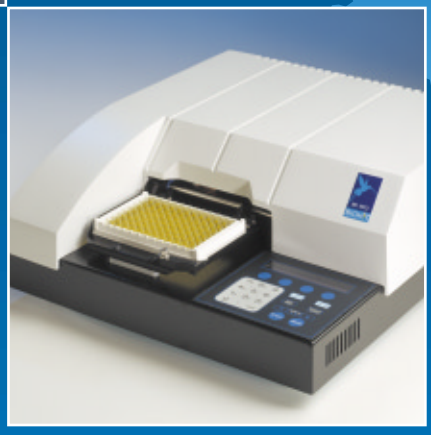
BIOHIT

ANNUAL REPORT 2002



Humming Bird

The qualities of the humming bird symbolize Biohit's product ranges of liquid handling, diagnostics, instruments, service and complete analyzing systems composed of these product groups.

Biohit's products are characterized by excellence in the selected areas of specialization and performance: versatility, flexibility, power, speed, light weight, design, ergonomics, accuracy and precision as well as safety in delicate operations.

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OVERVIEW ON BIOHIT IN 2002

Biohit develops and manufactures liquid handling products and diagnostic test systems for use in health care, research and industrial laboratories.

Biohit's liquid handling product range covers electronic and mechanical pipettors, and the range offered is currently the widest in the world. Biohit is the global market leader of electronic pipettors and the leading manufacturer of OEM[1]-electronic pipettors.

In the area of diagnostics Biohit develops and manufactures enzyme immunoassay (EIA) – based test kits and monoclonal antibodies for the screening of different types of diseases. Biohit's new diagnostic product range comprises a test panel (GastroPanel) for diagnosing *Helicobacter pylori*[2] -infection and atrophic gastritis[3] as well as for screening the risk of gastric cancer and peptic ulcer from a blood sample.

The GastroPanel-test and the GastroSoft-program interpreting its results enable to replace the invasive gastroscopy as the initial method when examining patients suffering from stomach pains and discomfort. There exist certain risks related with invasive gastroscopy, such as possible hemorrhage and infections. Furthermore, gastroscopy as a method is disliked by patients and cannot always be performed rapidly due limited health care resources. In the area of diagnostics Biohit offers also tests for the detection of systemic lupus erythematosus (SLE)[4] and lactose intolerance[5].

Biohit's product range covers, in addition to liquid handling products and diagnostics, instruments used for the analysis of test results, and related software. Moreover, Biohit offers maintenance, calibration and training services.

As a result of Biohit's aggressive innovation and patenting strategy the most relevant inventions have been protected by numerous patents in Finland and abroad.

Biohit's production plants are located in Kajaani and Helsinki, Finland. The sales and marketing subsidiaries are located in France, Germany, Italy, Japan, Russia, the U.K. and the U.S. Biohit's global distributor network covers altogether approx. 450 members in 70 countries. Moreover, Biohit co-operates with such multinational companies as Beckman Coulter, Becton Dickinson, bioMérieux, Johnson & Johnson and 3M.

In 2002 Biohit's MEUR 25.4 net sales was generated primarily by the sales of liquid handling products and maintenance. Exports accounted for 97% of the group net sales, and the degree of domestic production was approx. 95%. In 2002 altogether 59.1 % of the net sales was generated in Europe, 20.5% in the Americas and 20.4% in Asia and Russia.

Biohit listed on the New Market -list of the Helsinki Exchanges in June 1999. In 2002 the turnover of Biohit's B-share at the Helsinki Exchanges was EUR 3,017,824.28 and 1,178,003 in pieces. The highest price was EUR 4.40, the lowest EUR 1.40 and the average price EUR 2.56. The closing price at the end of 2002 was EUR 1.41.

Highlights in 2002

- Seventeen international evaluations were completed for the GastroPanel, which enables to diagnose *Helicobacter pylori* -infection and atrophic gastritis, as well as to screen the risk of gastric cancer and peptic ulcer
- Enlargement of the electronic eLINE product range
- Launch of the new mechanical pipettor range, the mLINE
- Continuation of the automation of the production premises in Kajaani

Mission of Biohit

The mission of Biohit is to create such innovations and products which promote the well-being and quality of life of people. In order to achieve this mission Biohit continues to focus on those business areas in which it possesses a solid background in multidisciplinary research, technology as well as innovations and products protected by patents.

The basis of Biohit's mission is an aggressive innovation and patenting strategy[6]. In pursuing this Biohit's management and numerous key persons have acted as pioneers and examples for many small and large companies as of the 1970s[7]. This foundation guarantees that Biohit is able to develop such products which promote efficient and safe laboratory practices as well as decentralized laboratory diagnostics and related targeted treatment (evidence-based medicine).

Vision of Biohit

The vision of Biohit for the next five years is to maintain its position as the leading manufacturer of electronic liquid handling devices in the world, and as one of the three leading manufacturers of mechanical liquid handling devices. Biohit conservatively estimates that the annual growth rate for the liquid handling business is 10% (the optimistic estimate is over 20%).

As to the business area of diagnostics Biohit estimates that, if the marketing of the test kits via Biohit's own sales organization, strategic alliances and licensing will be successful, the business generated by the sales of analyzing systems composed of diagnostics, instruments and liquid handling products could be at least twofold compared to the sales of liquid handling devices within the next five years.

1 Original Equipment Manufacturer refers to products which are tailor-made according to customer specifications.
2 *Helicobacter pylori* (H. pylori) causes atrophic gastritis and is related with the development of gastric cancer and peptic ulcer.
3 Atrophic gastritis refers to a loss of normal mucosal glands of the stomach, which is caused by prolonged *H. pylori* -infection. *H. pylori* -infection causes always an inflammation (gastritis) in the stomach.
4 Systemic Lupus Erythematosus (SLE) is a connective tissue disease which resembles rheumatic diseases.
5 Lactose intolerance is caused by the lack of the lactase enzyme, which breaks down milk sugar (lactose), in the mucosa of the small intestine.
6 In January 2000 Biohit possessed in Finland 16 patents and had submitted 31 Finnish patent applications. Altogether the twenty other recently listed companies in Finland had been awarded in total 11 patents and they had submitted 24 patent applications (Finnish Board of Patents and Registration, Taloussanomat 26.1.2000).
7 *Yksityislääkäri* (2003). Aggressive Innovation and Patenting Strategy: A Route to Success (in Finnish): No. 1: pp 96-98.

Key Financial Indicators of the Biohit Group

(EUR 1000 unless stated otherwise)	1998	1999	2000	2001	2002
Net sales	16 881	20 551	24 247	25 545	25 354
Change in net sales, %	16.6	21.7	18.0	5.4	-0.7
Return on equity, %	12.1	3.8	-4.6	-1.3	-11.7
Return on investment, %	12.2	8.5	-0.8	2.0	-5.5
Equity ratio, %	38.8	66.0	66.9	65.7	66.9
Investments in fixed assets	1 392	1 271	6 208	2 212	1 578
% of net sales	8.2	6.2	25.6	8.7	6.2
Research and development expenses	740	1 270	1 698	2 114	1 809
% of net sales	4.4	6.2	7.0	8.3	7.1
Personnel, average	164	184	222	289	303

Share Capital, Shares and Key Ratios

	1998	1999	2000	2001	2002
Number of shares, end of fiscal year	10 264 537	12 264 537	12 643 377	12 643 377	12 937 627
Key Rations					
Earnings per share (EPS), EUR	0.06	0.04	-0.06	-0.02	-0.14
Shareholders´ equity per share, EUR	0.69	1.33	1.30	1.28	1.15

Turnovers and Prices of Shares

Year	Turnover EUR	Turnover pieces	Average Price EUR	Lowest Price EUR	Highest Price EUR	Closing Price EUR	Market Capitalization EUR[8]
1999	5 624 694.27	1 240 212	4.54	3.75	6.00	4.13	50 652 538.00
2000	27 106 757.46	3 646 849	7.43	4.20	13.50	6.20	78 388 937.40
2001	4 863 535.92	908 660	5.35	3.00	7.20	4.28	54 113 654.00
2002	3 017 824.28	1 178 003	2.56	1.40	4.40	1.41	18 242 054.00

Financial Information of Biohit in 2003

- Publication of the financial statements: March 28
- Annual General Meeting: April 9 at Restaurant Pörssi, Fabianinkatu 14, 00100 Helsinki
- Interim Report 1-3/2003: May 7
- Interim Report 1-6/2003: August 6
- Interim Report 1-9/2003: November 5

8 Market price for capital stock assuming that the market price of the A-share is the same as that of the B-share.

LETTER FROM THE PRESIDENT

Osmo Suovaniemi, President & CEO

Net Sales of the Biohit Group and Result for 2002

The net sales of the Biohit Group for 2002 totalled MEUR 25.4 (MEUR 25.5). The loss after depreciations (MEUR 1.5), goodwill amortizations (MEUR 0.6), net financial expenses (MEUR 0.3), taxes (MEUR 0.3) and research and development expenses (MEUR 1.8) was MEUR 1.8. The net sales was generated primarily by the sales of Biohit Proline electronic and mechanical pipettors for two market segments, their disposable tips and service.

The share of diagnostic tests and related instruments was less than 5% of the group net sales. The profitability of liquid handling and their service was good. The result of the Biohit group has been affected by the expenses related with the research and development, production, evaluations and the preparation of the launch of Biohit's diagnostic tests. At the group level Biohit's result was weakened also by the decrease of sales and the unprofitability of Biohit Inc. in the U.S.

In order to improve profitability Biohit took into use in 2002 an adaptation program of its activities. Biohit has commenced to increase the efficiency and volume of its sales and marketing function, which, e.g., aims to support the efforts of the distributor network. Biohit also believes that increased sales by subsidiaries will improve the profitability of the group.

Liquid Handling - Safe Pipettors for Global Markets

The liquid handling products, i.e., pipettors developed and manufactured by Biohit are used in different types of laboratories in which liquids are handled and measured. The global market potential for pipettors and their disposable tips has been estimated to be approx. USD 500 million. It is possible to increase the potential of these markets threefold, e.g., with Biohit's new innovations and technologies. The sales of these products can be estimated to increase considerably especially in the developing countries if the special needs and special needs of these markets are taken into consideration.

In order to serve the global markets Biohit has identified and created new market segments. In the beginning of the 1990s Biohit created the Biohit Proline range for two segments, and thereafter has created products for four new segments. These six market segments differ from each other in terms of the area of application, performance and price. Moreover, in its development work of pipettors Biohit has paid special attention to safety and ergonomical aspects. The importance of these features in the prevention of work-related disorders, comfortability and the improvement of efficiency is fundamental[9,10].

In 2002 Biohit launched the new mechanical mLINE pipettor family for the volume range 0.5–5000 µl. The range is protected by numerous patents and patent applications. Biohit will complement the product family with the multichannel models in 2003. Moreover, in 2003 Biohit will launch the Biohit Basic -product family, which is targeted for the needs of the developing countries. Biohit's mechanical single- and multichannel Biohit Proline -range has captured a significant market share since its launch in the early 1990s.

In 2002 Biohit reinforced its three market segments of electronic pipettors with the new eLINE model for the volume range 100–5000 µl completing, thus, the entire single-channel family which covers the range 0.2–5000 µl. In 2003 Biohit will complement the electronic eLINE range with multichannel models. Biohit eLINE is the sole pipettor in the world which is equipped with electronic tip ejection. The said feature improves comfortability and reduces the risks of work-related diseases. In addition to the eLINE, the electronic pipettor range of Biohit includes the Biohit Proline and ePET product families.

Biohit has continued to develop further the electronic Biohit R-Line, which serves as a component of automated liquid handling and analyzing systems. Biohit offers the R-Line as single- and eight channel models. In 2002 Biohit continued to develop pipettor tips for new market segments.

In 2002 the accredited calibration laboratory of Biohit was accredited in accordance with the new ISO 17025 -quality standard. The maintenance and calibration service of pipettors continued to develop favorably. The same applies to the established OEM-business[11]. Biohit's OEM references includes, e.g.; such companies as 3M, Johnson & Johnson and bioMérieux. These companies complement their diagnostic analyzing systems with electronic pipettors produced by Biohit.

Diagnostics

In 2002 Biohit continued to develop further its diagnostic tests. The key components in the production of these tests are monoclonal antibodies[12] produced by certain hybridomas[13]. In addition, Biohit offers 30 monoclonal antibodies which can be used for research use and for the identification of different types of cancer from tissue samples. Biohit needs to conduct additional research and development work for the quick test for determining lactose intolerance[14] and the cellular fibronectin (cFn) -test for diagnosing

9 Mannonen S., Tiusanen T., Suovaniemi O. (2000). Major Sources of Error of Air Displacement Pipettors. *International Labmate*, April.
10 Mannonen S., Syrjä K. (2000). Safety in Pipetting. *International Labmate*, February.
11 Original Equipment Manufacturer refers to products which are tailor-made according to customer specifications.
12 The researchers Milstein and Köhler were awarded the Nobel prize in 1984 for the discovery of monoclonal antibodies.
13 Somatic cell hybrid formed by a fusion of cells.
14 Sipponen P, Suovaniemi O, Tamminen J (2000). Finnish patent 106212: *Method for the Determination of Disaccharidases and Kit therefor*

different types of cancer[15,16,17]. This is a prerequisite in order for Biohit to be able to offer these tests, not only for research use, but what is most important, also for clinical use.

The test kit for the determination of systemic lupus erythematosus (SLE), patented by Biohit, has been evaluated in Finland. Moreover, evidence exists that it would be possible to assess the clinical activity of the SLE[18]. It can be estimated that, as the SLE resembles rheumatic diseases, and, as in the diagnostics of the said diseases are used also other test kits, there exists market potential for Biohit's SLE-kit. Approx. 2% of the global population suffers from rheumatic diseases and 0.1–0.4% from SLE.

The GastroPanel, which has been patented by Biohit in numerous countries, enables to determine from a blood sample whether the patient suffers from *Helicobacter pylori* -infection and atrophic gastritis. The GastroPanel enables to reach the same results as those produced by invasive gastroscopy and the related microscopical examination of biopsy samples[19,20]. The GastroPanel and the GastroSoft-program, which interpretes the results of the GastroPanel (www.biohit.com), facilitate to diagnose the basis and nature of the dyspeptic symptoms of the patients. The GastroPanel and GastroSoft enable to assess whether the said symptoms are or have been caused by the *H. pylori* -based atrophic gastritis, as well as to determine the risk of gastric cancer and/or peptic ulcer[21,22]. The inflammation of the gastric mucosa, i.e., atrophic gastritis is symptomless or produces very few symptoms. However, atrophic gastritis underlies many diseases and it develops over time. Approx. 25% of the global population, i.e., 15 billion persons suffer from atrophic gastritis during their lifetime. Approx. 20% of the said population will suffer from peptic ulcer. Severe atrophic gastritis develops in 4–6% of the cases into gastric cancer or its premalignant stage, which is curable[23]. If a person has been diagnosed of gastric cancer at a late stage and treated at this late stage, 80–90 % of the patients will decease within the next five years. Approx. 10% of the patients suffering from atrophic gastritis will, most evidently, generate a state of severe atrophic gastritis[24]. The said patients face an exceptionally high risk to suffer from diseases related with the deficiency of vitamin B12. Due to corpus atrophy, the lack of nutrition and the celiac disease, as many as 30% of those who are over 65 years may suffer from the deficiency of vitamin B12. This may cause irreversible damages if the deficiency is not diagnosed.

Very often atrophic gastritis is not diagnosed or is diagnosed too late. The general opinion has been that atrophic gastritis is incurable. However, most research results and those received from clinical practice have demonstrated that it is possible treat and cure atrophic gastritis[25]. If atrophic gastritis is diagnosed and treated the risks of gastric cancer and peptic ulcer decrease. An untreated case of atrophic gastritis and the related deficiency of vitamin B12 may underlie dementia, deficiencies in the peripheral nervous system and heart and brain strokes. GastroPanel promotes also the diagnosis, treatment and prevention of these diseases.

The GastroPanel promotes the screening and diagnosis of atrophic gastritis and related diseases, and enhances preventive and targeted treatment (evidence-based medicine).

In order to promote the worldwide use of the GastroPanel Biohit concentrates on informing the general practitioners and service laboratories in collaboration with local specialists and medical companies. In addition, Biohit continuously aims to inform the public of the GastroPanel. The GastroPanel and the GastroSoft program serve as an aid especially for general practitioners for reaching improved diagnostics and targeted treatment. Decentralised laboratory diagnostics, performed close to the patient, enhances correct diagnostics and reduces its time and costs.

Analyzing Systems and International Collaboration

In order to develop decentralized laboratory diagnostics Biohit has complemented its product range with microplate instruments[26], which, together with its liquid handling and diagnostic products, enable Biohit to offer complete analyzing systems for its customer base. The said instruments are based on the principle of vertical photometry[27] and on multichannel pipetting.

The GastroPanel tests (Pepsinogen I and II, Gastrin-17 ja *H. Pylori*) as well as the tests for SLE and cFn are based on safe and accurate EIA-methods which utilize microplates[28].

The analyzing system developed by Biohit for the GastroPanel is flexible, easy to use and economical. Thus, it is easily applicable both for clinical and research use. Moreover, the system can, in addition for Biohit's test kits, be used also for immunodiagnostics.

15 *U.S.-patent 5,420,012 and European patent 0399271: Method for the Detection of Reactive Conditions*.

16 Ylätupa S. (1996). *The Development of a Method for Quantification of Cellular Fibronectin EDAcFn and Its Clinical Applications*, Ph.D. Dissertation, University of Helsinki.

17 Suovaniemi O., Härkönen M, Sipponen P. (2001). Finnish patent application 20011908: *Method for the Detection of Gastric Cancer.*

18 Salonen EM, Miettinen A, Valle TK, Koskenmies S, Kere J, Julkunen H: Anti-telomere Antibodies in Systemic Lupus Erythematosus (SLE): A Comparison with Five Antinuclear Antibody Assays in 430 Patients with SLE and Other Rheumatic Diseases. Submitted for publication.

19 Sipponen P, Ranta P, Helske T, Kääriäinen I, Mäki T, Linnala A, Suovaniemi O, Alanko A, Härkönen M. Serum levels of amidated gastrin-17 and pepsinogen I in atrophic gastritis. An observational case-control study. *Scand J Gastroenterol* 2002; 37: 785-791.

20 Nicolini G, Zagari R, Pozzato P, Lunedei V, De Luca L, Antonini F, Ricciardiello L, Fossi S, Beretti D, Martuzzi C, Fuccio L, Maltoni S, Sipponen P, Bazzoli F, Roda E. Diagnosis of atrophic gastritis based upon a combination of three non-invasive tests: Preliminary results of the Loiano-Monghidoro project. *J Gastroenterol Hepatol* 2002; 17 (Suppl): A264 and *Div Liver Dis* 2001; 33 Suppl.:A25.

21 Sipponen P, Seppälä K, Äärynen M, Helske T, Kettunen P. Chronic gastritis and gastroduodenal ulcer: a case control study of coexisting duodenal or gastric ulcer in patients with chronic gastritis. *Gut* 1989; 30: 922-929.

22 Sipponen P, Varis K, Fräki O, Korri UM, Seppälä K, Siurala M. Cumulative 10-year risk of symptomatic duodenal and gastric ulcer in patients with or without chronic gastritis. A clinicial follow-up study of 454 outpatients. *Scand J Gastroenterol* 1990; 25: 966-973.

23 Sipponen P, Kekki M, Haapakoski J, Ihamaki T, Siurala M. Gastric cancer risk in chronic atrophic gastritis: statistical calculations of cross-sectional data. *Int J Cancer* 1985; 35:173-7.

24 Varis K, Kekki M, Härkönen M, Sipponen P, Samloff IM, Serum pepsinogen I and serum gastrin in the screening of atrophic pangastritis with high risk of gastric cancer. 1991. *Scand J Gastroenterol*. (Suppl.) 186: 117-123.

25 Kokkola A, Sipponen P, Rautelin H, Härkönen M, Kosunen TU, Haapiainen R, Puolakkainen P. The effect of *Helicobacter pylori* eradication on the natural course of atrophic gastritis with dysplasia. *Aliment Pharmacol Ther*. 2002 Mar;16(3):515-20.

26 The intruments have been produced by BioTek.

27 Suovaniemi O. (1994). *Automated Instrumen-tation for Clinical and Research Laboratories – Innovations and Development of Vertical Light Beam Photometers and Electronic Pipettors*, Ph.D. Dissertation, University of Helsinki.

28 The U.S.-patent 5,308,584 of Biohit: *Cuvette Matrix Tray*.

Biohit is currently developing a new analyzing system which enables to determine more rapidly the results of the GastroPanel. In addition, Biohit aims to develop an automated and rapid analyzing system to be used close to the patient.

Biohit has promoted the use of the GastroPanel by adapting it to microplate-based automated analyzing systems. However, Biohit's diagnostic test kits can also be used in analyzing systems which are not based on the use of microplates. With regard to this matter Biohit has commenced negotiations with certain diagnostic companies and service laboratories in order to create possible strategic alliances.

The foundation for the success of international collaboration and strategic alliances lies in the experience of the management and key personnel of both Biohit Oyj and subsidiaries. Many of these persons have, as of the 1970s, been leading and internationally renown pioneers in the global business of biotechnology and high technology. We have been able to create standards to the areas of research, laboratory practice and diagnostics[29]. These standards have served as examples and bases for success for numerous companies. Furthermore, the said standards have promoted research, laboratory work and diagnostics worldwide[30]. Biohit's products, which conform with international quality standards and Biohit's patented technologies and innovations form the basis of our current and future international collaboration.

Production Capacity

The new production facility of Biohit was taken into use in Kajaani, Finland in 2000. The plant is equipped with most modern production tehnology and it specializes in the injection molding and the assembly of pipettors. Biohit has the capability to quadruple the production of liquid handling devices.

As to diagnostics, the current capacity for the production of test kits is 60.000, and Biohit has the capability of quadrupling also their production. The average customer price for the GastroPanel kits is EUR 400 of which the share of Biohit is EUR 200-400 depending on the sales channel.

One of Biohit's strengths is that the production has not been externalized. As a result, Biohit is able to control the utilization of its production technologies and reduce costs.

