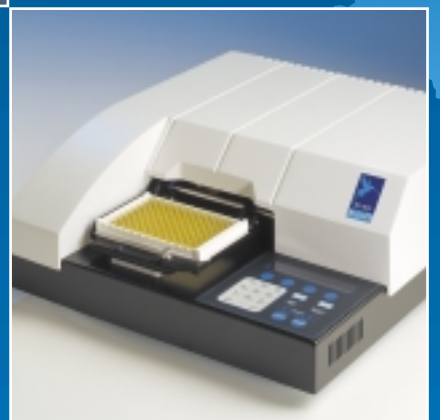


BIOHIT

# ANNUAL REPORT 2001





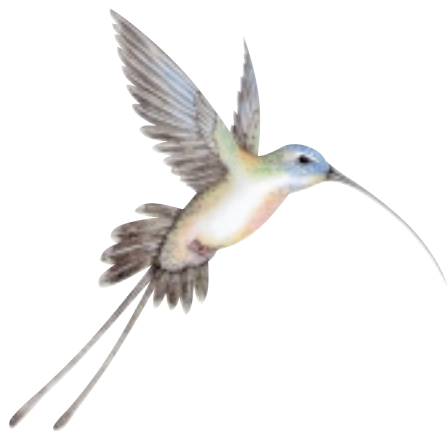
### **Humming Bird**

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 2001

Biohit develops and manufactures liquid handling products and diagnostic test systems for use in health care 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 -electronic pipettors in the world.

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*<sup>1</sup> -infection and atrophic gastritis<sup>2</sup> as well as for screening the risk of gastric cancer and peptic ulcer from blood samples. Moreover, Biohit has tests for the detection of lactose intolerance<sup>3</sup> and systemic lupus erythematosus (SLE)<sup>4</sup>.

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.

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 2001 Biohit's MEUR 25.5 net sales was generated primarily by the sales of liquid handling products and maintenance. Exports accounted for 96 % of the group net sales, and the degree of domestic production was approx. 95 %. In 2001 51 % of the net sales was generated in the European countries, 25 % in North America and the remaining 24 % primarily in Asia.

Biohit listed on the New Market -list of the Helsinki Exchanges in June 1999. In 2001 the share price varied between EUR 3.00 - EUR 7.20. The number of Biohit's shareholders totalled 4,184 on Dec. 28, 2001.

### Highlights in 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, and tests for diagnosing lactose intolerance and SLE.
- Marketing of the GastroPanel began for research use
- Development of a test kit for cellular fibronectin (cFn)<sup>5</sup>
- Completion of new production premises for diagnostics
- Service laboratory taken into use

### Biohit's Mission

Biohit's mission is to promote the well-being and quality of the life of people. In order to achieve this Biohit develops liquid handling products and diagnostic tests as well as analyzing systems composed of these product groups and instruments. These form the foundation for efficient and safe laboratory work and correct treatment, which is based on an accurate diagnosis (evidence-based medicine).

### Biohit's Vision

Biohit's vision to develop into one of the world's leading manufacturers of liquid handling products in the 1990s has been realized. Today Biohit is the global market leader of electronic liquid handling devices, and the range of liquid handling products developed and manufactured by Biohit is the widest in the world. Biohit is also the leading manufacturer of electronic OEM<sup>6</sup> -liquid handling devices. Biohit's vision for the next five years covers, e.g., the following:

- Strong broadening of Biohit's business portfolio with new safe and reliable product solutions and analyzing systems developed for decentralized laboratory diagnostics. These products are expected to promote research, preventive medicine and treatment founded on a correct diagnosis (evidence-based medicine)
- Taking efficiently advantage of market potential and promoting Biohit's new products towards global market leadership

### Biohit's Values

- Development of the competence and creativity of personnel and adoption of a common corporate culture
- Promoting the safety and well-being of Biohit's personnel, customers and co-operation partners (researchers, doctors and patients)
- Profitability through ethically sound operating principles

1 *Helicobacter pylori* (*H. pylori*) causes atrophic gastritis and is related with the development of gastric cancer and peptic ulcer.

