Science, including the respective medicinal products for *in vivo* diagnosis of different, widespreach common diseases. These *in vivo* diagnostics are non-invasive and offer competitive advantages in comparison with other diagnostic tools.
In 1997, the ^{13}C-urea breath test Helicobacter Test *INFAI*® was approved Europe-wide by the European Commission and later in many other countries worldwide. Helicobacter Test *INFAI*® is today the most widely used test for non-invasive diagnosis of infection with *Helicobacter pylori*.

In addition, INFAI is working on the development of other tests for the diagnosis of functional and metabolic disorders. These include:

- **Gastromotal**® - Gastric emptying test
- **Pancreo-Lip**® - test for slight to moderate degree of pancreatic insufficiency
- **Pancreo-Amyl**® - test for moderate to severe degree of pancreatic insufficiency
- **Kidney function test** - kidney insufficiency
- **Metabo Test**® - for congenital metabolic diseases
- **Lactoin**® - Lactose intolerance test

The approvals for these products are currently being processed.

In 2001, a new automated production line was installed at our factory in Bochum, Germany. Boasting an annual capacity of more than 3 million breath tests the INFAI production line is the largest in the world with a manufacturing process designed to comply with all pharmaceutical quality guidelines.

Quality management

INFAI has established an integrated quality management system based on ISO 9001, in compliance with national and international regulations. The high quality standards defined within this framework ensure the production of reliable and high-quality pharmaceutical products. Customer satisfaction is at the centre of all our activities. The permanent improvement of our quality management system enables us to act quickly upon changing market conditions.

CERTIFIED QUALITY MANAGEMENT SYSTEM ISO 9001:2000 DNV

INFAI GmbH · Gottfried-Hagen-Str. 60-62 · D-51105 Cologne, Germany
Phone: ++49 221 880 44-3 · Fax: ++49 221 880 44-55
www.infai.com · e-mail: mail@infai.com