Market Potential for the Products of Biohit

As of its establishment in 1988 Biohit has aimed to capture international markets. In 2002 97% of the net sales of the Biohit group was generated outside of Finland. The degree of domestic production was approx. 95%. During the past ten years Biohit has been able to simultaneously develop its product range, production technologies and a global network of co-operation partners including Biohit's seven subsidiaries abroad. In the beginning of 2003 Biohit established a representative office to Shanghai, China. The office focuses on the marketing and sales of analyzing systems, which are composed of liquid handling devices, diagnostic tests and instruments.

Biohit's seven subsidiaries, the representative office in Shanghai and the 60 main distributors together with their collaboration networks promote Biohit's products and the Biohit brand worldwide. In 2002 approx. 75% of the group net sales was generated by the subsidiary companies. Moreover, in 2002 Biohit continued to strengthen its collaboration with distributors and capture new market areas in South America, the Arab countries and Asia.

Biohit aims to increase its co-operation with the leading companies in this field. This offers Biohit the possibility to enter with its products and technologies into such market segments which otherwise would be inaccessible. Biohit continues to collaborate with such multinational companies as Beckman Coulter, Becton Dickinson, bioMérieux, Johnson & Johnson and 3M. Biohit is in the position to possibly conclude strategic alliances with these or other companies in order to beneficially utilize the existing market potential for diagnostics. The research work and evaluations made internationally with specialists and health care organizations for the GastroPanel form a basis for the said collaboration.

I am convinced that Biohit is currently in a stage of transition towards substantial and profitable growth. Biohit believes that all prerequisites exist that this growth is attainable during the next five years.

I wish to express my sincere gratitude to the personnel of Biohit in Finland and abroad, to all our shareholders and interest groups for the trust you have demonstrated towards Biohit. We believe that the future growth of Biohit will enable us to promote further research and human well-being.

Helsinki, March 1, 2003

Yours sincerely,

Osmo Suovaniemi, M.D., Ph.D., Professor
President and CEO of the Biohit Group

29 The adjustable single- and multichannel pipettor (Finnpipette), and the principle of vertical measurement together with its applications (e.g. Multiskan). Finnpipette and Multiskan are trademarks registered by Labsystems Oy. The electronic pipettors developed by Biohit are used by companies such as Becton Dickinson, bioMérieux, Eppendorf, Johnson & Johnson and 3M.

30 Suovaniemi, O. (1994). *Automated Instrumen-tation for Clinical and Research Laboratories – Innovations and Development of Vertical Light Beam Photometers and Electronic Pipettors*, Ph.D: Dissertation, University of Helsinki.

BIOHIT GROUP

Competence of Biohit

Biohit's present management and certain key persons developed and commercialized successfully two inventions made by professor Osmo Suovaniemi in the 1970s. The inventions were the single- and multichannel, adjustable, mechanical pipettes (Finnpipettes) and vertical light path photometry together with its instrument applications (e.g. FP-, Multiskan-, Fluoroskan, Luminoreader, Bioscreen-, Auto-EIA analyzers) and certain immuno-based measurements. The value of the global business for products based on the above inventions exceeds today USD 1.5 billion annually. These inventions have been utilized so extensively that they can justifiably be called global industrial standards.

The liquid handling instruments and systems based on these inventions, e.g., for the diagnosis of infectious and cancerous diseases (e.g., HIV and duodenal ulcer) served as the foundation for the global business and growth for Labsystems and joint venture Eflab, the companies founded by Suovaniemi in the 1970s. In a publication by the National Technology Agency of Finland these innovations by Suovaniemi have been assessed as follows: "The multichannel pipetting system and the vertical photometer capable of reading 96-well microtitre plates are Finnish innovations that revolutionised laboratory routines worldwide in the 1970s and 1980s." [31]

Biohit focuses solely on those business areas in which it possesses a solid multidisciplinary scientific base, technological expertise and inventions protected by patents. The management and key personnel of Biohit have a 10–30 years' experience in the R & D, manufacture and international marketing of liquid handling and diagnostic products, instruments and analyzing systems composed of these product groups. The experience, skills and accumulated intellectual assets of the personnel are Biohit's most crucial resources.

Business Environment of Biohit

The aforementioned annual business totalling USD 1.5 billion consists of different types of products used in, e.g., research and immunodiagnostics. Especially fast, even at an annual rate of 25–30%, are growing the markets for prod-

Numerous pipettor generations from the past 30 years. Biohit's current management and key personnel have developed the various pipettor generations following the glass pipettes: the adjustable single- and multichannel pipettors, as well as the mechanical and electronic liquid handling devices.

31 The National Technology Agency of Finland (2001). *Paving the Way for Evidence-Based Medicine: Diagnostics 2000.*

ucts used in PCR-[32] and HTS[33]-applications. The Nobel prize winning production method of monoclonal antibodies[34] and the PCR-technique[35] utilize applications related with multichannel liquid handling devices and the vertical measurement principle.

The rapidly developing DNA-chip technology for the screening and studying of genes has been developed by using multichannel liquid handling products and their accessories. These applications have recently been automated by developing liquid handling and measurement robots, and related software for the interpretation of results. The automation of the PCR-technique and DNA-chip technology enables the simultaneous studying of even tens of thousands of genes.

The future poses many challenges and much work for basic research and medicine, which utilize, e.g., instruments and products needed for the PCR- and HTS-techniques. The same applies for companies manufacturing this equipment. This area of work can be expected to expand when, in addition to human genes, also the genes of animals and plant microbes will be studied. Especially automated instruments based on vertical photometry have proven to be a success, e.g., for the multinational Perkin-Elmer, the Finnish company Wallac, which was acquired by Perkin and the Swiss Tecan Group (the market value of Tecan totalled on Dec. 31, 2000 USD 1.3 billion, i.e., eight times its net sales in 2000). For example, the HTS-equipment manufactured by these companies have rendered possible and facilitated considerably the Human Genome Project.

The development of enzyme immunoassay methods for research and, in specific, for the diagnosis of cancer and infectious diseases has resulted in the growth of the overall size of the markets to USD billions. It has been estimated that the value of the sales of services based on immunoassay methods by service laboratories in the U.S., Japan and Europe exceeds USD 40 billion annually.

Biohit has completed the following diagnostic tests for the immunoassay market: Test panel for determining' *Helicobacter pylori* -infection, atrophic gastritis and for screening the risk of gastric cancer and peptic ulcer from blood samples (GastroPanel and the GastroSoft-program for the interpretation of the results), and a test for diagnosing systemic lupus erythematosus (SLE). It has been estimated that the overall market potential for these tests, the test for diagnosing lactose intolerance and monoclonal antibodies totals USD 5.0 billion[36].

Biohit's Business Idea

Since its foundation in 1988 Biohit has established itself on the world market with its innovative, high technology liquid handling products. During the past decade Biohit has invested in R & D, launched numerous new products, invested in production technologies, automation and quality control, and established an extensive international sales and marketing network. Personnel resources have been strengthened and diversified through col-laboration with leading researchers at universities and research institutions.

32 The Polymerase Chain Reaction (PCR) technique is used for the amplification of small amounts of DNA.
33 High Through-Put Screening (HTS) refers to the study of large amounts of samples.
34 Milstein and Köhler received the Nobel prize for inventing monoclonal antibodies in 1984.
35 The PCR-technique was invented in 1983 by Kary Mullis, who received the Nobel prize for it in 1993.
36 MeritaNordbanken Research 6.3.2000

Biohit's business idea is to develop, manufacture and market liquid handling products, diagnostic tests, instruments as well as analyzing systems composed of these product groups.

The commitment and entrepreneurship of the personnel, members of the board and scientific advisors have been strengthened through ownership of shares and the option program targeted to the entire personnel.

In the early 1990s Biohit focused on liquid handling products and, in addition, continued to develop diagnostic tests and laboratory instruments for new business areas. As of 1999 Biohit's business idea has been to focus on the development of liquid handling products, diagnostic tests and laboratory instruments as well as on analyzing systems composed of these three product lines and their service.

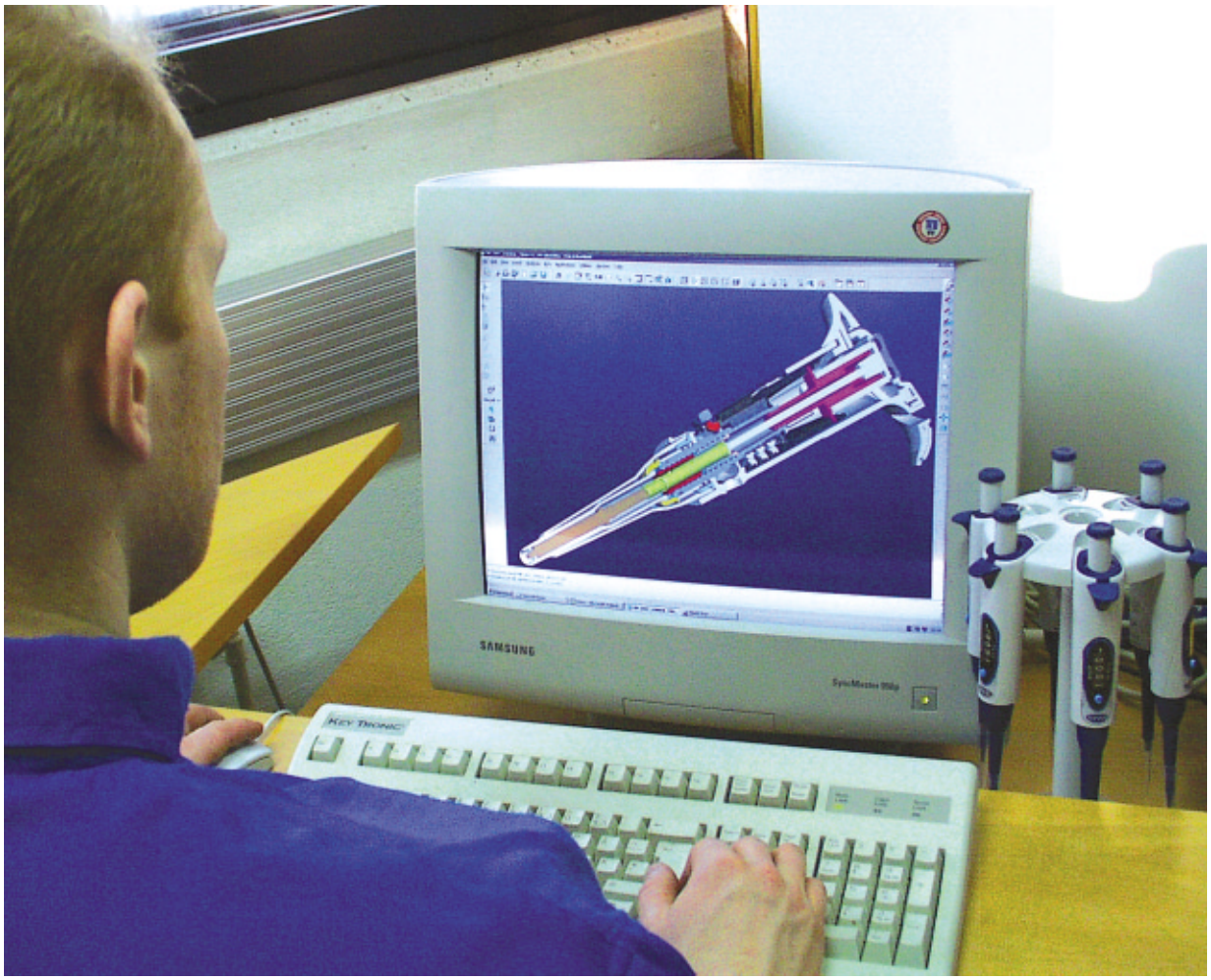
Research and Development

Biohit´s research and development combines expertise in various fields into integrated know-how. The key personnel are experts in the fields of biotechnology, chemistry, electronics, medicine, mechanics, molecular biology, optics, physics, and precision injection molding technology. Biohit's personnel together with scientific advisors representing various academic communities apply in the innovation work, basic and applied research, and R&D knowledge of these areas and different related high technologies.

This multidisciplinary approach, innovations and application of technologies has produced valuable results for the advancement of research and health care all over the world. A further strength of Biohit's multidisciplinary R & D is the ability to react quickly to new customer needs and product ideas.

In order to serve global markets Biohit has identified and created new market segments. In addition to the two market segments created for the Biohit Proline -pipettors in the early 1990s Biohit has developed four new market segments. These six segments differ from each other in terms of the area of use of the products, their performance and price. In its development work of pipettors Biohit has continuously paid attention to the safety and ergonomical aspects of its liquid handling product range. This reduces considerably the risk of developing work-related upper limb disorders, and enhances the safety and confortability at work.

In the area of diagnostics the evaluations of the test panel for determining H. pylori -infection and atrophic gastritis and for screening the risk of gastric cancer and peptic ul-



Biohit's research and development combine the expertise of various fields into integrated knowledge.

cer from blood samples (GastroPanel) continued according to plans. Evaluations were in progress in Finland and on the most important market areas abroad. The results of the evaluations completed in 2001 were positive and supported the results gained from evaluations completed earlier.

The research and development of Biohit's liquid handling and diagnostic products is carried out in Helsinki. In 2002 Biohit's R&D expenditure totalled MEUR 1.8.

Patent Policy

Biohit focuses solely on those business areas in which it possesses a solid multidisciplinary scientific base, technological expertise and inventions protected by patents.

Biohit possesses numerous patents, and its key personnel and management have a 10–30 years' experience in the R & D, manufacture and international marketing of liquid handling and diagnostic products, instruments and analyzing systems composed of these product groups. The experience of Biohit's President and CEO, Dr. Osmo Suovaniemi, is illustrated, e.g., by the fact that he has been awarded most patents in Finland[37,38] and a few hundred abroad in the fields of medical diagnostics, optics and mechanics.

37 *Tekniikka ja Talous (Technology and Economy)* 8.2.2001: 11
38 *Keksintöuutiset (Innovation News)*. (2001). 4-5: 7.

The comprehensive patent protection in Finland and abroad, which has resulted from Biohit's aggressive patenting policy has formed a solid and reliable basis for Biohit's growth and co-operation with other companies on the global level. Biohit's patents, the high quality of products and accurate deliveries have resulted in the continuation of long-term co-operation with companies such as Beckman Coulter, Becton Dickinson, bioMérieux, Johnson & Johnson and 3M. Biohit will continue to pay special attention on the development and protection of its multidisciplinary immaterial assets also in the future.

The basis of Biohit's mission is an aggressive innovation and patenting strategy[39]. In pursuing this Biohit's management and numerous key persons have acted as pioneers and examples for many small and large companies as of the 1970s[40]. This foundation guarantees that Biohit is able to develop such products which promote efficient and safe laboratory practices as well as decentralized laboratory diagnostics and related targeted treatment (evidence-based medicine).

39 In January 2000 Biohit possessed in Finland 16 patents and had submitted 31 Finnish patent applications. Altogether the twenty other recently listed companies in Finland had been awarded in total 11 patents and they had submittes 24 patent applications (Finnish Board of Patents and Registration. *Taloussanomat* 26.1.2000).
40 *Yksityislääkäri* (2003). Aggressive Innovation and Patenting Strategy: A Route to Success (in Finnish): No. 1: pp 96-98.

Osmo Suovaniemi, the President & CEO of the Biohit Group, received an honorary award from the Finnish Board of Patents and Registration on November 19, 2002. On June 29, 2002, which was the 160th jubilee of granting the first patent in Finland, Suovaniemi possessed most Finnish patents. On the said date the award was granted to three persons who have been inventors in at least fifty patents granted by the Finnish Board of Patents and Registration. Suovaniemi received the honor and name of professor from the President of Finland in 2002.

Production

The liquid handling products and disposable pipettor tips are manufactured according to the ISO 9001 -quality system standards in the Kajaani and Helsinki plants. The main production plant is located in Kajaani whereas the Helsinki production unit serves as a pilot plant.

Biohit's new facilities for the assembly of liquid handling products and injection molding of plastics were taken into use in Kajaani in 2000. The injection molding department produces precision molded plastic components, pipettor parts and disposable pipettor tips. Investments were made especially in the automation of injection molding, materials handling and production. The new premises enable to quadruple the current production volume of liquid handling products and plastics.

In the beginning of 2001 Biohit took into use a clean room unit for the production of diagnostic test kits. The premises enable the production of 60,000 test kits annually, and it is possible to quadruple the amount of test kits produced. The average customer price for the GastroPanel kits is EUR 400 of which the share of Biohit is EUR 200–400 depending on the sales channel.

One of Biohit's strengths is that the production has not been externalized. As a result, Biohit is able to control the utilization of its production technologies and reduce costs.

International Sales and Marketing

The foundation for the success of international collaboration and strategic alliances lies in the experience of the management and key personnel of both Biohit Oyj and subsidiaries. Many of these persons have, as of the 1970s, been leading and internationally renown pioneers in the global business of biotechnology and high technology. We have been able to create standards to the areas of research, laboratory practice and diagnostics. These standards have served as examples and bases for success for numerous companies. Furthermore, the said standards have promoted research, laboratory work and diagnostics worldwide. Biohit's products, which conform with international quality standards and Biohit's patented technologies and innovations form the basis of our current and future international collaboration.

The customer base of Biohit consists of leading laboratories of research institutes, universities, those of medical and biotechnology companies and hospitals. Also, the food industry and environmental control laboratories are important customers for Biohit. In addition, Biohit has numerous OEM-customers for which Biohit manufactures tailor-made products on the basis of its own technologies and know-how.

The international co-operation and customer service network for Biohit's liquid handling products, diagnostics, instruments and systems consists of:

- Subsidiary companies in France, Germany, Italy, Japan, Russia, the U.K. and the U.S. The companies are located on Biohit's most important market areas. The companies act as sales and marketing units for Biohit's products and also offer maintenance, calibration and training services locally. In addition to Biohit products, the units engage in the sales of OEM- and private label -products developed and manufactured by Biohit.
- Biohit's 60 main distributors, which together with their local distributors form a network of 450 members covering 70 countries.
- The global distribution networks of Biohit's most important OEM- and private label -customers.

In 2002 Biohit's MEUR 25.4 net sales was generated primarily by the sales of liquid handling products and the provision of maintenance services. Exports accounted for 97% of the group net sales, and the degree of domestic production was approx. 95%. In 2002 altogether 59.1% of the net sales was generated in Europe, 20.5% in the Americas and the remaining 20.4% in Asia.

Quality Systems

Biohit operates in a business area which requires definite accuracy and performance of the products. Today, the laboratory environment does not only require high quality products but also ones which are environmentally friendly both during their usage and thereafter.

Biohit has responded to these challenges by continuously developing its product ranges and its operative processes in order to meet well the existing and future demands posed by authorities, environmental bodies and customers.

Biohit participates annually in numerous exhibitions related with laboratory technology and medicine. Biohit at the Medica Exhibition in Germany in November 2002.

The quality systems of Biohit has been certified and it conforms with the following international standards:

- ISO 9001 ed. 1994: Quality System Standard
- ISO 13485 ed. 1996: Quality Systems, IVD / Medical Devices
- ISO 14001: Environmental Systems
- ISO 17025: Accreditation of the Calibration Laboratory

Biohit's production facilities in Kajaani enable to quadruple the current production volume of liquid handling products and accessories.

LIQUID HANDLING

In 2002 Biohit launched the new mLINE® mechanical pipettor range. In the development work of the pipettor special emphasis has been placed on the ergonomical aspects of the liquid handling device. The forces needed for pipetting and tip disposal are small which contributes to reducing the risk of work-related upper limb disorders (WRULDs). The picture displays also the new environmentally friendly and economic refill tip box system, which Biohit launched in 2002.

The liquid handling product range developed and manufactured by Biohit encompasses electronic and mechanical pipettors, their disposable tips and maintenance, calibration and training services. The liquid handling product range manufactured by Biohit is the widest in the world today.

Currently, Biohit is the global market leader of electronic pipettors holding an approx. 60% of the world markets. Biohit is also the leading manufacturer of electronic OEM-pipettors in the world. Biohit's OEM-customers include, e.g., Becton Dickinson, bioMérieux, Johnson & Johnson and 3M. As to mechanical liquid handling products, Biohit possesses an approx. 8% share of the world markets and in the area of disposables slighty under 2%. During the past couple of years the maintenance of liquid handling products has become a new, fastly growing and profitable business area. Biohit's liquid handling products comply with international quality standards and are GS[41]- and CE[42]-qualified.

Since its establishment in 1988 Biohit's management and key personnel have employed the aggressive innovation and patenting policy developed and applied by CEO Osmo Suovaniemi already in the 1970s and 1980s. At that time the policy served as a model also for other companies.

Biohit's current patents and patent applications feature various innovations, which together with the technologies developed and employed by Biohit, and which have been tested by various multinational companies, enable to offer many new products for different market segments. The current and new market segments vary in terms of the area of application, performance and price.

The value of the market for Biohit's current range of liquid handling products and disposable tips totals USD 500 million annually. This consists of the sales of over 1 million mechanical pipettors, approx. 50,000 electronic pipettors and over 10 billion disposable tips each year. It can be expected that the increasing number of electronic liquid handling applications to be integrated into automated laboratory instruments and analyzing systems, as well as the tightening safety, quality control and efficiency requirements, will considerably reinforce the demand for electronic liquid handling devices in the future.

The market potential for Biohit's current range of electronic and mechanical liquid handling products is significant. By maintaining the level of its existing products Biohit should be able to hold its annual growth of 10–20% and even increase its share on these traditional markets. When taking into consideration all Biohit's possible existing and new market segments in 2001 and 2002, it has been estimated that the market potential for the new liquid handling products is approx. USD 1.0 billion.

Between 2003-2007 Biohit's objective is to capture such new market segments for liquid handling products which Biohit can serve with its existing innovations, technologies and know-how.

41 Geprüft Sicherheit (GS): A German product safety standard.
42 Les Communautés Européennes (CE) –marking is a guarantee for authorities, importers and sellers that the product fulfils the requirements set by the European Union.

Electronic Liquid Handling

Biohit's electronic liquid handling products combine electronics, optics, fine mechanics and material technology in a way which simplifies and renders liquid handling more efficient and ergonomical. The microprocessor-controlled electronic pipettors contribute to minimizing human error when pipetting and improve the accuracy and precision of liquid handling.

Biohit's electronic pipettors are available in single- and multichannel configurations and cover the volume ranges of 0.2 µl[43] to 100 ml. They have opened up new dimensions in liquid handling'technology in terms of precision, ergonomics and functionality. The ergonomical design and light weight of the electronic pipettors take much of the strain out of pipetting and, thus, help to prevent fatigue and the development of work-related upper limb disorders (WRULDs). For example, the effort required for one pipetting action with a mechanical pipettor may even be the equivalent of moving a load of several kilograms with the thumb, whereas using an electronic pipettor requires only a fiftieth of this effort.[44,45,46,47,48,49] According to Hoskins et al. the Occupational Safety and Health Administration (OSHA) in the U.S. has determined that Repetitive Strain Injuries (RSIs) are the largest single category of injury in the workplace[50].