2 Atrophic gastritis refers to a loss of normal mucosal glands of the stomach, which is nearly always caused by prolonged *H. pylori* -infection. *H. pylori* -infection causes always an inflammation (gastritis) in the stomach.

3 Lactose intolerance is caused by the lack of the lactase enzyme, which breaks down milk sugar (lactose), in the mucosa of the small intestine.

4 Systemic Lupus Erythematosus (SLE) is a connective tissue disease which resembles rheumatic diseases.

5 An increase in the level of cFn in blood is related with the development of cancer in the gastrointestinal tract.

6 Original Equipment Manufacturer, i.e., the production of tailor-made products for customers.

## Key Financial Indicators (Group)

(EUR 1000 unless stated otherwise)	1997	1998	1999	2000	2001
Net sales	14 481	16 881	20 551	24 247	25 545
Change in net sales, %	14.6	16.6	21.7	18.0	5.4
Operating profit/loss	414	1 387	1 332	-482	237
% of net sales	2.9	8.2	6.5	-2.0	0.9
Profit/loss before extraordinary items and income taxes	176	451	825	-580	55
% of net sales	1.2	2.7	4.0	-2.4	0.2
Profit/loss before taxes	158	1 141	1 162	-341	55
% of net sales	1.1	6.8	5.7	-1.4	0.2
Return on equity, %	* 7	12.1	3.8	-4.6	-1.3
Return on investment, %	10.8	12.2	8.5	-0.8	2.0
Equity ratio, %	-5.1	38.8	66.0	66.9	65.7
Investments in fixed assets	867	1 392	1 271	6 208	2 212
% of net sales	6.0	8.2	6.2	25.6	8.7
Research and development expenses	622	740	1 270	1 698	2 114
% of net sales	4.3	4.4	6.2	7.0	8.3
Total assets	12 415	18 435	24 699	24 626	24 996
Personnel, average	154	164	184	222	289

## Share Capital, Shares and Key Ratios

	1997	1998	1999	2000	2001
Number of shares, end of fiscal year	6 253 537	10 264 537	12 264 537	12 643 377	12 643 377
Key Ratios					
Earning per share (EPS), EUR (group)	0.03	0.06	0.04	-0.06	-0.02
Shareholders' equity per share, EUR	-0.11	0.69	1.33	1.30	1.28

## Turnovers and Prices of Shares

Year	Turnover EUR	Turnover Shares	Average Price EUR	Lowest Price EUR	Highest Price EUR	Closing Price EUR	Market Capitalization EUR <sup>8</sup>
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	3 646 849.00	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

## Financial Information of Biohit in 2002

- Publication of the financial statements: March 15
- Annual General Meeting: March 27 at Restaurant Pörssi, Fabianinkatu 14, 00100 Helsinki
- Interim Report 1-3/2002: May 8
- Interim Report 1-6/2002: August 7
- Interim Report 1-9/2002: November 6

<sup>7</sup> Return on equity negative.

<sup>8</sup> 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 PRESIDENT**



*Osmo Suovaniemi, President & CEO*

Biohit's mission is to promote the well-being and quality of the life of people. In order to achieve this Biohit develops liquid handling and diagnostic products, which form the foundation for efficient and safe laboratory work and correct treatment based on an accurate diagnosis. Biohit's core value is the understanding of the needs of its personnel, co-operation partners and customers (researchers, doctors and patients). In order to be successful in this work and in taking care of its responsibilities even better in the future, Biohit focuses to an increasing extent also on good corporate governance.

Biohit's vision for the next five years is to maintain its position as one of the three leading manufacturers of liquid handling products in the world, and as the global market leader of electronic pipettors. Liquid handling and measurement instruments form, together with the diagnostic tests, synergistic systems which promote targeted treatment based on an accurate diagnosis (evidence-based medicine).

**Liquid Handling: New Market Segments and Improved Safety**

The size of the global market for liquid handling products (pipettors and tips) is approx. USD 500 million. The share of tips of this market is over half. In 2001 Biohit continued its aggressive innovation and patenting strategy. The

development of new technologies has formed a basis for capturing new markets segments. The market potential of these segments may increase the size of the existing liquid handling market to a level of USD 1.5 billion. Currently a strong demand exists for pipettors which contribute to safe laboratory work.