In order to improve further the safety of pipetting, most of Biohit's electronic pipettors are equipped with filters which protect the internal components of the pipettor from contamination and, as a result, the sample from carryover, e.g., in genetic studies[51,52]. In addition to providing enhanced ergonomics and safety, the electronic pipettor is, as a result of the microprocessor controls, an extremely versatile tool for numerous tasks; one unit can perform pipetting, multiple dispensing and diluting, and the electronic pipettor can also be used for mixing liquid samples.

Biohit has segmented the liquid handling markets on the basis of different customer needs and price sensitivity. The picture displays the ePET®-range designed in specific for the needs of research laboratories.

Biohit is the leading manufacturer of electronic liquid handling devices in the world. The structure, ergonomical design and light weight of Biohit's electronic pipettors take much of the strain out of pipetting and, thus, help to prevent the development of work-related upper limb disorders. Moreover, the microprocessor-controlled electronic pipettors contribute to minimizing humand error and, thus, improve the accuracy and precision of liquid handling. The picture exhibits the new generation eLINE® - product range which was developed for most demanding liquid handling applications. The eLINE® received an honorary mention in the Pro Finnish Design 2001 -competition arranged by Design Forum Finland.

43 1 µl = one millionth part of a liter.

44 Suovaniemi O. (1994). *Automated Instrumen-tation for Clinical and Research Laboratories – Innovations and Development of Vertical Light Beam Photometers and Electronic Pipettor*s, Ph.D. Thesis, University of Helsinki.

45 Björkstén M.G., Almby B., Jansson E.S. (1994). Hand and Shoulder Ailments among Laboratory Technicians Using Modern Plunger-Operated Pipettes. *Applied Ergonomics* 25: 88-94.

46 Fredriksson K. (1995). Laboratory Work with Automatic Pipettes: A Study on How Pipetting Affects the Thumb, *Ergonomics* 38 (5): 1067-1073.

47 McGlothlin J.D., Hales T.R. (1995). *NIOSH* (National Institute of Occupational Safety and Health) *Health Hazard Evaluation Report.*

48 Hodgson E. (1996). Work Related Upper Limb Disorders and the Laboratory. *World Directory of Environmental Testing, Monitoring and Treatment.*

49 David G., Buckle P. (1997). A Questionnaire Survey of the Ergonomic Problems Associated with Pipettes and Their Usage with Specific Reference to Work-Related Upper Limb Disorders. *Applied Ergonomics*, Vol. 28, No. 4: 257-262.

50 Hoskins D.B., Erickson J. (1998). Laboratory Ergonomics, the Wake-Up Call: A Case Study on How One Company Relieved Stress and Strain on Its Employees, *Chemical Health and Safety*, January /February.

51 Kolari M., Mannonen S., Takala T., Saris P., Suovaniemi O., Salkinoja-Salonen M.S. (1999). The Effect of Filters on Aseptic Pipetting Lifetime of Mechanical and Electronic Pipettors and Carryover during Pipetting. *Letters in Applied Microbiology* 29: 123-129.

52 Suovaniemi O. (2000). Finnish patent 104885: *Filter.*

The accredited calibration laboratory for liquid handling products reinforces Biohit's position as one of the leading manufacturers of liquid handling devices in the world.

As a result of the market segmentation made on the basis of different customer needs and price sensitivity Biohit's electronic pipettors can be divided into the following product groups:

- eLINE: The new generation electronic pipettor range for most demanding liquid handling applications. The ergonomical design of the eLINE® and the unique electronic tip ejector reduce considerably the risk for work-related disorders.
- Biohit Proline: Biohit's basic range of electronic pipettors.
- ePET: The most cost effective range of Biohit's electronic pipettors which serve as a more ergonomical alternative to mechanical pipettors.

and the following products for large volumes:

- ViscoPet: Electronic pipettor developed especially for the precise and accurate handling of viscous liquids. The device together with Viscotip capillaries makes the ViscoPet particularly suitable for the needs of laboratories processing food and dairy products.
- XL: Pipetting controller and electronic pipettor for the volume range 0.1–25 ml.
- Midi Plus: Pipetting controller for the volume range 1–100 ml.

Mechanical Liquid Handling

Today, mechanical liquid handling products continue to be some of the most commonly used tools in laboratories, and over million pieces are sold annually. The factors contributing to the popularity of the mechanical pipettors are that laboratory personnel are used to them and their lower price compared with electronic devices.

Biohit's mechanical pipettor range covers fixed and adjustable single- and multichannel models for the 0.1 µl – 5 ml volume range. In its development of mechanical pipettors Biohit has again paid special attention to ergonomical aspects. The light weight and smooth plunger action of the pipettors facilitate liquid handling. Moreover, as is the case with electronic pipettors, most of Biohit's mechanical pipettors are equipped with filters, which improve the quality and safety of pipetting[53,54].

Disposable Tips

The pipettors and injection molded plastic disposable tips manufactured by Biohit form together a reliable system[55,56]. Biohit guarantees the precision and accuracy of its pipettors when using tips developed and manufactured by Biohit. Further development of pipettor tips is always an integral part of the R & D work on the pipetting system. To support the safety and quality of pipetting Biohit's range of disposables includes, e.g., filter tips.

Maintenance and Calibration Services

As part of its product and marketing strategies Biohit provides maintenance, calibration and training services through its subsidiary and distributor network. During the past couple of years especially the maintenance of liquid handling products has become a new, fastly growing business area.

53 Kolari M., Mannonen S., Takala T., Saris P., Suovaniemi O., Salkinoja-Salonen M.S. (1999). The Effect of Filters on Aseptic Pipetting Lifetime of Mechanical and Electronic Pipettors and Carryover during Pipetting. *Letters in Applied Microbiology* 29: 123-129.
54 Suovaniemi O. (2000). Finnish patent 104885: *Filter*.
55 Suovaniemi O. (1994). *Automated Instrumen-tation for Clinical and Research Laboratories – Innovations and Development of Vertical Light Beam Photometers and Electronic Pipettors*, Ph.D. Thesis, University of Helsinki.
56 Mannonen S., Tiusanen T., Suovaniemi O. (2000). Major Sources of Error of Air Displacement Pipettors. *International Labmate*, April.

Today, due to tightening quality control regulations, the customers for liquid handling products are increasingly using accredited calibration laboratories. The calibration laboratory for Biohit's liquid handling products was accredited by FINAS[57] in 2000.

The accreditation of the calibration for liquid handling products performed in the production plants in Helsinki and Kajaani reinforces Biohit's market position as one of the leading manufacturers of liquid handling devices in the world. Currently, there exist only two accredited calibration laboratories in the world for companies manufacturing liquid handling devices. Of these Biohit's laboratory is the most accurate within the following scope of accreditation.

Quantity	Measurement Measurement Range	Measurement Capability (+/-)
Volume	0,1-5,0 µl	0,015 µl
	10 µl	0,025 µl
	50 µl	0,080 µl
	100 µl	0,100 µl
	200 µl	0,100 µl
	500 µl	0,520 µl
	1000 µl	0,520 µl
	5000 µl	3,600 µl

As a result of the accreditation Biohit is able to offer its customers worldwide calibration certificates for liquid handling devices, which are based on national and international measurement standards. Moreover, Biohit is able to fulfil the international (EN 45001) and national traceability requirements set for liquid handling devices. Traceable calibration certificates form already now an important part of the reliable analysis services provided by laboratories.[58] The number of Biohit's accredited calibration laboratory is K041.

Liquid Handling in 2002

In the area of liquid handling Biohit continued the development of new pipettor generations. This development work is based on Biohit's aggressive liquid handling product strategy in which new market segments have been identified and created. These segments differ from each other in terms of the area of application, performance and price.

In its development of liquid handling products Biohit has paid special attention to the safety and ergonomical aspects of pipettors, which contribute, e.g., to reducing the risk of work-related upper limb disorders[59,60].

In the area of liquid handling Biohit continued to broaden its electronic eLINE-range. During the reporting period Biohit launched the single-channel model for the volume range of 100–5,000 µl. As a result, the entire single-channel eLINE -product range has been completed. The said single-channel family covers the volume range of 0.2–5,000 µl.

Biohit's new generation electronic eLINE-range has been developed for the most demanding liquid handling applications. The microprocessor-control and novel construction enable maximum liquid handling performance with very high levels of accuracy and precision. The ergonomical design of the eLINE-range together with electronic tip ejection reduce considerably the risk of work-related upper limb disorders.

In 2002 Biohit launched the new mechanical pipettor range, the mLINE. In the development work of the pipettor special attention has been paid to its ergonomical design. The mLINE features low pipetting forces for operating the pipettor and also for tip ejection. These contribute to reducing the risk of repetitive strain injuries (RSI). Moreover, to reduce the risk of contamination the pipettors are equipped with tip cone filters. The launched single-channel mLINE covers the volume range 0.5–5,000 µl, and is fully autoclavable.

In 2002 Biohit was awarded the following patents:

- Finnish patent FI 109407 for the invention "Suction Device" (31.7.2002)
- Finnish patent FI 109882 for the invention "Pipette" (31.10.2002)
- US patent 6,482,361 for the invention "Suction Device" (19.11.2002)
- US patent 6,499,364 for the invention "Tip for a Suction Device" (31.12.2002).

In 2002 Biohit published the following articles related with the business area of liquid handling:

- Mannonen S, Hintikka V, Kaasinen J, Ekholm P: Reduced Tip Ejection and Pipetting Forces Prevent Repetitive Strain Injuries (RSI). Biomedical Products 2002, April, No. 4.
- Mannonen S, Hintikka V, Syrjä K. Choosing the Correct Electronic Pipettor. Clinical Laboratory International 2002, April.
- Mannonen S, Hintikka V, Syrjä K. The Benefits of Electronic Pipetting: How to Choose the Correct Pipettor. International Labmate Guide 2002/2003.

During the financial year the accredited calibration laboratory of Biohit was certified in accordance with the ISO 17025 -quality standard. Moreover, the capacity of the plastics production at the plant in Kajaani was increased considerably and the automation of production was continued.

57 The Finnish Accreditation Service (FINAS), a part of the Center for Metrology and Accreditation, is a body operating under the Ministry of Trade and Industry. FINAS is a member of the European Co-operation for Accreditation (EA).

58 Mannonen S., Riikonen S. (2000). Accredited Calibration and Future Demands for Pipettors. *International Biotechnology Laboratory*, April.

59 Mannonen S., Syrjä K. (2000). Safety in Pipetting. *International Labmate*, February.

60 Vaughton R. (1999). Taking the Strain Out of Pipetting. *International Biotechnology Laboratory*, September.

DIAGNOSTICS

In the business area of diagnostics Biohit develops, manufactures and markets enzyme immunoassay (EIA) -based test kits and monoclonal antibodies (MAbs) for the screening and detection of different types of disease. Biohit's diagnostic product range encompasses the following tests: Test panel for determining *Helicobacter pylori (H. pylori)* -infection and atrophic gastritis and for screening the risk of gastric cancer and peptic ulcer from blood samples (GastroPanel and GastroSoft), and tests for diagnosing lactose intolerance and systemic lupus erythematosus (SLE).

Test Panel for Determining *Helicobacter pylori* -Infection and Atrophic Gastritis

Background

Australian doctors, Barry J. Marshall and J. Robin Warren isolated the *Helicobacter pylori (H. pylori)* in 1982. This bacterium lives protected from gastric acids on the mucosa of the stomach. *H. pylori* -infection is usually caught in childhood and rarely in adulthood. The infection spreads orally (oral-oral transmission) and via the contents of the stomach (e.g. vomiting) and possibly also via feces. If untreated the infection lasts for a lifetime and causes an inflammation of the stomach, i.e., gastritis. Gastritis is nearly always caused by *H. pylori* -infection. In a small number of cases gastritis may develop as a result of an autoimmune disease. Over half of the global population are infected by *H. pylori* (approx. 3 billion persons) and related gastritis. In half of the infected cases (approx. 1.5 billion) the gastritis develops over the years into atrophic gastritis, which refers to the inflammation and atrophy of the mucosa of the stomach.

The isolation of the *H. pylori* changed the understanding of the causes of gastric cancer and peptic ulcer. Today it is known that the *H. pylori* -infection and gastritis are nearly always related with the development of gastric cancer and peptic ulcer. Before 1982, and even for a long time after that, it was believed that peptic ulcer develops primarily as a result of hypersecretion of acid, stress and anxiety.

In reality in 70–90% of the cases the primary cause of peptic ulcer is gastritis or atrophic gastritis caused by *H. pylori* -infection. Other causes are anti-inflammatory analgesics (NSAID drugs) and asperin. In 1994 the International Agency for Research on Cancer (IARC) operating under WHO presented a consensus statement, based on available research results, that gastric cancer is caused by *H. pylori* -infection. *H. pylori* -infection was considered to be related with the development of gastric cancer (carcinogenecity class 1) in a similar way as smoking is related with lung cancer. According to the consensus statement *H. pylori* -infection launches a chain of events, such as the development of atrophic gastritis, which in certain cases leads to gastric cancer.

Gastritis and atrophic gastritis appear in different patients in three different topographical types depending on whether the changes appear in the lower part of the stomach, i.e., the antrum (antrum gastritis), the upper part, i.e., the corpus (corpus gastritis) or both (pangastritis).

The risk for gastric cancer and peptic ulcer is very low when the stomach is normal. The risk of gastric cancer of a patient suffering from atrophic gastritis of the corpus is 5-fold compared with normal population. If both the corpus and antrum are severely atrophic the risk is approx. 90-fold. When only the antrum is severely atrophic the risk of gastric cancer is approx. 20-fold. In addition, the risk of peptic ulcer is approx. 25-fold compared with normal population. It has been estimated that in the U.S. approx. 20 million persons suffer from or develop a peptic ulcer during their lifetime[61]. The equivalent number in the Finnish population can be estimated to be slightly less than 500,000.

Atrophic gastritis and the early stage of gastric cancer are usually symptomless or show only weak symptoms. The surgical removal of an early stage gastric cancer is usually successful. However, the prognosis of a prolonged cancer case demonstrating symptoms is weak; the 5-year survival rate of those surgically treated is only 10–20%[62]. The equivalent survival rate of patients treated early in whom the cancer is restricted to the mucosa and submucosa is approx. 90%. The occurrence of gastric cancer is especially high in certain parts of the world, e.g., in Japan, Asia in general and South America.

Approx. 30% of the global population, i.e., nearly two billion persons, suffer from dyspepsia, the occasional or continuous pain or discomfort in the upper part of the stomach. The only method for examining whether a patient suffering from dyspepsia or *H. pylori* -infection suffers from atrophic gastritis has until now been the histological (microscopic) examination of biopsies taken in connection with gastroscopy.

As invasive gastroscopy is often uncomfortable for the patient, expensive and its availability limited, the patient is usually treated only on the basis of anamnesis, symptoms or clinical examination. Many cases have demonstrated the unreliability of an examination made on the basis of symptoms, which often leads to incorrect conclusions.

Severe consequences may result from delays in targeted treatment and further examinations based on a correct

Biohit participated in the Digestive Disease Week Symposium in the U.S. in 2002. On the right professor Barry Marshall, who together with Professor Robin Warren isolated the H. pylori in 1982. On the left Lea Paloheimo, Ph.D., who acts as the Specialist and Development Manager for diagnostics at Biohit.

61 Lim D. (1996). *Microbiology*, 2nd ed.: 522.
62 Wanebo H.J., Kennedy B.J., Chmiel J., Steele G.J., Winchester D., Osteen R. (1993). Cancer of the Stomach. A Patient Care Study by the American College of Surgeons. *Ann. Surg.* 218: 583-592.

diagnosis. Without a correct diagnosis the treatment may be delayed and the disease may become impossible to cure. This, at worst, may increase the risk of deaths, decrease the quality of life, and increase human suffering and health care costs.

The *H. pylori* -infection is diagnosed worldwide by using serological tests, breath tests and antigen tests of the feces. These tests enable to diagnose only whether the patient is infected or not. The GastroPanel makes a major contribution to these tests. On the basis of the results received so far only the Gastropanel enables to diagnose gastritis, its severity and quality equally reliably as gastroscopy and the examination of biopsy samples. Moreover, the tests conducted with the panel (levels of Pepsinogen I and Gastrin-17) enable to assess the condition and functioning of the entire mucosa of the stomach. As the severity of atrophic gastritis of the corpus area increases, the level of Pepsinogen I measured from the blood sample decreases. Likewise, as the severity of atrophic gastritis of the antrum increases the lower becomes the level of Gastrin-17 in blood.

Atrophic gastritis cannot be diagnosed on the basis of gastroscopy but it is necessary to study the biopsy samples histologically. It must also be noted that, on the basis of a few biopsies covering an area of a couple of square millimeters of the overall area of approx. 80 000 square millimeters, it is not possible to assess the condition and functioning of the entire mucosa of the stomach.

Diagnosis of Atrophic Gastritis from a Serum Sample

Atrophic gastritis, i.e., the inflammation and atrophy of the mucosa of the stomach, is a disease which is often symptomless or produces only unspecific symptoms. Atrophic gastritis, which may result in many diseases, develops over the years or decades and is not often diagnosed. It was earlier believed that atrophic gastritis is irreversible. Most recent research and observations indicate that atrophic gastritis is curable and that the atrophy can reverse if the Helicobacter pylori -infection, which is the most common cause of the atrophic gastritis, is treated in good time.

If atrophic gastritis is diagnosed and treated the risk of gastric cancer and peptic ulcer will decrease. In addition, atrophic gastritis, if not diagnosed and treated, may also result in and raise the risk of dementia, polyneuropathies, and heart and brain strokes due to the malabsorption of vitamin B12 and consequent abnormalities in the metabolism of homocysteine and methionine in extragastric tissues and cells.

Thus far, the only means for diagnosing atrophic gastritis has been gastroscopy and the microscopic examination of the endoscopic biopsy specimens. The Finnish company Biohit, together with its scientific collaborators, has developed the GastroPanel, which enables to screen and diagnose atrophic gastritis on the basis of a blood sample.

Helicobacter pylori -infection is one of the most common chronic infections. The infection causes to the major-

Test panel developed by Biohit for diagnosing atrophic gastritis and H. pylori -infection, and for screening the risk of gastric cancer and peptic ulcer from blood samples. GastroPanel® can replace gastroscopy as the initial method when examining patients suffering from stomach pains, discomfort and possible atrophic gastritis caused by H.pylori -infection.

ity of the global population severe diseases related with the gastrointestinal tract[63,64]. All patients infected by H. pylori will suffer from chronic gastritis. Approx. half of the global population are infected by H. pylori and suffer from related gastritis. Approx. 20% of those infected may suffer from peptic ulcer[65,66]. In half of the infected cases the gastritis develops over the years into atrophic gastritis, which increases considerably the risk of gastric cancer.[67,68]

Approx. 10% of the patients suffering from gastritis caused by *H. pylori* will develop severe atrophic gastritis of the corpus[69,70,71]. These patients face a considerably high risk of suffering from diseases related with deficiency of vitamin B12[72]. In accordance with the Maastricht 2000 -consensus the patients suffering from *H. pylori* should be treated. In order to avoid severe complications the consensus statement emphasizes that the patients suffering from *H. pylori* or severe gastric diseases (atrophic gastritis) must be treated[73]. Moreover, the symptoms of the patients suffering from severe gastric conditions should be diagnosed as well as perform gastroscopy at an early asymptomatic stage. Approx. 4–6% of the patients belonging to the said group have been diagnosed to suffer from gastric cancer or its premalignant phase[74].

GastroPanel Examination

GastroPanel enables to diagnose from a blood sample whether the patient suffers from *H. pylori* -infection and atrophic gastritis as well as assess the risks of gastric cancer and peptic ulcer[75,76,77]. This is done by measuring the levels of Pepsinogen I [78,79,80,81,82,83,84] and Gastrin-17 [85,86] -and the *H. pylori* -antibodies from a blood sample. On the basis of the results it is possible to determine whether the patient suffers from gastritis or atrophic gastritis and in which part of the stomach the changes are located (antrum, corpus or both) [87,88]. Patients suffering from atrophic gastritis belong to the risk group of diseases resulting from the deficiency of vitamin B12. The tests of the GastroPanel are based on the enzyme immunoassay method. GastroPanel is a non-invasive alternative for gastroscopy and the related examination of biopsy samples as an initial method for examining patients suffering from stomach pains and discomfort.

GastroSoft Program

Biohit has developed an easy-to-use computer program, the GastroSoft for the determination of the results of the GastroPanel. On the basis of the laboratory results the program draws up the diagnosis of *H. pylori* -infection and

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72 Ranta P, Helske T, Kääriäinen I, Mäki T, Saarinen P, Kekäläinen L, Suovaniemi O, Härkönen M, Sipponen P. Serum pepsinogen I test reveals cases of vitamin B12 deficiency without anemia in patients with gastric corpus atrophy. *Clin. Chem. Lab. Med*. 2001; 39: (suppl.): 328.

73 Malfertheiner P, Megraud F, O´Morain C, Hungin AP, Jones R, Axon a, Graham DY, Tytgat G. Current concepts in the management of *Helicobacter pylori* infection – The Maastricht 2 Concensus Report. Aliment Pharmacol Ther 2002; 16: 167-180.

74 Varis K, Sipponen P, Laxén F, Samloff IM, Huttunen JK, Taylor PR, Heinonen OP, Albanes D, Sande N, Virtamo J, Härkönen M. Implications of serum pepsinogen I in early endoscopic diagnosis of gastric cancer and dyspepsia. *Scand. J. Gastroenterol*. 2000: 9: 951-956.

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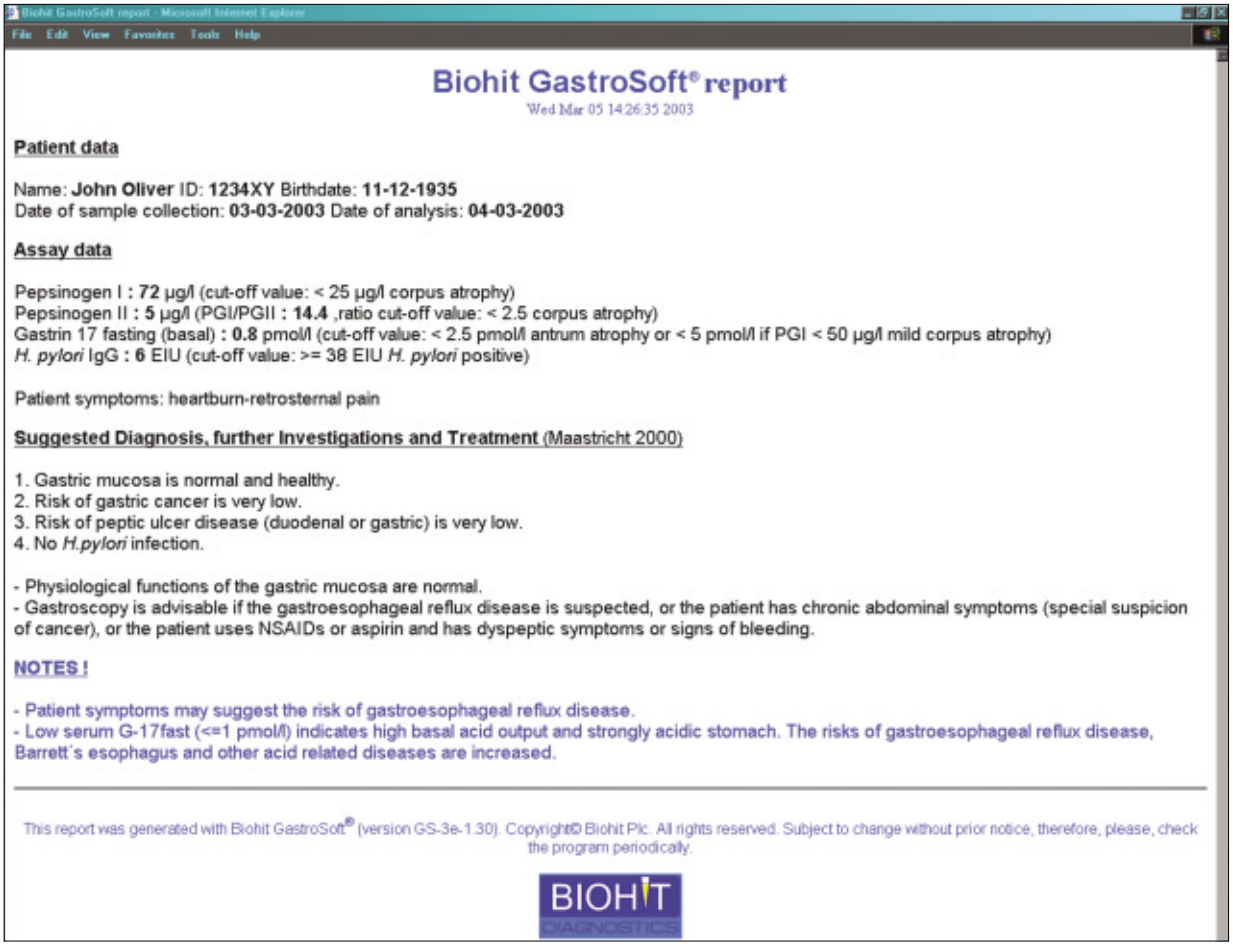

Biohit GastroSoft® report

Wed Mar 05 14:26:35 2003

Patient data

Name: **John Oliver** ID: **1234XY** Birthdate: **11-12-1935**
Date of sample collection: **03-03-2003** Date of analysis: **04-03-2003**

Assay data

Pepsinogen I : **72** µg/l (cut-off value: < 25 µg/l corpus atrophy)
Pepsinogen II : **5** µg/l (PGI/PGII : **14.4** ,ratio cut-off value: < 2.5 corpus atrophy)
Gastrin 17 fasting (basal) : **0.8** pmol/l (cut-off value: < 2.5 pmol/l antrum atrophy or < 5 pmol/l if PGI < 50 µg/l mild corpus atrophy)
H. pylori IgG : **6** EIU (cut-off value: >= 38 EIU *H. pylori* positive)

Patient symptoms: heartburn-retrosternal pain

Suggested Diagnosis, further Investigations and Treatment (Maastricht 2000)

1. Gastric mucosa is normal and healthy.
2. Risk of gastric cancer is very low.
3. Risk of peptic ulcer disease (duodenal or gastric) is very low.
4. No *H.pylori* infection.

- Physiological functions of the gastric mucosa are normal.
- Gastroscopy is advisable if the gastroesophageal reflux disease is suspected, or the patient has chronic abdominal symptoms (special suspicion of cancer), or the patient uses NSAIDs or aspirin and has dyspeptic symptoms or signs of bleeding.

NOTES !

- Patient symptoms may suggest the risk of gastroesophageal reflux disease.
- Low serum G-17fast (<=1 pmol/l) indicates high basal acid output and strongly acidic stomach. The risks of gastroesophageal reflux disease, Barrett´s esophagus and other acid related diseases are increased.

Biohit has developed an easy-to-use GastroSoft®-program for the interpretation of the results of the GastroPanel®. The program draws up a diagnosis of H. pylori -infection and possible atrophic gastritis and determines risk factors for gastic cancer and peptic ulcer. In addition, the program gives a recommendation on further investigations, which are based on the Maastricht 2 (2000) consensus on the treatment of H. pylori -infection.

possible atrophic gastritis as well as determines risk factors for gastric cancer and peptic ulcer. The program further gives recommendations based on the Maastricht 2000-consensus whether eradication therapy of *H. pylori* -infection is necessary[89].

The program further gives a recommandation whether gastroscopy, examination of biopsy samples and the measurement of the levels of vitamin B12 and homocysteine are necessary. Depending on the symptoms of the patient and the results of the GastroPanel GastroSoft also provides an indication of possible risks related with the reflux disease and Barrett's oesophagus.

Areas of Use of the GastroPanel

GastroPanel promotes the accurate diagnosis of diseases of the upper abdomen and mucosa of the stomach, and serves as an aid for assessing the risks and causes of related diseases. Testing by GastroPanel promotes the prevention of certain diseases, accurate diagnoses and targeted treatment (evidence-based medicine). GastroPanel is useful in:

1) Examination of the causes of dyspepsia, i.e., pain or discomfort in the upper abdomen (prevalence of dyspepsia: approx. 30% of global population):
- Functional dyspepsia (over half of the dyspeptic cases). In these cases, the results from GastroPanel and gastroscopy indicate that the mucosa of the stomach is normal (no atrophy, no inflammation, no *H. pylori* -infection)[90,91,92].

89 Malfertheiner P, Megraud F, O´Morain C, Hungin AP, Jones R, Axon a, Graham DY, Tytgat G. Current concepts in the management of *Helicobacter pylori* infection – The Maastricht 2 Concensus Report. *Aliment Pharmacol Ther* 2002; 16: 167-180.

90 Sipponen P, Ranta P, Helske T, Kääriäinen I, Mäki T, Linnala A, Suovaniemi O, Alanko A, Härkönen M. Serum levels of amidated gastrin-17 and pepsinogen I in atrophic gastritis. An observational case-control study. *Scand J Gastroenterol* 2002; 37: 785-791.

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- Organic gastric diseases underlying dyspepsia. In these cases, the GastroPanel helps to find the proper diagnosis non-endoscopically. Possible causes are gastric cancer, peptic ulcer or reflux disease. Prevalence of reflux disease: approx. 20% of global population [93,94,95,96,97,98,99].
- The GastroPanel enables the assessment of the risk of Barrett's oesophagus

2) Diagnosis of *H. pylori* -infection (prevalence on the average over 50% of population) and atrophic gastritis (prevalence: approx. half of those infected by H. pylori) and risk assessment of gastric cancer (prevalence approx. 0,1%) and peptic ulcer (prevalence approx. 10%).[100,101,102.]
3) Diagnosis and screening of corpus atrophy, which causes a deficiency of vitamin B12[103]. The deficiency may be related to many diseases, such as dementia and polyneuropathies[104,105,106,107]. The deficiency of vitamin B12 is one factor which increases the level of homocysteine in the tissue and cells[108], which is an independent risk factor for atherosclerosis and heart and brain strokes[109,110,111]. As many as 30% of those over 65 years may suffer from the deficiency of vitamin B12.

Benefits of the GastroPanel

Up until now atrophic gastritis has been diagnosed solely by gastroscopy and the related examination of biopsy samples. However, GastroPanel enables to diagnose atrophic gastritis from a blood sample. An early diagnosis of atrophic gastritis and the eradication of *H. pylori* form a basis for the treatment of atrophic gastritis and the prevention of related diseases[112,113,114,115].

It has been estimated that the use of the GastroPanel for screening and diagnostic purposes saves at least EUR hundreds of million per year in healt care costs if the preventive and treatment aspects of diseases related with atrophic gastritis are taken into consideration.

Vitamin B12 and Homocysteine

Atrophic gastritis of the corpus caused by *H. pylori* -infection or more rarely by an autoimmune disease results in the malabsorption of vitamin B12. Approximately 10% of patients with atrophic gastritis will suffer from severe atrophic gastritis of the corpus area of the stomach. Yhe risk of the said patients to suffer form diseases related with the deficiency of vitamin B12 is very high. The deficiency of vitamin B12 increases the level of homocysteine in the body. Homocysteine is an intermediate product of metabolism. The increased level of homocysteine in blood and tissues signal a serious disturbance of methionine metabolism in the cells. The deficiency of vitamin B12 is related with dementia, depression, damages of the peripheral nervous system, and increases the risk of these diseases.[116] An elevated level of homocysteine in the body increases the risk of atherosclerosis and heart and brain strokes [117,118,119].

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116 See http://www.b12.com.
117 See http://www.homocysteine.com.
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Humans and other mammals gain the necessary vitamin B12 from nutrition. The reason is that only micro-organisms are able to produce the said vitamin. The absorption of vitamin B12 from the small intestine requires a healthy, normally functioning mucosa of the corpus. Those patients suffering from atrophic gastritis need substitute treatment for vitamin B12.

An observation, which needs to be taken seriously, is that the damages of the brain tissue and peripheral nervous system are irreversible and develop already years before the pernicious type of anemia caused by the deficiency of vitamin B12 occurs.

Cellular Fibronectin

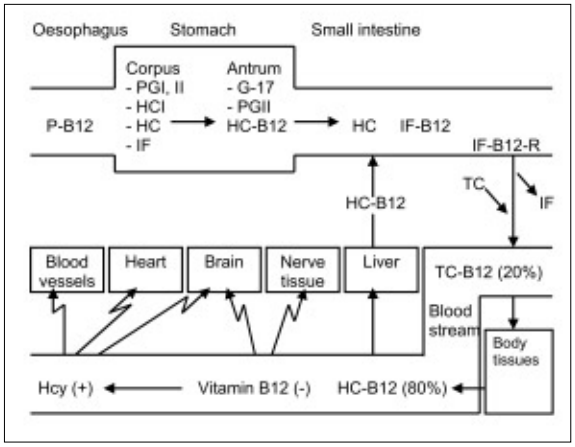
In the 1990s Biohit developed a blood test which serves as an indicator of the cancer of the gastrointestinal tract or its early stages. Biohit patented the method in the U.S. in 1995 and in Europe in 1996[120]. The invention enables possibly to trace gastric cancer or the cancer of the large intestine by measuring the level of cellular fibronectin (cFn) in blood[121].

Fibronectins are adhesive glycoproteins that have a role in a variety of cell contact processes, cell differentiation, and oncogenic transformation. When cancer is developing in the gastrointestinal tract the concentration of cellular fibronectin in blood increases. As to gastric cancer it has been demonstrated that as the cancer advances the level of cFn increases in blood.

Biohit's cFn-test aims to complement the GastroPanel-examination. If the GastroSoft-program, which interpretes the results of the test panel, indicates an increased risk of gastric cancer and the level of cFn is elevated, it may indicate that the patient suffers from gastric cancer or is at a high risk of it. If the interpretation provided by GastroSoft is normal but the level of cFn is elevated the treating doctor should look for cancer elsewhere in the gastrointestinal tract. If the result of the GastroPanel and the level of cFn are normal it is unlikely that the patient suffers from gastric cancer. Biohit filed a patent application of the combined use of the GastroPanel, GastroSoft and cFn in 2001[122]. Biohit continues research on the topic with specialists.

Biohit's cFn -test kit, which is protected by patents and patent applications, is based on a monoclonal antibody developed by Biohit and a hybridoma producing the antibody. The markets for the cFn-test as a tumor marker can be considered large and even larger when combined with the GastroPanel and GastroSoft. The markets for a useful tumor marker may very well be over USD 100 million. For example, the size of the global markets for a colon cancer marker are over USD 100 million[123].

120 U.S.-patent 5,420,012 and EP-patent 0399271: *Method for the Detection of Reactive Conditions*.
121 Ylätupa S. (1996). *The Development of a Method for Quantification of Cellular Fibronectin EDAcFn and Its Clinical Applications*, Ph.D. Thesis, University of Helsinki.
122 Suovaniemi O., Härkönen M., Sipponen P. (2001). Finnish patent application 20011908: *Method for Detecting Gastric Cancer*.
123 McGrath & Associates, Inc. (2002).



Metabolism of Vitamin B12 and Consequences of Its Distortions

The absorption of vitamin B12 from nutrition is distorted when the mucosa of the corpus area of the stomach is atrophic. This results from the fact that the atrophic mucosa of the corpus does not secrete the intrinsic factor (IF) and haptocorrin (HC). In nearly 90% of the cases the atrophy of the mucosa is caused by Helicobacter pylori -infection and in less than 10% of the cases by autoimmune disease. If the atrophy of the mucosa becomes chronic the risk of gastric cancer and peptic ulcer increases. This risk can be determined by measuring from a blood sample the concentration of Pepsinogen I secreted by the mucosa of the corpus and the concentration of Gastrin-17 secreted by the mucosa of the antrum.

Gastric acid and proteolytic enzymes in the stomach release vitamin B12 from the proteins of food. The haptocorrin (HC) of the gastric juice binds the vitamin B12. The protease enzyme secreted by the pancreas breaks down the HC-B12 complex produced, and the vitamin B12 released is bound by the intrinsic factor. The IF-B12 complex is absorbed by the epithelial cells of the small intestine by the receptors of the cell membranes. The vitamin B12, released from the IF-B12 complex, binds with transcobalamin (TC). This results in the TC-B12 complex (holo-transcobalamin). The TC-B12 complex is released into the blood stream and is subsequently recognized and taken up by specific receptors present in all cell types. This complex, which is physiologically active, includes approx. 20% of the total amount of vitamin B12 present in blood. Its concentration decreases rapidly if the absorption of vitamin B12 is distorted. The half-life of the TC-B12 complex in the body is only 0.75 day and that of the HC-B12 complex approx. 9 days. The HC-B12 complex is stored in the liver and kidneys.[1]

Vitamin B12 is solely produced by micro-organisms. Thus, vitamin B12 must be received from nutrition, and if the corpus area of the stomach is atrophic, by injections of vitamin B12. The lack of vitamin B12 in the body is an increasingly growing health problem worldwide and it concerns especially the elderly.

The lack of vitamin B12 leads in less than a year to distortions of the activity of the neural tissues, depression and dementia. These illnesses begin to develop already before the development of noticeable pernicious type of anemia, and they can become irreversible if the diagnosis and treatment are delayed.[2] *Moreover, in connection with the lack of vitamin B12, the concentration of homocysteine (Hcy) in tissues and blood increases, which increases the risk of atherosclerosis and thromboembolic diseases*[3].

1 Holo-transcobalamin: The Physiologically Active Vitamin B12 Metabolite. *Clinical Laboratory International*, Vol. 24, No.8 (2000): 8.
2 http://www.b12.com
3 http://www.homocysteine.com

Biohit's GastroPanel® -test and the GastroSoft® -program interpreting the results can replace gastroscopy (in the picture) as the initial method when examining patients suffering from stomach pains and discomfort, and atrophic gastritis. Gastrosocopy is relatively expensive, disliked by patients and cannot be performed on all occasions due to limited health care resources.

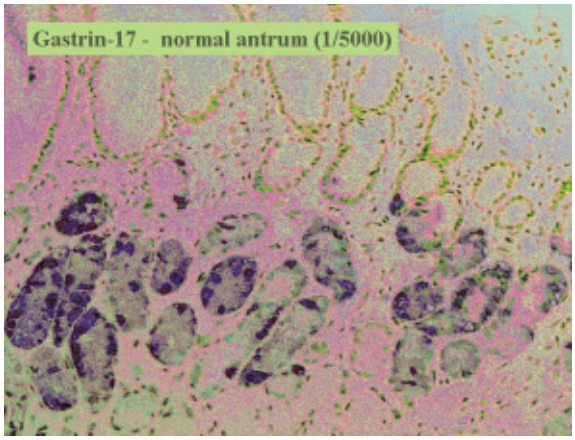
Monoclonal Antibodies

The different test kits of the GastroPanel are based on immunodiagnostics and on the use of Biohit's monoclonal antibodies (MAbs)[124] and microplates[125], which can be used in vertical measurement applications[126].

Biohit manufactures Pepsinogen I, Pepsinogen II and Gastrin-17 -antibodies which are related with the GastroPanel. These have been proven to be highly specific also for immunohistochemical analyses. This expands the area of use of the said antibodies also to, e.g., pathological laboratories.

Biohit also manufactures and markets 27 other MAbs, which are suited for immunohistochemistry and used in basic research as well as for classifying different types of cancer from tissue samples[127,128,129,130]. These MAbs have been developed specifically for human extracellular matrix components, human integrins, human cytoskeletal polypeptides, human neurotransmitter substances, human spectrins and human endothelial cell surface markers.

124 Milstein and Köhler invented monoclonal antibodies and received the Nobel Prize for this invention in 1984.
125 Vauramo, K. (1994). U.S. -patent 5,308,584: *Cuvette Matrix Tray*.
126 Suovaniemi O. (1994). *Automated Instrumentation for Clinical and Research Laboratories – Innovations and Development of Vertical Light Beam Photometers and Electronic Pipettors*, Ph.D. Thesis, University of Helsinki.
127 Linnala A. (1998). *Tenascin, Fibronectin, Laminin and Their Integrin Receptors in Human Cell Cultures*, Ph.D. Thesis, University of Helsinki.
128 Jahkola T., Toivonen T., Nordling S., von Smitten K., Blomqvist C., Virtanen I. (1996). Expression of Tenascin in Invasion Border of Early Breast Cancer Correlates with Higher Risk of Distant Metastasis. *Int. J Cancer (Pred. Oncol.)* 69: 445-447.
129 Jahkola T., Toivonen T., Nordling S., von Smitten K., Virtanen I. (1998). Expression of Tenascin-C in Intraductal Carcinoma of Human Breast: Relationship to Invasion. *European Journal of Cancer*, Vol. 34, No. 11: 1687-1692.
130 Ylätupa S. (1996). *The Development of a Method for Quantification of Cellular Fibronectin EDAcFn and Its Clinical Applications*, Ph.D. Thesis, University of Helsinki.



Immunohistochemical staining of a normal antrum sample with Biohit's monoclonal Gastrin-17 antibody. The mucosa is normal. The cells secreting Gastrin-17 peptide located in the mucosal glands are clearly positively stained (the dark color). This means that the Gastrin-17 peptide is present in the cells. The peptide is not present in the other cells. An equivalent staining of the other cells is negative. This indicates that the Gastrin-17 peptide is formed solely in the antrum area of the stomach. The range of monoclonal antibodies offered by Biohit includes e.g. the following related with the GastroPanel®: Pepsinogen I, Pepsinogen II and Gastrin-17.

Diagnosis of Systemic Lupus Erythematosus

Biohit has developed a novel method for diagnosing systemic lupus erythematosus (SLE). SLE is a prototype of autoimmune diseases, which with its various symptoms resembles rheumatic diseases. The development and technology of the test are based on an international patent acquired exclusively by Biohit[131].

The presence of DNA antibodies in the blood of a patient is typical of SLE. Unlike in the conventional DNA antibody tests, which use purified calf thymus DNA as capture antigens for autoantibodies, the newly developed Biohit anti-telomere antibody assay is based on the use of the double-stranded telomeric DNA as the capture antigen for the binding of SLE antibodies.

Biohit's telomere antibody test measures in a sensitive and specific enzyme immunoassay procedure (EIA) telomere antibodies in the serum of an SLE patient. On the basis of the titers of these antibodies it is possible to distinguish SLE, e.g., from rheumatoid arthritis.[132,133] The observation that telomerase activity is detected in 85% of all cancers has made the telomerase enzyme a new cancer marker and added special interest on telomere research itself[134]. The renowned researcher on rheumatic diseases and SLE, professor D.J. Wallace, together with his research team has published positive results on the SLE-test[135].

The test kit patented by Biohit for determining SLE from a blood sample has been evaluated in Finland. Moreover, there exists evidence that the test kit enables to assess the clinical activity of the SLE[136]. As SLE resembles rheumatic diseases the SLE test can be used among other tests in determining the said diseases. Approximately 2% of the global population suffer from rheumatic diseases and 0.1–0.4 % from SLE.

Phytoestrogens and the Prevention of Cancer

Biohit's policy is to continue to develop unique diagnostic tests in the fields of cancer detection and prevention. For this purpose Biohit aims to develop in the long range, in collaboration with Professor Herman Adlercreutz, tests for urine and serum phytoestrogens. These tests, which are performed using enzyme immunoassay techniques and monoclonal antibodies, are based on over 20 years of basic research. Biohit currently has monoclonal antibodies for these tests.

Low concentrations of phytoestrogens may signal a risk for certain forms of cancer, e.g., large bowel, breast and prostate[137,138,139,140], as well as for ischemic heart disease[141]. In such cases the prevention of the diseases involves changes in diet to include more whole grain bread, berries, certain vegetables and soybean products[142,143]. People are more and more interested in nutrition and health. For this reason research work on phytoestrogens is undertaken very intensively worldwide.

Diagnosis of Lactose Intolerance

Over 17% of the adult population in Finland suffer from lactose intolerance. In Asian and African countries there may be as many as 90% of the population suffering from the disease. Lactose intolerance is caused by the deficiency or a very low level of the lactase enzyme, which breaks down milk sugar (lactose), in the surface epithel of the mucosa of the small intestine. The deficiency causes disorders of the stomach, e.g., diarrhea and swelling when consuming milk products.