In 2001 Biohit launched the new electronic eLINE®-pipettor which promotes reliability in liquid handling and reduces risks for work-related upper limb disorders. Biohit's ePET®-range, competing with mechanical pipettors, contributes also to safety-at-work. Biohit believes that the ePET®, as a result of its more user-friendly properties, will capture a significant portion of the over 1,000,000 pieces market of mechanical pipettors.

The current market size of electronic pipettors is only approx. 50,000 units annually. Biohit has captured a 60% share of this market. The electronic R-Line, a pipetting module for automated liquid handling and analyzing systems, is opening up new market segments for Biohit. Biohit's new range of mechanical pipettors, which promotes high quality and safe laboratory work, and is currently under development will, in the coming years, compete in the high price market segment for mechanical pipettors. The size of this segment is approx. 600,000 units annually.

Biohit's maintenance and calibration services for pipettors demonstrated a significant growth in 2001. Moreover, Biohit continued to offer OEM-products for such customers as 3M and Johnson & Johnson, who complement their diagnostic product ranges with Biohit's tailor-made electronic pipettors. Biohit's patented products, which also conform with international standards of quality, enable to continue this long-term co-operation.

**Treatment Based on a Correct Diagnosis**

Biohit has researched and developed diagnostic tests and related technologies for over ten years. As a result, Biohit possesses a large number of hybridomas<sup>9</sup> for the limitless production of monoclonal antibodies<sup>10</sup>. Approx. 30 of these antibodies are used for the detection of different types of cancer from tissue samples. Plant estrogen antibodies are used for research, and in the future also for tests, which measure the levels of plant estrogens in the body. Plant estrogens prevent, e.g., the development of breast cancer and cancer of the large intestine. Certain monoclonal antibodies are the key components of diagnostic test kits.

In 2001 Biohit's test kits were delivered to hospitals and researchers for testing and clinical use both in Finland and abroad. Numerous scientific publications have been drawn up on the basis of these results, and many are currently in progress. Biohit's tests are protected in Finland and abroad by patents and patent applications.

Nearly half of the world population suffer from intestinal symptoms caused by milk sugar, i.e., lactose. Every sixth person in Finland, 90 % of the population in Southern Italy and nearly everyone in Thailand suffer from lactose intolerance<sup>11</sup>. Biohit has developed a POC-test<sup>12</sup>, which enables to detect from tissue samples taken in

9 A somatic cell hybrid formed by a fusion of cells.  
 10 A common antibody produced by plasmocytoma cells belonging to the same cell clone (all cells produce the same antibody). Milstein and Köhler received the Nobel prize in 1984 for inventing monoclonal antibodies.  
 11 Palotie L. (2002). In the Beginning All Suffered from Lactose Intolerance. *Helsingin Sanomat* 11.2.  
 12 Point-of-Care (POC) -test is performed close to the patient.

connection with gastroscopy whether the patient suffers from lactose intolerance, i.e., whether the activity of the lactase enzyme present in the cells of the intestine has decreased.

Moreover, Biohit has a unique test for determining systemic lupus erythematosus (SLE) from blood samples. SLE is a prototype of autoimmune diseases, which with its various symptoms resembles rheumatic diseases. 0.1-0.4% of the world population suffer from SLE. Approx. 2% of the global population suffer from rheumatic diseases. The SLE-test will complement the tests used for diagnosing rheumatic diseases. Since Biohit's tests for detecting lactose intolerance and SLE improve the reliability of diagnostics, and simultaneously contribute to reducing health care expenses, it can be estimated that demand will exist for these tests on the world market.

Biohit's GastroPanel and the GastroSoft-program interpreting the results ([www.biohit.com](http://www.biohit.com)) facilitate especially the work of general practitioners when determining the causes of dyspepsia<sup>13</sup> or whether the patient suffers from atrophic gastritis<sup>14</sup> caused by *H. pylori* -infection. Until now gastroscopy and the microscopic examination of biopsy samples has been the only means for diagnosing these diseases and their severity. Gastroscopy is relatively expensive, unpleasant for the patient and it is not often available immediately. Thus, the doctor often relies on trial treatments, which are expensive and seldom successful. At worst the trial treatments delay the diagnosis of the disease and may even result in the death of the patient.