Patients seeking medical treatment due to undefined stomach disorders are often ordered to a gastroscopy. However, lactose intolerance cannot be diagnosed on the basis of gastroscopy or the microscopical evaluation of biopsy samples. This is due to the fact that the lack of the enzyme does not show on the biopsies and, as a result, the structure of the mucosa seems normal. The lack of the lactase enzyme must be determined biochemically from a biopsy sample in the laboratory or on the basis of a lactose load or breath test. All these tests are time-consuming, strenuous for the patient and expensive.

Biohit's quick test for determining lactose intolerance (hypolactasia of the small intestine) is based on the fact that, in connection with gastroscopy, a biopsy taken from the mucosa of the upper part of the small intestine is examined immediately. After 15 minutes the change in the color of the test liquid informs whether the lactase enzyme is present in the biopsy sample or not. Normally the color changes as the lactase enzyme of the sample breaks the lactose, i.e., the milk sugar, in the reagent. If the color remains unchanged or changes slightly, the patient suffers from lactose intolerance (hypolactasia of the small intestine). Biohit's unique POC-test[144,145] enables, when performing gastroscopy, to find quickly those patients who suffer from lactose intolerance. For this reason the quick test should be used in connection with gastroscopy for determining possible lactose intolerance.

131 Salonen E-M. (1997). U.S. patent 5,700,641: *Diagnostic Method, Test Kit, Drug and Therapeutic Treatment for Autoimmune Disease.*

132 Salonen E-M., Ruuskanen L., Friman C. (1996). Anti-Telomere Antibodies in SLE. *Arthr. & Reum.* 39: 40.

133 Salonen E-M., Wallace D.J., Metzger A., Morris R., Avaniss-Aghajani E. (1998). Anti-Telomere Antibodies Are Highly Specific for Systemic Lupus Erythematosus (SLE). *Arth. & Reum*. 41: 247.

134 Shay J.W. (1997). Telomerase in Human Development and Cancer. *Journal of Cellular Physiology* 173: 266-270.

135 Wallace D.J., Salonen E-M., Avaniss-Aghajani E, Morris R., Metzger A.L., Pashinian N. (2000). Anti-Telomere Antibodies in Systemic Lupus Erythematosus: A New ELISA Test for Anti-DNA with Potential Pathogenetic Implications. *Nature* 9: 328-332.

136 Salonen E.M., Miettinen A, Valle T.K., Koskenmies S., Kere J., Julkunen H.: Anti-telomere Antibodies in Systemic Lupus Erythematosus (SLE): A Comparison with Five Antinuclear Antibody Assays in 430 Patients with SLE and Other Rheumatic Diseases. Submitted for publication.

137 Adlercreutz H., Fotsis T., Heikkinen R., Dwyer J.T., Woods M., Goldin B.R., Gorbach S.L. (1982). Excretion of the Lignans Enterolactone and Enterodiol and of Equal in Omnivorous and Vegetarian Women and in Women with Breast Cancer. *Lancet* 2: 1295-1299.

138 Adlercreutz H. (1990). Western Diet and Western Diseases: Some Hormonal and Biochemical Mechanisms and Associations. *Scand. J. Clin. Lab. Invest.* 50, Suppl. 201: 3-23.

139 Adlercreutz H., Mazur W. (1997). Phyto-Oestrogens and Western Diseases. *Ann. Med*. 29: 95-120.

140 Adlercreutz H., Mazur W., Kinzel J., van Reijsen M., Bertels P., Elomaa V.-V., Watanabe S., Wähälä K., Mäkelä T., Hase T., Landström M., Bergh A., Damber J.-E., Åman P., Zhang J.-X., Hallmans G. (1997). Phytoestrogens and Prostate Disease. In *Fundamentals of Cancer Prevention* (Ed. Conney A.H., Ito N., Sugimura T., Terada M., Wakabayashi K., Weinstein I.B.). Princess Takamatsu Cancer Research Fund, Tokyo, pp. 22-24.

141 Adlercreutz H., Mazur W. (1997). Phyto-Oestrogens and Western Diseases. *Ann. Med*. 29: 95-120.

142 Adlercreutz H., Mazur W. (1997). Phyto-Oestrogens and Western Diseases. *Ann. Med*. 29: 95-120.

143 Griffiths K., Adlercreutz H., Boyle P., Denis L., Nicholson R.I., Morton M.S. (1996). Nutrition and Cancer. *ISIS Medical Media, Oxford*, pp. 1-173.

144 Point-of-Care (POC) –test is performed quickly close to the patient.

145 Sipponen P., Suovaniemi O., Tamminen J. (2000) Finnish patent 106212: *Method for the Determination of Disaccharidases and Kit Therefor.*

Biohit's production premises for diagnostics and the service laboratory are located in Helsinki, Finland.

Biohit's Service Laboratory

In August 2001 Biohit commenced to offer paid laboratory services, which received a permission from the State Provincial Office of Southern Finland, Department for Social and Health Affairs on May 8, 2001. The purpose of the service laboratory is to collect, first in Finland, patient samples, e.g., from health care centers, occupational health service centers, other medical centers as well as regional and central hospitals. Samples will be collected also abroad from general practitioners and other service laboratories. Biohit's service laboratory will also engage in the research and development of diagnostic tests and the analysis of different types of patient data in co-operation with scientific communities in Finland and abroad.

The purpose of Biohit's service laboratory is to promote the diagnostic tests and analyzing systems and, thus, to encourage the users of the laboratory service to begin making the necessary analyses themselves with the help of the analyzing system purchased from Biohit. In this way the customer will be able to receive the test results more easily, rapidly and at a lower cost.

The performance of the analyses as close as possible to the patient and doctor promotes decentralized laboratory diagnostics, which is usually the most optimal, and for this reason the most recommendable way. Decentralized laboratory diagnostics which promotes evidence-based medicine should be striven for not only for the benefit of the patient and the doctor but also since it decreases the costs of health care.

Biohit's service laboratory performs the following analyses:

- GastroPanel
  - o Helicobacter pylori IgG (S-HepyAbG),Pepsinogen I (S-Pepsin1), Gastrin-17 (S-Gastr17-S)
  - o S-HepyAbG, S-Pepsin1, S-Pepsin2, S-Gastr17-S
- Cellular fibronectin (cFn -tumor marker)
- Vitamin B12, fS-B12-vit, KL 1137
- Folat, fS-Folaat, KL 1416
- Folat from erythrocytes, fE-Folaat, KL1414
- Homocysteine, S-Hcyst, KL 1868
- Telomere-DNA IgG-antibodies, S-dsDNAAb
- Celiac panel: Gliadin IgA and IgG, tissue transglutaminase IgA, S-AGAAbA KL 3399, S-AGAAbG KL 3400, S-tTGAbA KL 1885
- Determination of lactase and saccharase from biopsies of the small intestine, Ts-Laktaas, KL 2182, Ts-Sakraas, KL 2601
- Microscopic examination of the endoscopic biopsy samples of the gastrointestinal tract, Ts-PADGast, KL 4043

The results of the GastroPanel are analyzed with Biohit's GastroSoft-program (www.biohit.com). The program functions and is allowed to be used only in connection with Biohit's test panel. The program is based on analyses made with Biohit's tests. Comments on the use and further development of the program can be sent via the Contact us -form found under GastroSoft at www.biohit.com.

Instructions for taking samples and delivering the samples to the service laboratory can be ordered from Biohit Oyj, sales@biohit.com, fax: +358-9-773 86 200 or tel: +358-9-773 861.

Diagnostics in 2002

The evaluations of the GastroPanel for determining *Helicobacter pylori* -infection and atrophic gastritis and for screening the risk of gastric cancer and peptic ulcer from blood samples continued according to plans.

By the end of 2002 seventeen clinical evaluations related with the GastroPanel had been completed. Thirteen had been made in Europe, three in Asia and one in North America. The number of patients studied in the evaluations totalled 3,208. The results of the said evaluations have been published internationally in numerous scientific articles. During the reporting period altogether twelve evaluations were in progress. Eight evaluations were in progress in Europe, two in Africa, one in Asia and one in the Near East. The number of patients to be studied in these evaluations totals 4,280. By the end of 2002 preliminary agreements had been made or negotiations begun to commence eleven new evaluations in Europe, three in North and South America and three in Asia.

In 2002 Biohit received the first customer orders for the GastroPanel test. Biohit concluded distribution agreements for the GastroPanel in Italy and numerous South American and Near Eastern countries, in which the prevalence of *Helicobacter pylori* -infection is approx. 90%. Especially on these markets and in the developing countries the GastroPanel serves as the only easy and economically sound alternative for diagnosing the *H. pylori* -infection, atrophic gastritis and for assessing the risk factors for related diseases, e.g., gastric cancer and peptic ulcer. During the reporting period the GastroPanel was used at the Jorvi Hospital (HUCH: The Helsinki University Central Hospital) in Finland and in service laboratories in Finland, Germany and Italy.

In 2002 Biohit was awarded in the area of diagnostics the following patents:

- European patent 0804737 for the Method for Screening the Risk of Gastric Cancer (13.2.2002).
- European patent 0812421 for the Method for Diagnosing Systemic Lupus Erythematosus (19.6.2002).
- U.S. patent 6,416,961 for the Method for the Diagnosis of Early Gastric Cancer (9.7.2002)

In 2002 Biohit published together with its collaborating parties the following articles related with diagnostics:

- Altavilla N, Moussa AM, Seghini P, Cerati E, Cavallaro LG, Cavestro GM, Dal Bo N, Pilotto A, Cannizzarro R, Maino M, Leandro G, franze A, DiMario F. Sucrose Test and Serum Pepsinogens as Markers of Inflammation and Damage in Helicobacter pylori -Related Gastritis. *Gut* 2002: Suppl II Vol 51; A30.
- Cavallaro LG, Moussa AM, Seghini P, Aragona G, Iori V, Cavestro GM, Dal Bo N, Pilotto A, DiMario F. Topoghraphy of Gastric Damage in H.pylori Infection: Evaluation by Serum Pepsinogen Levels. *Gut* 2002. Suppl II Vol 51; A30.
- Laheij RJF, Oijen MGH, Paloheimo LI, Jansen JBMJ. Vitamin B12 Deficiency and Gastric Functioning in Patients with Cardiovascular Disease. *Gut* 2002: Suppl III Vol 51;A152.
- DiMario F, Seghini P, Moussa AM, Iori V, Aragona G, Cavestro GM, Dal Bo N, Maino M, Mantovani N, Ingegnoli A, Pilotto A, Franze A. Influence of Different Epidemiological, Pharmacological and Biological Factors of Serum Pepsinogen Levels. *Gut* 2002: Suppl II Vol 51; A29.
- Goetze JP, Rehfeldt JF. Impact of Assay Epitope Specificity in Gastrinoma Diagnosis. *Clin Chem* 2003: 49: No 2.
- Ingegnoli A, Moussa AM, Altavilla N, Seghini P, Cerati E, Mantovani N, Aragona G, Caruana P, Cavestro GM, Leandro G, Dal Bo N, Dimario F. Serum Pepsinogens and Sucrose Test in Helicobacter pylori Related Gastritis. *Gut* 2002. Suppl II Vol 51. A29.
- Moussa AM, Iori V, Aragona G, Seghini P, Cerati E, Campi L, Cavestro GM, Comparato G, Leandro G, Battaglia G, Dal Bo N, Franze A, DiMario F. Relationship between Direst and Indirect Methods for Diagnosis of H.pylori Infection. *Gut* 2002. Suppl II Vol 5; A110.
- Nicolini G, Zagari R, Pozzato P, Lunadei V, De Luca L, Antonini F, Ricciardiello L, Fossi S, Berretti D, Martuzzi C, Fuccio L, Maltoni S, Sipponen P, Bazzoli F, Roda E. Diagnosis of Atrophic Gastritis Based upon a Combination of Three Non-invasive Tests: Preliminary Results of the Ioiano-Monghidoro Project. *J Gastroenterol Hepatol* 2002; 17 (Suppl); A264.
- Plebani M. *Un Approccio Non Invasivo: Alla Diagnosi Delle Malattie Gastrointestinali*. EDRA Medical Publishing and New Media.
- Sipponen P. et al. Value of the Test Panel Composing of Serum Assays of Pepsinogen I, Gastrin-17 and H. pylori Antibodies in Non-Endoscopic Diagnosis of Gastritis and Atrophic Gastritis. A Preliminary Prospective Study. Presentation at the World Congress of Gastroenterology, Bangkok, Thailand Feb 24 - March 1, 2002.
- Sipponen P. Gastric Cancer: Pathogenesis, Risks, and Prevention. *J Gastroenterol* 2002;37 (Suppl XIII):39-44.
- Sipponen P, Härkönen M, Alanko A, Suovaniemi O. Diagnosis of Atrophic Gastritis from a Serum Sample. *Minerva Gastroenterol Dietol* 2003, in press.
- Sipponen P, Härkönen M, Alanko A, Suovaniemi O. Diagnosis of Atrophic Gastritis from a Serum Sample. *Clin Lab* 2002; 48:505-515.
- Sipponen P et al. Helicobacter Pylori Infection and Related Risks and Diseases - Towards Optimal Diagnostics and Evidence Based Medicine.. 5th Nordic-Baltic Congress on Infectious Diseases, 22-25 May 2002, Saint-Petersburg, Russia.
- Sipponen P, Ranta P, Helske T, Kääriäinen I, Mäki T, Linnala A, Suovaniemi O, Alanko A. Serum levels of Amidated Gastrin-17 and Pepsinogen I in Atrophic Gastritis: An Observational Case-Control Study. *Scand J Gastroenterol* 2002;37:785-791.
- Suovaniemi O. Test Panel for the Determination of Helicobacter pylori -Infection and Atrophic Gastritis. UEMS, Compendium 2002: 28-31.
- Suovaniemi O. Determination of H. pylori -related diseases. *Innovations in Pharmaceutical Technology*, Vol 02, Issue 10, 2002.
- Suovaniemi O, Härkönen, M, Paloheimo LI, Sipponen P. Diagnosis of Atrophic Gastritis from a Serum Sample. *Jordan Medical Journal* 2002: 2 (Vol 36); 117-121
- Väänänen H, Vauhkonen M, Helske T, Kääriäinen I, Rasmussen M, Tunturi-Hihnala H, Koskenpato J, Sotka M, Turunen M, Sandström R, Ristikankare M, Jussila A, Sipponen P. 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, in press.
- Zagari R, Nicolini G, Casaniva S, Fiocca R, Pozzato P, Lunedei V, Di Marco M, De Luca L, Ricciardello L, Martuzzi C, Fuccio L, Maltoni S, Grigioni W, Panuccio D, Sipponen P, Roda E, Bazzoli F. Diagnosis of Atrophic Gastritis in the General Population Based upon a Combination of Three Non-Invasive Tests. *Gut* 2002: Suppl II Vol 51;A39.

INSTRUMENTS

Biohit's microplate readers and washers are delivered preprogrammed for Biohit's diagnostic tests. The picture displays the BP 800 microplate washer and the Gastrin-17-test kit of the GastroPanel®.

The business idea of Biohit is to offer its customer base complete analyzing systems, which consist of liquid handling products, diagnostic tests, instruments used for the analysis of the results, software as well as maintenance and training services. In the business area of instruments Biohit supplies products for the following three market segments: instruments used in research, those used in clinical applications, and instruments used in industrial applications.

Biohit's GastroPanel and other test kits as well as the analyzing systems are very well suited for decentralized laboratory diagnostics performed close to the patient by the doctor. Decentralized laboratory diagnostics is a prerequisite for the close interlinkage between the examination and treatment of the patient (evidence-based medicine).

Research and Development of Instruments and Market Potential

As early as the 1970s the current management of Biohit and key personnel developed and commercialized two inventions made by Dr. Osmo Suovaniemi at the end of 1960s: the single- and multichannel adjustable mechanical liquid handling devices (Finnpipettes[146]), and vertical photometry and its instrument applications (e.g. Multiskan[147]).

Biohit has researched and developed further vertical measurement principles since the end of the 1980s[148,149]. It has been estimated that the current annual sales volume of microplate readers, multichannel pipettors, microstrips as well as other products developed on the basis of the vertical measurement principle together with their accessories already exceeds USD 1.0 billion annually[150,151].

The instruments based on vertical photometry have made possible the extensive research and fast development of the enzyme immunoassay (EIA) -technology and related applications such as analyzing and screening of cancer and infectious diseases. During the past ten years, the EIA-technology has been followed by the rapid development of molecular biology techniques, such as the Polymerase Chain Reaction (PCR) –technique, which is used for the amplification of DNA. Vertical measurement applications have been widely used in recent years in connection with the PCR-technique and similar applications. Especially

146 Finnpipette is a registered trademark of Labsystems Oy.
147 Multiskan is a registered trademark of Labsystems Oy.

148 Suovaniemi O. (1994). Automated Instrumen-tation for Clinical and Research Laboratories – Innovations and Development of Vertical Light Beam Photometers and Electronic Pipettors, Ph.D. Thesis, University of Helsinki.
149 Tiusanen T. (1992). Inner-Filter Correction with a Fluorometer-Based Multifunctional Instrument, Ph.D. Thesis, University of Helsinki.
150 McGrath & Associates, Inc. (1999).
151 Suovaniemi O. (1994). Automated Instrumentation for Clinical and Research Laboratories – Innovations and Development of Vertical Light Beam Photometers and Electronic Pipettors, Ph.D. Thesis, University of Helsinki, p.46.

fast are growing the investments in equipment by companies specializing in automated molecular biology methods and the development of biologically active molecules. It has been estimated that these markets grow at an annual rate of 25–30%.

In order to serve its customer base also with complete analyzing systems, Biohit began the purchases of private label liquid handling and microplate instruments from Bio-Tek Instruments, Inc. in 2000. In fact, the vertical measurement principle and its applications invented by Osmo Suovaniemi at the end of the 1960s have served as examples for the development of Bio-Tek's instruments.

Product Range of Instruments and Software

Biohit's range of instruments comprises microplate readers and washers, and related software developed by Biohit for its diagnostic tests. The instruments with integrated keyboard, LCD-display, interface and extensive menu-driven software can serve as stand-alone instruments or as part of a larger laboratory information management system (LIMS) when connected to a host device, such as a PC. Although Biohit's readers and washers are intended for a wide range of assays they are delivered with pre-programmed protocols for Biohit's ELISA assays, e.g., for Pepsinogen-I, Gastrin-17 and Helicobacter pylori. This ensures ease-of-use, optimal operation and verified test reporting and results.

BP800 Microplate Reader

The BP800 microplate reader has all the features of a modern microplate photometer with dual wavelength measurement, UV-optics and versatile microplate format support. The instrument is delivered with preprogrammed assay protocols for Biohit's diagnostic tests. With the help of the intuitive user interface new test protocols can be made fast and easily. Extensive on-board data analysis includes several curve-fitting options, transformations and control validation. In addition to the printer interface, the instrument has a serial interface to be controlled with a PC for the further processing and distribution of data. The reader is supported by Biohit e-Lisa XL measurement and data distribution software.

BP808 Microplate Reader

The BP808 microplate reader is a top performance 8-channel microplate photometer with four-zone incubation and plate shaking functionality. Due to the fast reading capability the unit is suitable not only for end-point but also for kinetic applications. With the help of the intuitive user interface new test protocols can be made fast and easily. Extensive on-board data analysis includes several curve-fitting options, transformations and control validation. Automatic report printing is carried out with the help of an external printer. The instrument has a serial interface to be controlled with a PC for the further processing and distribution of data, e.g., with Biohit's e-Lisa XL software. The product is delivered with preprogrammed assay protocols for Biohit's diagnostic tests.

Biohit's microplate washer, which may, as a result of featuring a precise micro-stepping syringe pump, be used also as a rapid microplate dispenser.

e-Lisa XL

The e-Lisa XL is an easy-to-use software utility for supporting the BP800/808 Biohit readers with end point type assays such as Biohit Pepsinogen I, Gastrin-17 and Helicobacter pylori ELISA tests. It has been designed for use together with Microsoft Excel™, providing a huge amount of possibilities for data processing. The e-Lisa XL is delivered with ready made Excel templates for several Biohit assays. These serve as immediate use of Biohit test results or as examples to design your own templates for your assays.

BW50 Microplate Washer

The BW50 microplate washer is a self-contained and programmable microplate washer suitable for different ELISA, FIA, RIA and DNA probe and cellular assays. It allows for full control of precise fluidic delivery from the gentle dripping of a simple squeeze bottle to the full force of pressure delivery systems. The washer is delivered preprogrammed for Biohit diagnostics.

The know-how, innovations and experience of Biohit's key personnel have formed a solid basis for the development of the instrument business. The development of instruments, related software and liquid handling products is guided by the diagnostic tests.

The liquid handling instruments used for the automated handling of samples and reagents as well as the instruments used for the reading and interpretation of the analyses intended for research, PCR-, HTS-applications and Point of Care (POC) -diagnostics offer Biohit an additional, strong base for growth. In this area the markets of the said instruments and larger systems composed of them is estimated to demonstrate a growth of 25–30% annually. Moreover, the markets of different types of plastic disposables, which are used in the above applications, are estimated to grow over 30% each year.

BOARD OF DIRECTORS´ REPORT

Biohit manufactures liquid handling products and accessories and diagnostic test systems for use in research, health care and industrial laboratories. Biohit's product range encompasses also instruments and related software, which together with the liquid handling products and diagnostic tests, enable to offer complete analyzing systems for customers.

In the business area of liquid handling Biohit's main products are electronic and mechanical liquid handling devices and disposable tips. Biohit's diagnostic product range encompasses the following tests: Test for diagnosing atrophic gastritis and *Helicobacter pylori* -infection as well as for screening the risk of gastric cancer and peptic ulcer from blood samples; tests for diagnosing lactose intolerance and systemic lupus erythematosus (SLE).

Net Sales

The net sales of the Biohit Group decreased by 0.7% and totalled MEUR 25.4 (MEUR 25.5). The net sales decreased especially in the market areas of the U.S., Russia and Germany. However, the decrease in net sales was compensated by the increase in sales on the market areas of France, the U.K. and Asia. The group net sales was primarily generated by the sales of liquid handling products. However, towards the end of the year also the sales of diagnostics began to demonstrate signs of the anticipated growth. The sales of diagnostics continued to be hindered by numerous international evaluations of which most were completed in 2002.

In 2002 exports accounted for 97% of group net sales. The most important market area was Europe which generated 59% of the net sales. Biohit considers North America and Asia as the future growth areas. The sales of liquid handling products increased especially in China in 2002.

Result

The operating loss for the financial year totalled MEUR 1.2 (MEUR 0.2 profit in 2000). The operating loss before goodwill amortization totalled MEUR 0.6 (MEUR 1.2 profit).

The board of Biohit decided on 27.8.2002 to prolong the goodwill amortization period related to Locus genex Oy from seven to 20 years. The decision of this change is based on the information on the market and, e.g., on the feedback of GastroPanel evaluations, according to which the company estimates that the accumulated income effect is longer than it was estimated at first, and at least 20 years. According to the board decision there was no amortizations from the Locus genex goodwill during the last half of the year 2002, because the amortization according to plan (MEUR 0.4) made for the first half year was based on the original 7 years´ amortization period.

The Group result was weakened by the development of net sales, which did not reach the anticipated level, and by the increase of fixed costs. The increase in fixed costs resulted primarily from investments made in international sales and marketing which, on their part, increased personnel costs. The dismissals and personnel reductions made at the parent company during the last quarter of 2002 did not yet have an improving effect on the overall cost structure of the Group.

Net financial expenses totalled MEUR 0.3 (MEUR 0.2).

The income taxes (MEUR 0.3) have been accounted for on the basis of the result for the financial year. However, deferred tax assets relating to the tax loss carry forwards have not been accounted for. MEUR 0.2 of the income taxes charged to the income statement result from the decrease in the deferred tax assets relating to the dissolution loss on Locus genex Oy.

Earnings per share was MEUR -0.14 (MEUR -0.02).

The loss for the reporting period totalled MEUR 1.8 (MEUR 0.2).

Liquidity

The net cash flow provided by operating activities was MEUR 0.5 negative (MEUR 1.9 positive).

The cash flow from operating activities was weakened considerably due to the payment of 2001 taxes (MEUR 1.1) related to the voluntary dissolution of Locus genex Oy. The Group's liquid assets totalled MEUR 1.4 (MEUR 2.5) at the end of the fiscal year.

The equity ratio was on December 31, 2002 66.9% (65.7%).

Investments

The gross investments totalled MEUR 1.6 (MEUR 2.1). The major part of the investments consisted of machinery, equipment acquired to the Kajaani plant for the automation of liquid handling products, as well as of injection moulding tools used in the production of liquid handling devices.

The Group research and development expenditure totalled MEUR 1.8 (MEUR 2.1), i.e., 7.1% (8.3%) of net sales.

Administration and Personnel

During the financial year the following persons have been the members of the Board of Directors of Biohit Oyj: Professor Reijo Luostarinen as the Chairman and docent Arto Alanko, Professor Hannu Seristö, Professor Osmo Suovaniemi and Professor Mårten Wikström as members.

PricewaterhouseCoopers Oy have acted as the auditors and Hannele Selesvuo as the responsible Authorized Public Accountant.

The average number of personnel in the Biohit group totalled 303 (289) of which 181 (176) worked at the parent company and 122 (113) at the subsidiary companies.

Prospects for 2002

Net sales is expected to develop favorably in 2003. However, the uncertainties relating with the general economic development of the major market areas renders the drawing up of forecasts difficult. The positive expectations relating with liquid handling products result from the favorable feedback received from the markets for the new mechanical pipettor range (mLINE), which was launched at the end of 2002. Moreover, during 2003 Biohit will launch new liquid handling products. Although it is estimated that the major part of net sales will be generated by liquid handling devices in 2003 Biohit anticipates that the sales of diagnostics will demonstrate an increase in 2003.

In order to improve the profitability Biohit took into use in 2002 an adaptation program of its activities. In accordance with the program the company aims, e.g., to intensify marketing efforts and cut costs. Biohit will continue the adaptation program also during 2003. It is expected that the measures will improve significantly the profitability of the Group.

INCOME AND CASH FLOW STATEMENTS

INCOME STATEMENT January 1 – December 31		Group		Parent company	
EUR 1 000	Note	2002	2001	2002	2001
NET SALES	2.1.	25 354	25 545	14 994	15 525
Change in inventories of finished goods and work in progress		-216	244	-121	318
Other operating income		208	501	194	182
Materials and services	2.2.	-4 644	-5 460	-2 855	-2 966
Personnel expenses	2.3.	-11 010	-9 883	-6 457	-5 904
Depreciation and value adjustments	3.1.	-2 140	-2 268	-1 308	-2 384
Other operating expenses		-8 780	-8 442	-4 645	-4 591
OPERATING PROFIT/LOSS		-1 227	237	-199	180
Financial income and expenses	2.4.	-317	-182	-472	-309
PROFIT/LOSS BEFORE EXTRAORDINARY ITEMS		-1 545	55	-671	-129
Extraordinary items	2.5.	0	0	0	0
PROFIT/LOSS BEFORE INCOME TAXES		-1 545	55	-671	-129
Income taxes		-282	- 273	-195	21
Minority interest		26	- 14	0	0
NET LOSS		-1 800	- 232	-865	-107

CASH FLOW STATEMENT January 1 – December 31	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
CASH FLOWS FROM OPERATING ACTIVITIES				
Profit/loss before extraordinary items	-1 545	55	-671	-128
Adjustments:				
Depreciations	2 140	2 268	1 308	2 383
Financial income and expenses	317	182	472	309
Other adjustments	0	24	0	-38
Cash flow before change in net working capital	912	2 529	1 109	2 526
CHANGE IN NET WORKING CAPITAL				
Increase (-)/decrease (+) in non-interest bearing receivables	-283	424	-225	-269
Increase (-)/decrease (+) in inventories	613	-468	167	-401
Increase (+)/decrease (-) in non-interest bearing liabilities	-461	- 77	-141	243
Funds generated before financial items and income taxes	781	2 408	911	2 099
Interests and other financial items paid	-218	-442	-141	-321
Interests received	147	153	233	148
Income taxes paid	-1 164	-243	-1 119	-75
Cash flow before extraordinary items	-454	1 876	-115	1 851
Net cash flow from operating activities (A)	-454	1 876	-115	1 851
NET CASH FLOW FROM INVESTING ACTIVITIES				
Investments in tangible and intangible assets	-1 730	- 2 170	- 1 452	-1 904
Proceeds from disposition of tangible and intangible assets	0	33	0	33
Loans given	0	0	-430	-189
Grants received	66	425	66	425
Investments in subsidiaries	0	-42	0	-129
Repayments of loan receivables	0	0	110	82
Dividends received from investments	5	6	5	6
Net cash flow from investing activities (B)	-1 659	-1 748	-1 701	-1 676
NET CASH FLOW FROM FINANCING ACTIVITIES				
Proceeds from share issue	569	0	569	0
Increase in capital loan	0	111	0	111
Increase in long-term loans	927	73	829	64
Repayments of long-term loans	-467	-870	-477	-870
Net cash flow from financing activities (C)	1 028	-686	921	-695
Net increase (+)/decrease (-) in cash and cash equivalents (A+B+C)	-1 084	-558	-895	-520
Cash and cash equivalents at January 1	2 458	3 016	1 831	2 351
Cash and cash equivalents at December 31	1 374	2 458	936	1 831

BALANCE SHEET December 31

ASSETS EUR 1 000	Note	Group 2002	 2001	Parent company 2002	 2001
FIXED ASSETS AND OTHER LONG-TERM INVESTMENTS					
Intangible assets	3.1.1.	1 188	1 182	6 431	6 408
Goodwill	3.1.1.	3 049	3 671	0	0
Tangible assets	3.1.2.	6 425	6 370	5 755	5 724
Shares and holdings	3.2.	119	216	5 785	6 074
Total fixed assets and other long-t.investments		10 781	11 439	17 971	18 206
CURRENT ASSETS					
Inventories	3.3.	3 600	4 253	1 999	2 167
Deferred tax assets	3.7.	1 320	1 516	0	190
Long-term receivables	3.4.	0	0	477	186
Short-term receivables	3.4.	5 339	5 330	5 644	5 808
Cash at bank and in hand		1 374	2 457	936	1 831
Total current assets		11 633	13 556	9 057	10 182
TOTAL ASSETS		22 414	24 995	27 028	28 388

SHAREHOLDERS' EQUITY AND LIABILITIES EUR 1 000	Note	Group 2002	 2001	Parent company 2002	 2001
SHAREHOLDERS' EQUITY					
Share capital	3.5.1.	2 199	2 149	2 199	2 149
Share premium fund	3.5.1.	15 425	14 906	15 425	14 906
Accumulated profit/loss from prior years	3.5.1.	-1 003	-600	1 133	1 241
Net loss	3.5.1.	-1 800	-232	-865	-107
Capital loans	3.5.4.	1 243	1 243	1 243	1 243
Total shareholders' equity		16 066	17 466	19 136	19 432
MINORITY INTEREST		75	111	0	0
APPROPRIATIONS	3.6.	0	0	359	359
LIABILITIES					
Deferred tax liability	3.7.	104	104	0	0
Long-term liabilities	3.8.1.	2 535	2 080	2 345	1 998
Short-term liabilities	3.8.2.	3 634	5 234	5 188	6 599
Total liabilities		6 273	7 418	7 534	8 597
TOTAL SHAREHOLDERS' EQUITY AND LIABILITIES		22 414	24 995	27 028	28 388

NOTES TO THE FINANCIAL STATEMENTS

1. ACCOUNTING PRINCIPLES

The financial statements have been prepared in accordance with Finnish Accounting Act.

Preparation of the financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts and figures in the financial statements. Actual results could differ from those estimates.

Amounts are presented in euro and are based on the original value of transactions.

PRINCIPLES FOR VALUATION AND RECOGNITION OF REVENUES AND COSTS

Valuation of Fixed Assets

Fixed assets are recorded in the balance sheet at historical cost net of grants received and depreciation. Depreciation is calculated on straight-line basis over the useful life of the assets.

The useful life times are:

Intangibles	5–10 years
Goodwill (group)	3–20 years
Goodwill (parent)	10 years
Buildings	20 years
Other capitalized costs	5–10 years
Machinery and equipment	3–10 years

The board of Biohit has 27.8.2002 decided to prolong the goodwill amortization period related to Locus genex Oy from seven to 20 years. The decision of this change is based on the information on the market and, e.g., on the feedback of GastroPanel evaluations, according to which the company estimates that the accumulated income effect is longer than it was estimated at first, and at least 20 years. In 2002 the goodwill amortization totalled MEUR 0.4. This corresponds with the amortization made on the first half of 2002 based on the original 7 years' amortization period.

The amortization period of the goodwill at the parent company, which consists of the patents and liquidation loss transferred to Biohit Oyj as a result of liquidation of Locus genex Oy, was correspondingly prolonged from 5 to 10 years. The current amortization period agrees with the amortization period in taxation. The change was carried out retroactively so that no amortizations were recorded in 2002.

Valuation of Inventories

Inventories are stated at the lower of cost, on a first-in-first-out (FIFO) basis, or net realizable value. The value of finished goods include an appropriate proportion of production overheads in addition to the direct costs.

R & D Expenses

From 1998 on R & D costs are recorded as expense when occurred.

Revenue Recognition

Net sales are calculated as gross sales less indirect sales taxes and discounts. Revenues from products and services are recognized upon delivery.

Maintenance and Repairs

Costs for maintenance and repairs are recorded as expenses when occurred. The costs of renovating rented premises have been capitalized under other capitalized expenses and will be depreciated on a straight-line basis over the remaining rental period.

Pensions

The pension schemes and any additional pension benefits required by Finnish law are arranged through pension insurance companies. Pension costs are charged to the income statement for the period when earned. In foreign subsidiaries pension costs are accounted for in accordance with the local practice.

Foreign Currency Translation

Receivables and liabilities in foreign currencies are translated into euro at the exchange rate quoted by the European Central Bank on the balance sheet date.ss Exchange gains and losses are recorded to profit and loss account with the exception that the unrealized exchange gain on the non-current USD-based loan receivable from a subsidiary company was in 2001 financial statements of the parent company disclosed under accrued liabilities.

ACCOUNTING PRINCIPLES OF CONSOLIDATION

Scope of Consolidated Financial Statements

The consolidated financial statements include Biohit Oyj and all companies in which the Group holds more than 50 % of the voting rights. Subsidiary companies are included in the consolidated financial statements from the date of acquisition.

Intragroup Shareholdings

The consolidated financial statements have been prepared using the purchase method. The difference between the acquisition cost and the shareholders' equity corresponding to the acquired holding is presented as goodwill.

Intragroup Transactions and Margins

Intragroup transactions, unrealized internal profits, receivables and debts as well as intragroup distribution of profits are eliminated in the consolidated financial statements.

Translation Differences

The income statements of foreign group companies are translated into euro at the average exchange rate for the year and the balance sheets at the exchange rate on the balance sheet date. Differences arising from the translation as well as those from translating shareholders' equity are recorded in the consolidated financial statements under "Accumulated profit/loss from prior years".

Deferred Taxes

Deferred income tax liabilities and receivables have been accounted for on timing differences based on tax rates enacted at the balance sheet date. The deferred tax liability has been fully provided for while the deferred tax assets has been stated at the recoverable amount. No deferred tax assets has been recognised on tax loss carry forwards.

2. NOTES TO THE INCOME STATEMENT

2.1. Net sales by Geographical Area	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
Finland	579	964	871	975
Scandinavia	1 739	817	1 705	817
Rest of Europe	12 662	11 228	7 500	7 187
America	5 191	6 368	2 771	3 945
Other countries	5 182	6 168	2 146	2 601
Total	25 354	25 545	14 994	15 525

2.2. Materials and Services	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
Materials				
Purchases during the year	4 299	5 287	2 769	3 040
Change in inventories	46	- 95	45	-83
Total materials	4 344	5 191	2 814	2 957
External services	299	268	41	9
Total materials and services	4 644	5 460	2 855	2 966

2.3. Personnel Expenses and Number of Personnel	Group		Parent company	
Personnel Expenses, EUR 1 000	2002	2001	2002	2001
Salaries and wages	8 780	7 975	5 197	4 758
Pension expenses	1 136	1 067	828	737
Other personnel expenses	1 094	841	432	409
Total	11 010	9 883	6 457	5 904

Salaries and Fees of the Management

The salaries of the Group's Presidents totalled TEUR 625 (TEUR 706 in 2001). The fees to the members of the Board of Directors were TEUR 49 (67) in the parent company and Group. Any other notable pension arrangements other than those laid down by law have not been made with the Presidents of Group companies.

	Group		Parent company	
Personnel *)	2002	2001	2002	2001
Office personnel	211	188	89	75
Factory personnel	92	101	92	101
Total	303	289	181	176
Personnel at end of the year	283	294	158	184

*) temporary dismissals are not included

2.4. Financial Income and Expenses	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
Dividend income from outside the Group	5	6	5	6
Interest income from long-term investments				
From companies within the Group	0	0	132	115
Other interest and financial income:				
From companies within the Group	0	0	17	25
From others	147	247	97	120
Total	147	247	245	260
Value adjustments of shares and holdings			-275	-275
Interest expense and other financial expenses:				
For companies within the Group	0	0	-2	-1
For others	-469	-436	-444	-299
Total financial income and expenses	-317	-182	- 472	- 309
Net foreign exchange losses included in ”Financial income and expenses”	168	35	245	37

2.5. Income Taxes	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
Current income taxes on extraordinary items	0	0	0	0
Current income taxes on ordinary operations	-85	-1 521	-5	-169
Change in deferred income tax liability/assets	-197	1 248	-190	190
Total	-282	-273	-195	21

3. NOTES TO THE BALANCE SHEET

3.1. Tangible and Intangible Assets

3.1.1. Intangible Assets Group EUR 1 000	Intangibles	Goodwill	Other capitalized expenses	Total
Acquistion cost at beginning of year	948	6 547	1 075	8 570
Additions	159	0	160	319
Acquisition cost at end of year	1 107	6 547	1 235	8 889
Accumulated depreciation and value adjustments at beginning of year	-373	-2 875	-467	-3 715
Depreciation for the year	-110	-623	-204	-937
Accumulated depreciation and value adjustments at end of the year	-483	-3 498	-671	-4 652
Net book value at end of year	624	3 049	564	4 237

3.1.1. Intangible Assets Parent company EUR 1 000	Intangibles	Goodwill	Other capitalized expenses	Total
Acquisition cost at beginning of year	971	6 558	883	8 412
Additions	159	0	160	320
Acquisition cost at end of year	1 131	6 558	1 043	8 732
Accumulated depreciation and value adjustments at beginning of year	-397	-1 312	-296	-2 005
Depreciation for the year	- 110	0	-186	-296
Accumulated depreciation and value adjustments at end of the year	- 506	-1 312	-483	-2 301
Net book value at end of year	624	5 247	560	6 431

Goodwill in parent company consists of patents (TEUR 5 045) transferred as a result of the dissolution of Locus genex Oy and liquidation loss (TEUR 1 513).

3.1.2. Tangible Assets **Group**

EUR 1 000	Buildings	Machinery and equipment	Total
Acquisition cost at beginning of year	2 309	7 450	9 759
Additions	0	1 336	1 336
Disposals	0	- 78	- 78
Acquisition cost at end of year	2 309	8 708	11 016
Accumulated depreciation and value adjustments at beginning of year	-144	-3 245	-3 389
Depreciation during the year	-115	-1 088	-1 203
Accumulated depreciation and value adjustments at end of the year	-259	-4 333	-4 591
Net book value at end of year	2 050	4 376	6 425

3.1.2. Tangible Assets **Parent company**

EUR 1 000	Buildings	Machinery and equipment	Total
Acquisition cost at beginning of year	2 309	6 320	8 628
Additions	0	1 043	1 043
Acquisition cost at end of year	2 309	7 363	9 671
Accumulated depreciation and value adjustments at beginning of year	-144	-2 761	-2 904
Depreciation during the year	-115	-897	-1 013
Accumulated depreciation and value adjustments at end of the year	-259	-3 658	-3 916
Net book value at end of year	2 050	3 705	5 755

The book value of production machinery and equipment is TEUR 3 176.

3.2. Shares and Holdings

Group

EUR 1 000	Shares
Book value at beginning of year	216
Disposals	-97
Book value at end of year	119

Parent Company

EUR 1 000	Shares Group companies	Shares other	Loans receivable from companies within the Group	Total
Book value at beginning of year	4 384	161	1 528	6 073
Additions	230	0	0	230
Disposals	0	0	-244	-244
Value adjustments	-230	-45	0	-275
Book value at end of year	4 384	117	1 284	5 785

Other shares consist mainly of the shares in Nordea and Elisa Communications, which have been recorded at their market value on 31 December 2002.

Group Companies	Group holding	Parent company shareholding
Biohit Ltd., Great Britain	100%	100%
Pipette Doctor Ltd., Great Britain	100%	0%
Biohit S.A., France	91%	91%
Biohit s.r.l., Italy	90%	90%
Biohit Deutschland GmbH, Germany	100%	100%
Biohit Japan Co., Ltd., Japan	100%	100%
Biohit Inc., USA	95%	95%
Finnbio Ltd., Russia	100%	49%
Biohit OOO, Russia	100%	100%
Finnhit OOO, Russia	100%	100%
Oy Finio Ab, Finland	100%	100%
Locus genex Oy, Finland	100%	100%
Vantaan Hienomekano Oy, Finland	100%	100%

Vantaan Hienomekano Oy, Locus genex Oy and Biohit OOO did not have business operations in 2002. The maintenance business of Pipette Doctor Ltd. has in its entirety been transferred in the beginning of 2002 to Biohit Ltd. As a result, Pipette Doctor Ltd. is dormant. Likewise, nearly all of the business operations of Finnbio Ltd. have been transferred to Biohit OOO in 2002. Locus genex Oy is under voluntary liquidation process.

3.3. Inventories

	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
Materials	953	1 043	995	1 041
Finished products/goods	2 640	3 150	1 004	1 126
Advance payment	8	59	0	0
Total inventories	3 600	4 253	1 999	2 167

3.4. Receivables

	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
LONG-TERM RECEIVABLES				
Receivables from Group companies				
Loans receivable	0	0	477	186
SHORT-TERM RECEIVABLES				
Receivables from companies within the Group				
Accounts receivable	0	0	3 445	3 864
Loans receivable	0	0	113	84
Other receivables	0	0	198	238
Receivables from other companies				
Accounts receivable	4 639	4 493	1 571	1 201
Loans receivable	0	8	0	8
Other receivables	285	334	170	174
Prepayments and accrued income	415	494	149	239
Total short-term receivables	5 339	5 330	5 644	5 808

3.5. Shareholders' Equity

3.5.1. Shareholders' Equity	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
Share capital at beginning of year	2 149	2 149	2 149	2 149
Share issue	50	0	50	0
Share capital at end of year	2 199	2 149	2 199	2 149
Share premium fund at beginning of year	14 906	14 906	14 906	14 906
Premium from share issue	519	0	519	0
Share premium fund at end of year	15 425	14 906	15 425	14 906
Profit/loss from prior years at beginning of year	-832	-619	1 133	1 241
Translation difference	-171	19	0	0
Profit/loss from prior years at end of year	-1 003	-600	1 133	1 241
Loss for year	-1 800	-232	-865	-107
Capital loans at beginning of year	1 243	1 132	1 243	461
Increase	0	111	0	783
Decrease	0	0	0	0
Capital loans at end of year	1 243	1 243	1 243	1243
Total shareholders' equity	16 066	17 466	19 136	19 432

As a result of the subscription of shares made on the basis of the 1999 personnel option program and the option program targeted to Jencons Scientific Ltd., the share capital of Biohit increased during the reporting period by EUR 50,022.50 (294,250 shares) to EUR 2,199,396.59 (12,937,627 shares). The share premium of EUR 518,657.50 has been recorded in the premium fund.

3.5.2. Distributable equity at 31 December	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
Profit/loss from prior years	-1 003	-600	1 133	1 241
Loss for the year	-1 800	-232	-865	-107
Unrecorded interest on capital loans	-480	-421	-480	-421
Accelerated depreciation recorded in shareholders´equity	-255	-255	0	0
Total	-3 537	-1 508	-213	713

The calculation above demonstrates that, on the basis of the Companies Act, Biohit does not have distributable earnings as at 31.12.2002.