Approx. 30%, i.e., nearly two billion persons suffer from dyspepsia<sup>15</sup>. If the symptoms of the dyspeptic patient or his overall condition do not indicate any severe disease, the GastroPanel serves as the primary means for a general practitioner to study the causes of dyspepsia. In over half of the cases the causes of dyspepsia are functional, i.e., the results of the examination of biopsy samples and those produced by the GastroPanel are normal.

Over half of the global population, i.e., approx. three billion persons suffer from *H. pylori* -infection and related inflammation of the mucosa, i.e., gastritis. Half of these patients will eventually suffer from atrophic gastritis which increases the risk of gastric cancer and peptic ulcer<sup>16</sup>. The screening and early diagnosis of atrophic gastritis, which is often symptomless, contribute to the prevention of gastric cancer and peptic ulcer and effective treatment.

GastroPanel and GastroSoft enable to diagnose *H. pylori* -infection which causes atrophic gastritis, the severity of atrophic gastritis and in which part of the stomach (corpus, antrum or both) the gastritis is located. GastroSoft also draws up risk factors for possible gastric cancer and peptic ulcer. Moreover, the program provides a recommendation for treating *H. pylori* -infection and recommendations for further examinations (gastroscopy and the measurement of the levels of vitamin B12 and

homocysteine in blood). GastroPanel enables to find those patients who, in accordance with the Maastricht 2000 consensus<sup>17</sup> need immediately *H. pylori* -eradication, gastroscopy and the examination of biopsy samples in order to diagnose possible gastric cancer or peptic ulcer.

The atrophy of the corpus area of the stomach caused by *H. pylori* -infection leads to a deficiency of vitamin B12. This, on its part, may lead to dementia and damages of the peripheral nervous system ([www.b12.com](http://www.b12.com)). The lack of vitamin B12 increases the level of homocysteine in the body, which is a risk factor for atherosclerosis and heart and brain strokes ([www.homocysteine.com](http://www.homocysteine.com)). The GastroPanel-examination opens up new possibilities for the prevention and treatment of these diseases.

In order to promote the adoption of the GastroPanel worldwide Biohit focuses on informing general practitioners and clinical and service laboratories in co-operation with different national experts and medical companies. The ultimate objective of doctors and medical companies is the diagnosis of the causes of stomach pains and related targeted treatment (evidence-based medicine). In addition, Biohit aims to inform also the general public of the benefits of the GastroPanel. The reasons for this are:

- Patients suffering from stomach pains and disorders do not prefer to undergo trial treatments but instead wish to be examined before commencing treatment. Instead of the expensive and unpleasant gastroscopy the GastroPanel-examination done from a blood sample reduces the need for trial treatments, promotes evidence-based medicine and the well-being of patients, and decreases health care costs.
- GastroPanel is suitable for the screening of patients belonging to risk groups and it complements other examinations. For example, elderly and weak patients, over 50 years old men who smoke, those suffering from reflux disease<sup>18</sup> and persons whose relatives have suffered from gastric cancer belong to the risk groups.
- GastroPanel is suitable also for such healthy individuals who wish to follow their health in a similar manner as, e.g., the levels of lipids are followed.
- As to occupational health services, the GastroPanel provides additional information on the health of the employee. As to the prevention of diseases, it is more comfortable for the patient and contributes to reducing health care costs.

Biohit's GastroPanel and GastroSoft enable especially general practitioners to reach a more accurate diagnosis, which forms the basis for targeted treatment. Decentralized laboratory diagnostics, which is rapidly available and performed close to the patient and doctor, promotes strongly evidence-based medicine.

### Analyzing Systems for Research Use and Decentralized Laboratory Diagnostics

Biohit's analyzing systems, which are composed of liquid handling products, diagnostic tests, instruments and related software, are well suited for research use and clinical laboratories. The flexibility and ease-of-use of this reasonably priced system can be estimated to increase its use in Finnish health care centers and private medical

13 Dyspepsia refers to pain or discomfort in the upper part of the stomach.

14 Atrophic gastritis refers to a loss of normal mucosal glands of the stomach, which is nearly always caused by prolonged *H. pylori* -infection. *H. pylori* -infection causes always an inflammation (gastritis).