3.5.3. Share capital of the parent company	2002		2002		2001	
	No. of shares	EUR	% of shares	% of votes	No. of shares	EUR
A-shares (20 votes per share)	3 875 500	658 835	29.96	89.53	3 875 500	658 835
B-shares (1 vote per share)	9 062 127	1 540 562	70.04	10.47	8 767 877	1 490 539
Total	12 937 627	2 199 397	100.00	100.00	12 643 377	2 149 374

The shares of Biohit Oyj comprise of A and B shares. At meetings of shareholders shares of series A entitle to 20 votes each and shares of series B to one vote each. In distribution of dividends, the dividend payable on shares of series B shall be higher by two per cent (2%) of the nominal value compared with the dividend payable on shares of series A.

3.5.4. Capital Loans

On December 31, 2001, the parent company and Group held TEUR 1 243 in capital loans. The terms for the capital loans conform to section 5, paragraph 1 of the Finnish Companies Act. TEUR 880 of the capital loans are from the company's main shareholders.

3.6. Appropriations	Parent company	
EUR 1 000	2002	2001
Untaxed reserves	359	359

The appropriations derive from the accelerated depreciation.

3.7. Deferred income tax liabilities and assets	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
Deferred income tax assets				
From consolidation entries	1 320	1 327		
From temporary differences	0	190	0	190
Deferred income tax liabilities				
From temporary differences	104	104	0	0
Net	1 216	1 413	0	190

Deferred income tax assets from consolidation entries include taxes paid as a result of dissolution of Locus genex Oy of TEUR 1 038 which are deferred in the group accounts over the remaining amortization period of 16 years of the goodwill relating to Locus genex Oy.

The deferred income tax assets in the parent company on December 2001, resulted from the different amortization period of the goodwill, resulting from the dissolution of Locus genex Oy, for accounting (5 years) and taxation (10 years) purposes.

Cumulative tax losses of the group companies, including the losses of the current year, amount to approximately MEUR 1,7. The relating deferred tax assets, MEUR 0,5, has not been accounted for in the financial statements.

3.8. Liabilities

3.8.1. Long-term Liabilities	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
Loans from financial institutions	1 720	1 291	1 588	1 241
Other long-term debt	815	789	757	757
Total long-term liabilities	2 535	2 080	2 345	1 998
Debts falling due in more than five years				
Loans from financial institutions	119	33	85	33
Other long-term debt	284	378	284	378

3.8.2. Short-term Liabilities	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
Loans from financial institutions	801	796	801	796
Advances received	146	148	2	58
Accounts payable	837	1 246	430	717
Other liabilities	677	727	2 906	2738
Accrued liabilities	1 172	2 317	999	2 279
Liabilities from Group companies				
Accounts payable	0	0	51	10
Total short-term liabilities	3 634	5 234	5 189	6 599

Accrued liabilities consist mainly of holiday pay and related social security accruals.

4. OTHER NOTES

4.1. Pledges given, Commitments and Contingencies

Pledges given	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
Loans for which mortgages and pledges have been given				
Loans from financial institutions	2 143	1 906	2 143	1 906
Corporate mortgages	3 389	3 389	3 389	3 389
Pledges on leaseholds	1 500		1 500	
Other long-term liabilities	757	757	757	757
Mortgages on real estate	757	757	757	757

The parent company has given pledges of MEUR 0.4 on behalf of Group companies.

Leasing commitments	Group		Parent company	
EUR 1 000	2002	2001	2002	2001
Due for payment in the following year	1 389	1 190	690	575
Due for payment at a later date	2 723	2 855	1 744	1 906
Total	4 112	4 045	2 434	2 481

Leasing commitments include mainly fixed-term leasing and rental agreements which are effective more than one year.

Interest on capital loans

On December 31, 2002, accumulated, unrecorded interest on capital loans was TEUR 480 (TEUR 421) for the parent company and for the Group.

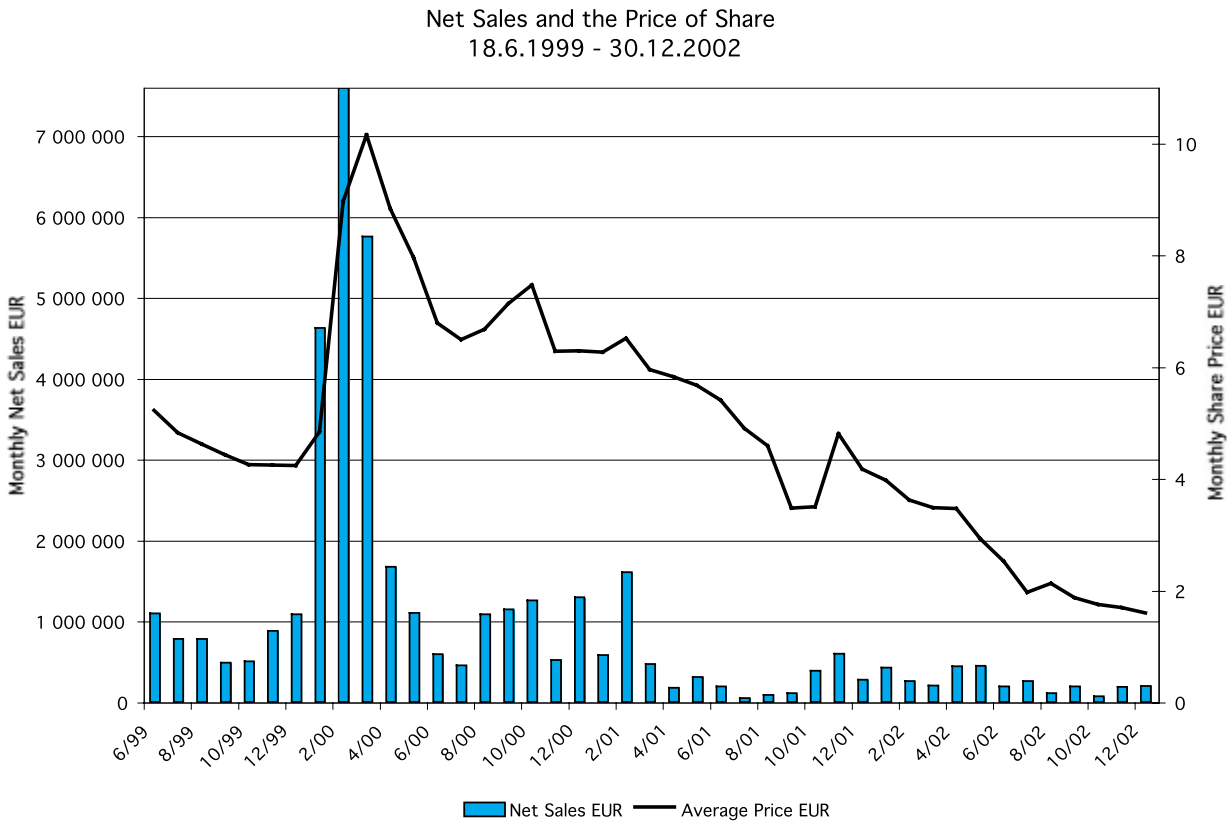
Derivative contracts

The group has no off-balance sheet financial instruments.

4.2 Ratios

Financial ratios	1998	1999	2000	2001	2002
Net sales	16 881	20 551	24 247	25 545	25 354
Increase in net sales %	16.6 %	21.7 %	18.0 %	5.4 %	-0.7%
Operating profit/loss	1 387	1 332	-482	237	-1 227
% of net sales	8.2 %	6.5 %	-2.0 %	0.9 %	-4.8%
Profit/loss before extraordinary items and income taxes	451	825	-580	55	-1 545
% of net sales	2.7 %	4.0 %	-2.4 %	0.2 %	-6.1%
Profit/loss before voluntary provisions and taxes	1 141	1 162	-341	55	-1 545
% of net sales	6.8 %	5.7 %	-1.4 %	0.2 %	-6.1%
Return on equity, %	12.1 %	3.8 %	-4.6 %	-1.3 %	-11.7%
Return on investment, %	12.2 %	8.5 %	-0.8 %	2.0 %	-5.5%
Equity ratio, %	38.8 %	66.0 %	66.9 %	65.7 %	66.9 %
Investments in fixed assets	1 392	1 271	6 208	2 212	1 578
% of net sales	8.2 %	6.2 %	25.6 %	8.7 %	6.2 %
Research and development	740	1 270	1 698	2 114	1 809
% of net sales	4.4 %	6.2 %	7.0 %	8.3 %	7.1 %
Total assets	18 435	24 699	24 626	24 996	22 414
Personnel, average	164	184	222	289	303

Ratios per share	1998	1999	2000	2001	2002
Earnings per share, EUR	0.06	0.04	-0.06	-0.02	-0.14
Equity per share, EUR	0.69	1.33	1.30	1.28	1.15
Price/earnings (P/E)	-	102	-101	-233	-10
Dividend per share, EUR	0	0	0	0	0
Dividend per earnings, %	0	0	0	0	0
Effective yield of shares, %	0	0	0	0	0
Price development of B-share, EUR					
- average price	-	4.54	7.43	5.35	2.56
- lowest price	-	3.75	4.20	3.00	1.40
- highest price	-	6.00	13.50	7.20	4.40
- price on December 31, 2001	-	4.13	6.20	4.28	1.41
Market price for the entire capital stock EUR 1 000 (assuming that market price of A-share is the same as B-share´s)	-	50 653	78 389	54 114	18 242
Development of exchange of B-shares, pcs 1 000	-	1 240	3 647	909	1 178
- % of total amount of shares	-	16.58 %	41.93 %	10.36 %	13.16 %
Average number of shares, adjusted for share issues	6 264 526	11 354 957	12 573 123	12 643 377	12 827 781
Number of shares at the balance sheet date, adjusted for share issues	10 264 537	12 264 537	12 643 377	12 643 377	12 937 627



4.3 Shares and shareholders

Shares and voting rights

The shares of Biohit Oyj are divided into A and B shares. At shareholders' meetings the series A is entitled to 20 votes each and series B shares to one vote each. As to the distribution of dividends, the dividend payable on series B shares shall be two per cent (2%) higher of the nominal value compared with the dividend payable on series A shares.

Share capital of the parent company	**2002**		**2002**		**2001**	
	No. of shares	EUR	% of shares	% of votes	No. of shares	EUR
A-shares (20 votes per share)	3 875 500	658 835	29.96	89.53	3 875 500	658 835
B-shares (1 vote per share)	9 062 127	1 540 562	70.04	10.47	8 767 877	1 490 539
Total	12 937 627	2 199 397	100.00	100.00	12 643 377	2 149 374

According to the Articles of Association, the Company´s minimum share capital is EUR 1 063 101.29 and the maximum share capital EUR 4 252 405.16 within which limits the share capital can be raised or lowered without amending the Articles of Association.
The Company does not possess own shares. The Board of Directors does not have outstanding authorization to issue shares, convertible bonds or option loans or acquire shares in the Company. The Company does not currently have an option plan.

Ownership of shares by sector on Dec. 30, 2002

A-Shares	No. of shareholders		No. of shares	
	pieces	%	pieces	%
1. Companies	2	22.22	919 990	23.74
2. Households	7	77.78	2 955 510	76.26
Total	9	100.00	3 875 500	100.00

B-Shares	No. of shareholders		No. of shares	
	pieces	%	pieces	%
1. Companies	213	4.90	1 978 932	21.84
2. Households	6	0.14	141 708	1.56
3. Public organizations	2	0.05	519 600	5.73
4. Non-profit organizations	20	0.46	89 230	0.98
5. Households	4 080	93.77	6 141 955	67.78
6. Foreign	30	0.69	185 110	2.04
Shares which are not entered into the book-entry system			5 592	0.06
Total	4 351	100.00	9 062 127	100.00
Nominee-registered shares	4		132 730	1.46

Ownership according to the number of shares owned on December 30, 2002

A-Shares	No. of shareholders		No. of shares	
	pieces	%	pieces	%
1-1 000	1	11.11	10	0.00
1 001-5 000	0	0.00	0	0.00
5 001-10 000	0	0.00	0	0.00
10 001-50 000	1	11.11	19 990	0.52
Over 50 000	7	77.78	3 855 500	99.48
Total	9	100.00	3 875 500	100.00

B-Shares	No. of shareholders		No. of shares	
	pieces	%	pieces	%
1-1 000	3 775	86.68	1 313 944	14.50
1 001-5 000	468	10.75	1 024 369	11.30
5 001-10 000	59	1.35	449 140	4.96
10 001-50 000	34	0.78	666 308	7.35
Over 50 000	19	0.44	5 602 774	61.83
Total	4 355	100.00	9 056 535	99.94
Shares which are not entered into the book-entry system			5 592	0.06
Total			9 062 127	100.00

Major shareholders on December 30, 2002

10 major shareholders according to number of shares	A-sharest	B-shares	Total no. of shares	%
Suovaniemi, Osmo	2 285 340	2 271 072	4 556 412	35.22
Erja-Yhtymä Oy	900 000		900 000	6.96
Suovaniemi, Ville	208 280	371 300	579 580	4.48
Suovaniemi, Joel	208 280	343 700	551 980	4.27
Härkönen, Matti	57 200	449 300	506 500	3.91
Suovaniemi, Oili	121 600	314 135	435 735	3.37
Suovaniemi, Vesa	74 800	292 417	367 217	2.84
LEL Työeläkekassa		361 600	361 600	2.79
Adlercreutz, Herman		250 970	250 970	1.94
Tech Know Oy Ltd	19 990	141 300	161 290	1.25

10 major shareholders according to number of votes	A-shares	B-shares	Total no. of votes	%
Suovaniemi, Osmo	45 706 800	2 271 072	47 977 872	55.42
Erja-Yhtymä Oy	18 000 000		18 000 000	20.79
Suovaniemi, Ville	4 165 600	371 300	4 536 900	5.24
Suovaniemi, Joel	4 165 600	343 700	4 509 300	5.21
Suovaniemi, Oili	2 432 000	314 135	2 746 135	3.17
Suovaniemi, Vesa	1 496 000	292 417	1 788 417	2.07
Härkönen, Matti	1 144 000	449 300	1 593 300	1.84
Tech Know Oy Ltd	399 800	141 300	541 100	0.63
LEL Työeläkekassa		361 600	361 600	0.42
Adlercreutz, Herman		250 970	250 970	0.29

Ownership by management on December 30, 2002

The members of the Board and the President of the Company owned a total of 2 285 340 A-shares and 2 355 308 B-shares on December 30, 2002.This in total stands for 35.87% of all shares and 55.52% of the votes in the Company.

Formulas used in calculating key ratios

Return on equity, %

$$\frac{\text{Profit before extraordinary items – income taxes for the period x 100}}{\text{Shareholders´equity – capital loans + minority interest (average over the year)}}$$

Return on capital employed, %

$$\frac{\text{Profit before extraordinary items + interest and other financial expenses x 100}}{\text{Total assets – non-interest-bearing liabilities (average over the year)}}$$

Equity ratio, %

$$\frac{\text{Shareholders´equity – capital loans + minority interest x 100}}{\text{Total assets – advance payments received}}$$

Earnings per share, EUR

$$\frac{\text{Profit before extraordinary items – income taxes for the period – minority interest}}{\text{Average number of shares, adjusted for share issue}}$$

Equity per share, EUR

$$\frac{\text{Shareholders´equity – capital loans}}{\text{Number of shares at the balance sheet date, adjusted for share issues}}$$

Dividend per share, EUR

$$\frac{\text{Dividend for the period}}{\text{Number of shares at the balance sheet date, adjusted for share issues}}$$

Dividend per earnings, %

$$\frac{\text{Dividend/share x 100}}{\text{Earnings per share}}$$

Effective dividend yield, %

$$\frac{\text{Dividend, adjusted for share issue/share x 100}}{\text{Stock exchange price on December 31, adjusted for share issues}}$$

Price/earnings, (P/E)

$$\frac{\text{Stock exchange price on December 31, adjusted for share issues}}{\text{Earnings per share}}$$

PROPOSAL OF THE BOARD OF DIRECTORS AND AUDITORS´ REPORT

Proposal for the Handling of the Loss

The Company does not have distributable earnings.

The Board of Directors proposes that no dividends be paid and that the loss for the period of EUR 865 470.37 will be transferred to the retained profit/loss account from previous years.

Helsinki, February 14, 2003

Reijo Luostarinen
Chairman of the Board
of Directors

Osmo Suovaniemi
Member of the Board
of Directors

Mårten Wikström
Member of the Board
of Directors

Arto Alanko
Member of the Board
of Directors

Hannu Seristö
Member of the Board
of Directors

AUDITORS' REPORT

To the shareholders of Biohit Oyj

We have audited the accounting records, the financial statements and the corporate governance of Biohit Oyj for the financial period 1.1. - 31.12.2002. The financial statements, which include the report of the Board of Directors, consolidated and parent company income statements, balance sheets and notes to the financial statements, have been prepared by the Board of Directors and the Managing Director. Based on our audit we express an opinion on these financial statements and the corporate governance of the parent company.

We have conducted our audit in accordance with the Finnish Standards on Auditing. Those standards require that we perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used as well as evaluating the overall financial statement presentation. The purpose of our audit of corporate governance is to examine that the members of the Board of Directors and the Managing Director of the parent company have legally complied with the rules of the Companies' Act.

In our opinion the financial statements have been prepared in accordance with the Accounting Act and other rules and regulations governing the preparation of financial statements. The financial statements give a true and fair view, as defined in the Accounting Act, of the result of operations as well as the financial position of the group and the parent company. The financial statements including the consolidated financial statements can be adopted and the members of the Board of Directors and the Managing Director of the parent company can be discharged from liability for the financial period audited by us. The proposal by the Board of Directors regarding the handling of the loss for the financial period is in compliance with the Companies' Act.

Helsinki, March 6, 2003

PricewaterhouseCoopers Oy
Authorised Public Accountants

Hannele Selesvuo
Authorised Public Accountant

ADMINISTRATION AND SCIENTIFIC ADVISORS

BOARD OF DIRECTORS

Reijo Luostarinen, D.Sc.(Econ.). *Internationalization and Strategic Planning.* Current Chairman of the Board of Biohit and member of the Board of Biohit since 1993. Professor of International Business at the Helsinki School of Economics (HSE). Head of the faculty and Director of the International Business (IB) Program and Director of the Center for IB-Research. Chairman or member of the board of many other educational units at HSE. Vice-Rector of HSE 1990-1995. Docent at the Helsinki University of Technology and at the University of Vaasa. Visiting professor or guest lecturer in 23 different countries. Asla Fulbright scholar at the University of Michigan. President of the European International Business Academy and Regional Chairman of the Academy of International Business (USA) in Europe 1989-1990. Board member of six scientific foundations. Chairman of four international academic conferences. Senior advisor of international business for different U.N.-organizations, some governments and ministries. Owner of two consulting firms, chairman and shareholder of 3 companies and board member of altogether ten companies in 1980-1997. Author of 15 books, chapters in five books, editor of two books and author of seventy articles, working papers and research papers. Editorial board member of six international scientific journals. International operations and global business strategy expert in companies located in different countries. Holdings in Biohit on December 30, 2002: 76,500 B-shares.

Arto Alanko, M.D., Ph.D. *Co-operation with Health Care Units.* Member of the Board of Biohit since 2001. Docent of surgery. Docent Alanko has acted since 2001 as the Provincial Medical Officer of Southern Finland and from 2002 the Medical Counsel of the Province. Between 1997-2000 docent Alanko served as the Director of Jorvi Hospital and participated, e.g., in the preparation and development of the strategy for the hospital district. Previously docent Alanko has acted, e.g., as the Administrative Medical Officer of the Helsinki University Central Hospital, as the Senior Medical Officer of the Hospital Department of the National Board of Health, as researcher in surgical oncology and as surgical and administrative consultant in various hospitals. The quality management project directed by Arto Alanko at the Helsinki University Central Hospital won the Arthur Andersen / Ed Crosby -prize granted by the International Hospital Federationin (IHF) for a good managerial innovation in 1995. Arto Alanko has also participated in numerous national work groups. The number of scientific articles and publications prepared by docent Alanko totals 140. Holdings in Biohit on December 30, 2002: 7,400 B-shares.

Hannu Seristö, D.Sc. (Econ.). *International Marketing and Competitive Strategies.* Member of the Board of Biohit since 2002. Professor of International Business at the Helsinki School of Economics (HSE). Prof. Seristö got his Master's degree in 1987 and worked in managerial positions of international business and international marketing at Finnair Oy, McKinsey & Co. Inc. and Suunto Oy. He started doctorate studies in 1992, got his licentiate degree in 1993, and earned his doctorate from HSE in 1995 after research work at Cranfield University in England. Prof. Seristö's teaching and research focuses on international business strategies, international marketing, and business in the context of the European Union. He is the chairman of the board of the HSE International Center, which provides the leading Master of Business Administration (MBA) Program in the Nordic countries. Holdings in Biohit on December 30, 2002: 336 B-shares.

Mårten Wikström, M.D., Ph.D. *Development of Co-operation with Scientific and Research Communities.* Member of the Board of Biohit since 1997. Professor of Medical Chemistry at the University of Helsinki. Academy professor since 1996. He is actively engaged in basic scientific research (biochemistry, biophysics, molecular biology) at the University of Helsinki where he directs the Helsinki Bioenergetics Group, an international research team. Moreover, he acts as the Research Director of the program on structural biology and biophysics at the Institute of Biotechnology, University of Helsinki. Prof. Wikström has over 160 original publications on basic research in internationally renowned journals and he has received several scientific awards, e.g., the Anders Jahre Medical Prize for young researchers (1984), the A. I. Virtanen Prize (1989), the Matti Äyräpää Prize (1993), and the main Anders Jahre Medical Prize (1996). He is member of Societas Scientarum Fennica and foreign member of the Royal Swedish Academy of Sciences. In 1985-1989 he served as the Director of Research and as Operative Director at Eflab Oy and Labsystems Oy. No shareholdings on December 30, 2002.

Osmo Suovaniemi, M.D., Ph.D., Professor. *Management and Development of the Operative Activities of the Group. Development of the Liquid Handling and Diagnostic Product Ranges.* Founder, President and CEO and member of the Board of Biohit. His background as the founder, main shareholder, Chairman and CEO of Labsystems Oy and Eflab Oy until 1986, and as a major innovator of the products of those companies, demonstrates his experience and skills in this field of business. He received the M.D. in 1972 and the Ph.D. in 1994, both from the University of Helsinki, Finland. He has also completed the JOKO Executive Education study program at the Helsinki School of Economics in 1976-1977 and at the Finnish Institure of Management (LIFIM) in 1982. In 1976 he was awarded by the Finnish Foundation of Inventors for the single- and multichannel Finnpipette invention. He has served as board member, Vice-Chairman and Chairman of the General Industry Group in Finland between 1978-1986 and as board member of the Confederation of Finnish Industry in 1986. In 1984 the Finnish economic reporters awarded him an honorary prize for his economic achievements in 1983. Dr. Suovaniemi has been awarded 66 patents in Finland and a few hundred worldwide, mainly in the fields of medical diagnostics, optics and mechanics. He received an honorary award from the Finnish Board of Patents and Registration on November 19, 2002. On June 29, 2002, which was the 160th jubilee of granting the first patent in Finland, Suovaniemi possessed most Finnish patents. Suovaniemi received the honor and name of professor from the President of Finland in 2002. Holdings in Biohit on December 30, 2002: 2,285,340 A-shares and 965,207 B-shares.

MANAGEMENT TEAM

Osmo Suovaniemi. *President & CEO.*

Erik Forsblom. *Diagnostics.* M.Sc. (Biochemistry). Mr. Forsblom has an over 20 years' experience within the field of clinical chemistry. Between 1973-1981 Mr. Forsblom worked as laboratory technician and chemist (assistant chemist and departmental chemist) at the Clinical Laboratory Center and at the United Clinical Laboratories in Helsinki. In 1981 he joined Labsystems Oy as research chemist. Between 1984 and 1988 he acted as Production Manager of the Diagnostics Division and between 1988-1990 as Assistant Director of the Diagnostics Division of Labsystems Oy. In 1990 Mr. Forsblom joined Biohit Plc. where he acted as Marketing Manager/Regional Export Manager until 1996.

Jussi Heiniö. *Administration and Legal Affairs.* LL.M. With Biohit since 1997. Mr. Heiniö graduated from the Faculty of Law at the University of Helsinki in 1988. Between 1988-1992 he acted first as an assistant lawyer and from 1992 as an Attorney-at-Law at Law Office Matti Oksala Ky. Between 1989-1990 he worked as a junior lawyer undergoing court training and later on as a judge in the District Court of Vantaa, Finland.

Helena Hentola. *Corporate Communications and Information Resources.* M.Sc. (Econ., International Business). With Biohit since 1995. Mrs. Hentola received the M.Sc. from the Helsinki School of Economics (HSE) in 1992 upon which she continued her studies at HSE and the University of Helsinki. In 1992 she studied at the Monterey Institute of International Studies in the U.S. She has acted as Project Coordinator of the Finland's International Business Operations (FIBO) -Research Program at HSE in 1995, as Research Associate and additional lecturer at the Dept. of International Business at HSE between 1994-1995 and as Researcher of the FIBO-Program between 1993-1994 and 1990-1991.

Kalle Härkönen. *Production.* M.Sc. (Business Economics of Forestry). With Biohit since 2001. Mr. Härkönen received the M.Sc. from the University of Helsinki in 1999 and a B.Sc from the Finnish Business College in 1992. He acted as Factory Manager at Delipap Oy in 2001. He worked in several positions at the packaging factory Tetra Pak Oy between 1996-2000, latest as Production Manager. He has also been an international trainee in the U.S. studying international marketing and business economics at the University of Maine between 1995-1996.

Semi Korpela. *Finance.* M.Sc (Econ.). With Biohit since 2003. Graduated from the University of Jyväskylä in 1996. Additional studies in the universities of Tampere, Helsinki and Universitat Autónoma de Barcelona and Universidad de Valladolid. During 1997-2003 he worked in the Sonera Corporation in various duties related to financial issues, latest as an international business controller in the Baltic Operations unit (Estonian Telecom, Lietuvos Telekomas) and Sonera Carrier Networks subgroup.

Sari Mannonen (née Ylätupa). *Sales and Marketing.* Ph.D., (Biochemistry). With Biohit since 1995. Mrs. Mannonen received the M.Sc. in 1990 and Ph.D. in 1996 from the University of Helsinki. She has completed the Business Unit Management Program at the JOKO Executive Education Oy organized by the Helsinki School of Economics in 2002. She has taken a course in Good Laboratory Practise (GLP) in the Netherlands in 1990. She has acted as biochemist and Product and Marketing Manager at Locus genex Oy between 1989-1995, in duties related to the development of diagnostic tests at Labsystems Oy between 1987-1988 and as assistant and teacher at the Dept. of Biology at the University of Helsinki between 1987-1988.

Seppo Riikonen. *Quality Systems.* Measurement and Adjustment Technician. With Biohit since 1989. In addition to having completed the study program offered by the Helsinki Institute of Technology in 1982, Mr. Riikonen has received the Diploma in Marketing from the Institute of Marketing, Helsinki in 1992. He has acted as Service Manager at Nordion Instruments Oy Ltd between 1985-1989, as Service Technician at Oriola Oy between 1984-1985 and as Project Technician at Orion Analytica Oy between 1982-1984.

Seppo Sirviö. *Information Technology.* B.Sc. (Information Technology) from the University of Kuopio. Mr. Sirviö joined Biohit in 2002. Before joining Biohit he worked, e.g., as Manager, Customer Support, at Novo Group Plc. between 2000-2001, and as Systems Manager at Neste Chemicals Ltd. (currently Dynea Ltd.) between 1995-2000. He has also experience of e-Business systems.

Erkki Vesanen. *Research and Development.* M.Sc. (Engineering, Electronics). With Biohit since 1989. Mr. Vesanen has acted as Managing Director of Innomedia between 1986-1989 and between 1976-1986 at Labsystems Oy in several duties related to product development, production, marketing and international operations.

MANAGING DIRECTORS OF SUBSIDIARIES

Régis Carnis. *France.* Managing Director of Biohit S.A. since its establishment in 1991. M.Sc. (Biochemistry). Mr. Carnis received his M.Sc. from the University of Paris in 1976. During his studies he worked as laboratory technician at the Department of Medical Chemistry in the laboratories of haematology and bacteriology. In 1976-1983 he received experience in the diagnostic field when working as Sales Engineer, Product Manager, and later as Sales Director in the French company Sebia S.r.l. specializing in electrophoresis and biochemistry analyzers. He acted as Sales Director for Ames, an American dry chemistry company, before setting up a subsidiary of Labsystems in France in 1984.

Mirjana Franjevic. *Germany*. Sales and Product Manager of Biohit Deutschland GmbH. With Biohit since October 2000. Qualified as a laboratory technician for industrial chemistry. In 1988-1993 she worked for Roche Diagnostics (R&D) in Switzerland and received experience in the characterization and application of newly developed ELISA -kits for automated systems. In 1994 she moved back to Germany and joined Pharmacia - Wallac Diagnostics and acted until July 2000 as Application Manager for Wallac DELFIA -kits and instruments.

Robert P. Gearty. *U.S.* Managing Director of Biohit Inc. since April 2000. Mr. Gearty earned a B.A. in Biology from St. Michael's College in Winooski, Vermont in 1977. After graduation, Mr. Gearty was employed by Rossignol Ski Company, Williston, Vermont. In 1979, he joined Vangard International, Inc., a U.S. distributor of laboratory products, including the line of liquid handling products manufactured by Labsystems Oy. The association with Dr. Suovaniemi's products continued into the 1990's with Vangard's U.S. introduction and subsequent distribution of the Biohit line of liquid handling products. At Vangard Mr. Gearty most recently served as Sales Manager. In April 2000 Mr. Gearty was appointed Managing Director of Biohit Inc. upon Biohit's acquisition of Vangard International.

Enrico Marzi. *Italy.* Managing Director of Biohit s.r.l. since its establishment in 1992. Mr. Marzi graduated in 1968 with a Diploma of Industrial Chemical Technology from Fabriano High School and further in 1974 with a Degree in Chemistry from Camerino University MC, Italy. Up to 1980 Mr. Marzi acted as Professor of Organic Chemistry and at the same time studied at the Postgraduate School Mario Negri Institute specializing in drug metabolism. He spent 1980 at the Pharmacological Department of the University of Manchester for a specialization in pharmacokinetics. In 1981 he acted as Product Specialist for the EKTACHEM line at KODAK, Italy. In 1982 he joined Farmitalia Carlo Erba Diagnostic Division as Product Manager for Clinical Chemistry Instruments. In 1985 he began to cooperate with Labsystems Oy as consultant in order to study the Italian diagnostic market. In 1986-1991 he acted as General Manager of Labsystems Italy. In 1991 he joined Menari as the Italian General Manager for the Diagnostic Division.

Victor Peppi. *Russia.* Managing Director of Finnbio Ltd. since May 2001. Mr. Peppi graduated in 1999 with a diploma of law from Tcheljabinsk State University and further in 2001 with a degree in Master of Business Administration from the International Management Institute in St. Petersburg. During his studies he worked for the largest subsidiary of the pharmaceutical company Natur Product in Russia - from sales representative to deputy of General Director. In 1999 he relocated to St. Petersburg, and until 2001 he was responsible for the co-ordination of production plans and production capacity at the head office of Natur Product in St. Petersburg to meet the demand of the Russian markets.

Takao Saito. *Japan.* Managing Director of Biohit Japan Co., Ltd. since 1998. With Biohit since 1994. Mr. Saito graduated from the University of Waseda in 1969 with a bachelor of commerce degree. Upon graduation he was employed by a trading company for electronic equipment and parts, and engaged in the export business. In 1975 he joined Nichiryo Co., Ltd., a manufacturer of liquid handling instruments. He started the export business and developed distributor contacts in over 30 countries. Export sales totalled eventually 40% of the total sales of the company. In 1989 he joined Lasertech Co., Ltd., a manufacturer of semiconductor inspection systems and laser scanning microscopes. He stayed in California, U.S. as the executive vice president of Lasertech's U.S. subsidiary and engaged in the sales of these products to major U.S. contacts for 3 years.

Richard Vaughton. *U.K.* Managing Director of Biohit Ltd. since its establishment in 1992. Mr. Vaughton qualified as a medical microbiologist and worked in the U.K. and Saudi Arabia until 1985. He then relocated to Scotland working for Flow Laboratories in microbiology Product Management and export sales. He then moved to Lugano, Switzerland and subsequently to Milan, Italy to work as an International Product Manager for Flow International S.A. After the takeover of Flow Laboratories by ICN Biomedicals, he was appointed Marketing Manager, Microplate Technology at ICN International in the U.K. ICN relocated these offices a year later to California, and Mr. Vaughton left to become a Director of Bio-Consult Ltd., working for an Italian company on a Biosensor project and for a number of other laboratory-focused companies, including Biohit. He also jointly founded and successfully sourced U.K. and U.S. funding for a new company manufacturing laboratory equipment in Scotland, which was later sold to a U.K. public limited company.

SCIENTIFIC ADVISORS

Herman Adlercreutz, *M.D., Ph.D.*, Professor (emer.) of Clinical Chemistry at the University of Helsinki. Director of Folkhälsan Research Center and Head of the Institute for Preventive Medicine, Nutrition and Cancer. At Biohit advisor for diagnostics and laboratory instrumentation. Current focus on the development of test kits for phytoestrogens.

Hannu Harjunmaa, *Ph.D.*, Principal Scientist, VivaScan Corporation, Massachusetts, U.S. At Biohit advisor for liquid handling and laboratory instruments. Current focus on the research and development of new techniques for liquid handling.

Matti Härkönen, *M.D., Ph.D.*, Professor (emer.) of Clinical Chemistry at the University of Helsinki. At Biohit advisor for diagnostics and laboratory instrumentation including liquid handling. Current focus on the gastric test panel.

Frank Laxén, *M.D., Ph.D.*, Consultant Gastroenterologist, Department of Medicine, University of Turku, has actively studied the screening and endoscopic detection of gastric precanceroses and early gastric cancer since 1978. At Biohit advisor for diagnostics.

Aavo Mikelsaar, *M.D., Ph.D.*, Professor at the University of Tartu, Estonia in the field of human biology and genetics. Director of the Institute of General and Molecular Pathology, Medical Faculty. At Biohit advisor for cancer diagnostics.

Arto Orpana, *Ph.D.*, Docent in biochemistry at the University of Helsinki. A clinical biochemist with a back-ground of over 10 years in basic scientific research. At Biohit advisor for diagnostics and instruments (PCR- and liquid handling equipment) and development of PCR- and other applications.

Aarno Palotie, *M.D., Ph.D.*, Professor, University of California Los Angeles, Dept. of Pathology and Laboratory Medicine. Acts at Biohit as an expert in genetic laboratory diagnostics.

Ari Ristimäki, *M.D., Ph.D.*, Docent of Cell Biology, is actively engaged in basic science research (molecular cell biology) at the University of Helsinki and the Helsinki University Central Hospital. At Biohit advisor for diagnostics. Current focus on cyclooxygenase-2, basic research and general applications.

Eeva-Marjatta Salonen, *Ph.D.*, docent. Helsinki University Central Hospital Laboratories, Division of Virology. At Biohit advisor for diagnostics. Current focus on telomere research.

Nils-Erik Saris, *Ph.D.* 1964, M.D. h.c. 1990, Professor (emer.), University of Helsinki. Actively engaged in basic scientific research (biochemistry, biophysics, clinical chemistry). At Biohit advisor for laboratory instruments including liquid handling.

Seppo Sarna, *Ph.D.*, Professor of Biometrics at the University of Helsinki. At Biohit provides biostatistical and epidemiological expertise.

Pentti Sipponen, *M.D., Ph.D.*, Professor, is currently the Head of the Department of Pathology, Jorvi Hospital, Espoo, Finland which is a laboratory engaged in large histopathological routine and research. At Biohit advisor for diagnostics and diagnostic devices. Current focus on the gastric test panel and lactose intolerance test.

Agu Tamm, *M.D., Dr.Med.* Professor of Laboratory Medicine, University of Tartu, Estonia. At Biohit advisor for diagnostics of dyspepsia, hypolactasia and gastric test panel.

Auditors

The auditors of Biohit Oyj are Authorized Public Accountants PricewaterhouseCoopers Oy, Hannele Selesvuo, APA.

CORPORATE GOVERNANCE

Biohit Oyj adheres to the application guideline on the administration of public listed companies issued by the Central Chamber of Commerce of Finland and the Confederation of Finnish Industry and Employers (1997). Moreover, the Board of Directors has ratified a written corporate governance guideline in which the duties and areas of responsibility of the different governance bodies are defined.

The Board of Directors and the President & Chief Executive Officer (CEO) are responsible for the management of the company. The Managing Directors of the subsidiaries and the members of the Management Team assist and support the President & CEO in the management of the company.

GOVERNANCE BODIES

Board of Directors

The Board of Directors, which comprises 3–6 members elected by the Annual General Meeting (AGM), are responsible for the administration of the company and its appropriate organization. The Board elects a chairman among its members. The AGM elects the members of the Board of Directors for one year at a time and simultaneously decides on their remuneration.

In addition to the duties stipulated by law the Board ratifies the operating principles, the business plan and the budget of the Group. Moreover, the Board decides on the possible redirection of operations, organization structure, investments and other significant matters. The decision making of the Board is based on reports drawn up by operative management and auditors on the activities and development of the Group and the business areas.

The Board decides on the internal division of its duties so that the expertise and experience of the Board members can be benefited from in an optimal way. Information on the Board members, their share ownership and division of duties is given on page 45–46.

The Board convened 16 times during 2002.

The total remuneration for the members of the Board totalled EUR 49,627.85.

President and Chief Executive Officer

The President and CEO, appointed by the Board of Directors, is responsible for the day-to-day management of the Group. It is the duty of the President & CEO to manage the operative activities, realization of the budget and to inform the Board of matters related with business operations and administration. The President & CEO reports to the Board of matters pertaining to the business areas and changes taken place monthly and of significant changes immediately. The Board of Directors approves the annual salary and other terms of the President & CEO.

Management Team

The Management Team comprises the President & CEO and the directors of different functions.

Information on the members of the Management Team, their communities of interest and the division of duties is given on page 46–48.

The President & CEO appoints the members of the Management Team and approves the terms of employment in accordance with instructions given by the Board of Directors.

The duty of the Management Team is to assist and support the President & CEO in managing the business areas and administration, and in realizing the budget.

Managing Directors of Subsidiaries

The Managing Directors of subsidiaries and the Boards of Director of the subsidiaries are responsible for the day-to-day management of the subsidiary activities. The Managing Directors of subsidiaries operate under the management and control of the President & CEO and the Director of Administration. The Boards of Director of the subsidiaries are composed of the Managing Director and a necessary number of the members of the Management Team.

The Managing Directors of subsidiaries are responsible for ensuring that the business operations are managed and developed in accordance with the operating principles of the Group.

The President & CEO approves the salaries of the Managing Directors of subsidiaries in accordance with instructions given by the Board of Directors.

Information on the Managing Directors of subsidiaries and their communities of interest is given on page 48–49.

Insiders

Biohit Oyj applies the Guidelines for Insiders approved by the Helsinki Exchanges on October 28, 1999.

Biohit's permanent insiders comprise the members of the Board of Directors, the President & CEO and the members of the Management Team.

Control System

The Board of Directors is responsible for ensuring that accounting and the control of the financial matters of the company are properly managed. The President & CEO is responsible for the operational management of book keeping and financial control.

The President & CEO and Director of Administration are responsible for the operational management of the subsidiaries of Biohit Oyj. The financial administration and auditors support the President & CEO and Director of Administration in this task.

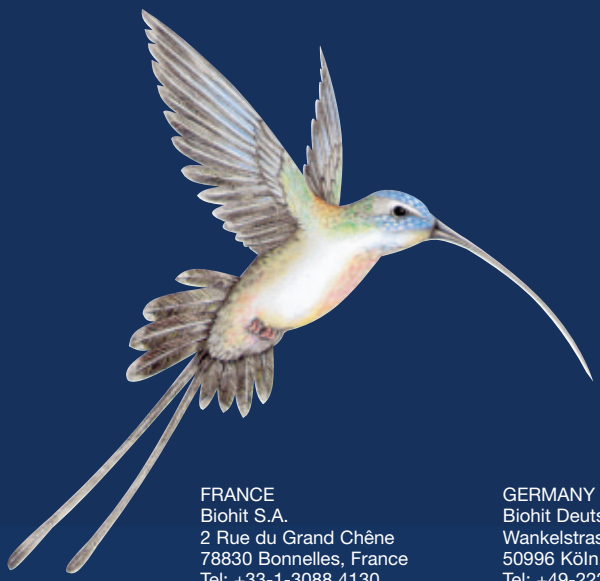
The auditor elected by the AGM is responsible for the audit stipulated by law. In 2002 PricewaterhouseCoopers Oy (Authorized Public Accountants) acted as the auditor of the Biohit Group with Hannele Selesvuo, APA, as the principal auditor. In connection with the publication of the financial statements the auditors issue their statutory report to the shareholders. The auditors report to the Board of Directors and the President & CEO.

MAJOR EVENTS IN BIOHIT'S HISTORY

Year	Events	Net sales EUR 1 000
1988	– Establishment of Biohit Oy – Basic research and market surveys – Electonic pipettor development – Establishment of Locus genex Oy, the current doagnostics division of the Biohit Group	
1989	– TEKES[152] funding received for the development of the electronic and mechanical pipettors, pipettor tips as well as microplates	125
1990	– Worldwide introduction of the electronic pipettor – Assembling of pipettors and injection moulding begins in Kajaani, Finland – Introduction of the first monoclonal antibodies	491
1991	– TEKES funding for the development of mechanical pipettors – First deliveries of electronic pipettors – Establishment of the first subsidiary in France – Introduction of new monoclonal antibodies	2 143
1992	– Launch of the mechanical pipettor – Launch of the multichannel electronic pipettor – Establishment of subsidiaries in Italy and the U.K. – Ph.D. Thesis of Tapani Tiusanen: An application invention of vertical measurement; the self-correcting, multiparameter measuring instrument	4 244
1993	– Launch of the multichannel mechanical pipettor – Co-operation with Eppendorf and bioMérieux begins	6 419
1994	– Development of the renewed electronic pipettor – Co-operation with Ortho Diagnostic Systems of Johnson & Johnson begins – Establishment of joint venture in Japan – Ph.D. Thesis of Osmo Suovaniemi: The vertical measurement invention, its applications and the invention of electronic liquid handling devices	8 425
1995	– Launch of several new liquid handling products – Establishment of subsidiary in Germany – Co-operation with Eastman Kodak Co. Clinical Diagnostic Systems, later acquired by Johnson & Johnson begins	10 550
1996	– Reinforcement of international sales and marketing – Improvement of the cost structure and quality of products – The GastroPanel program begins – Ph.D. Thesis of Sari Ylätupa: An application invention of vertical measurement and immunoassays; the determination of cFn from blood samples and its importance in cancer diagnostics	12 638
1997	– Moving into new facilities in Helsinki – ISO 9001 –quality system certification – Co-operation with Becton Dickinson and 3M begins – Receiving EUREKA[153] status on the basis of which TEKES funding received for the GastroPanel program	14 481

152 TEKES = The National Technology Agency of Finland.
153 EUREKA = Europe-Wide Network for Industrial R & D. A framework through which industry and research institutes from 26 European countries and the European Union develop and exploit the technologies crucial to global competitiveness and a better quality of life.

Year	Events	Net sales EUR 1 000
1998	– Assembling of pipettors and injection moulding begins in Helsinki – Locus genex Oy and Biohit Systems, Inc. become Biohit Group companies – External evaluation of the first test kit (Pepsinogen I) in the GastroPanel program – Ph.D. Thesis of Auli Linnala: Basic research on Biohit's monoclonal antibodies (cFn and tenascin), which are related with cancer diagnostics	16 881
1999	– Listing on the New Market –list of the Helsinki Exchanges – Continuation of aggressive patenting policy	20 551
2000	– Completion of new production premises in Kajaani – Accreditation of the calibration laboratory for liquid handling products – Preparation to commence the global marketing and sales of diagnostic tests and analyzing systems – Commencement of the sales of instruments – Reinforcement of international collaboration and customer service organization through acquisitions in the U.S. and Russia	24 247
2001	– Clinical evaluations carried out in various countries for assessing the reliability of the following diagnostic tests: GastroPanel for diagnosing *Helicobacter pylori* -infection and atrophic gastritis, as well as for screening the risk of gastric cancer and peptic ulcer from blood samples, and tests for diagnosing SLE and lactose intolerance. – Marketing of the GastroPanel begins for research use – Development of test kit for cellular fibronectin (cFn) – Completion of new production premises for diagnostics in Helsinki, Finland – Service laboratory taken into use	25 545
2002	– Launch of the new mLINE mechanical pipettor range – Enlargement of the electronic eLINE pipettor product range – Continuation of the automatization at the production premises in Kajaani	25 354



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