15 Knill-Jones R.P. (1991). Geographical Differences in the Prevalence of Dyspepsia. *Scand. J. Gastroenterol.* 26 Suppl 182: 17-24.

16 Sipponen P., Härkönen M., Alanko A. (2001). Determination of Atrophic Gastritis from Serum Samples. *Finnish Medical Journal* 38: 3833-3839. Sipponen P. et al. (submitted in 2002). Serum Levels of Amidated Gastrin-17 and Pepsinogen I in Atrophic Gastritis: An Observational Case-Control Study. *Scand. J. Gastroenterol.* See also [www.biohit.com](http://www.biohit.com).

17 Updated guidelines on the management of *H. pylori* -infection drawn up by European general practitioners, national gastroenterological societies and specialists from around the world in 2000.

18 The reflux disease causes the backward flow of the contents of the stomach to the esophagus.

centers. This is especially the case when the system is marketed in connection with Biohit's diagnostic tests. As a result, as laboratory diagnostics moves close to the patient and the doctor, it is possible to improve the quality of diagnostics and related treatment of patients suffering from dyspepsia and atrophic gastritis. Biohit's analyzing system is also suitable for all immunoassays which are based on the extensive use of multichannel pipettors<sup>19</sup>, vertical measurement<sup>20</sup> and microplates<sup>21</sup> all over the world. Hundreds of such immunoassays are available, e.g., for the diagnosis of infectious and cancer diseases.

Biohit aims to develop a rapid and automated analyzer for decentralized laboratory diagnostics. This analyzer will employ the concepts of multichannel pipetting, the microplate and the vertical measurement principle. By employing these innovations numerous companies both in Finland and abroad have during the past three decades reached rapid and profitable growth. The products of these companies have formed the basis, e.g., for the development of the aforementioned immunoassays and gene research. For the area of gene research Biohit is developing a new instrument. This instrument is related with the techniques of multichannel pipetting, microplates and vertical measurement which are used in studying the structures and functions of genes and diseases caused by gene defects. These techniques have contributed to the development and extensive use of the HTS<sup>22</sup>- and PCR<sup>23</sup>-techniques.

**Production Capacity and Channels for Capturing New Markets**

During the past ten years Biohit has in an exceptional way been able to develop simultaneously its products and production technologies and establish a global co-operation and customer service network. Our success has not been random but has been based on the experience of our personnel in Finland and abroad in the area of biotechnology. Biohit's management and key personnel have since the 1970s been leading and internationally renowned pioneers in the global business of biotechnology and related technologies. We have created standards for research, laboratory work and diagnostics<sup>24,25</sup>, which have served as examples and bases for success for numerous companies. These standards have promoted research and the development of laboratory practices and diagnostics worldwide<sup>26</sup>.

Our new production plant, which was taken into use in Kajaani in fall 2000, enables to quadruple the current production volume of liquid handling products. The Helsinki unit offers additional capacity for the injection molding of pipettors and other plastic components and for the pilot and mass production of new pipettors. In March 2001 the clean room unit for the production of diagnostic tests was taken into use in Helsinki. One of Biohit's strengths is that our production has not been externalized. Instead, we use to a certain extent reliable subcontractors. In this way Biohit has control of the core production technologies and costs.

Biohit's sales and marketing network covers all continents. Our seven subsidiaries and 60 main distributors together with their customer service networks contribute to strengthening the Biohit brand and company image all over the world. Co-operation with multinational companies has enabled us to enter such market segments which otherwise would be beyond our reach. Our co-operation partners include, e.g., Beckman Coulter, Becton Dickinson, bioMérieux, Johnson & Johnson and 3M.

During 2001 Biohit strengthened its co-operation with researchers and scientific communities in Finland and abroad. The purpose of this is to promote especially the extensive adoption of our diagnostic products. Likewise, we are beginning to co-operate with large service laboratory chains in different countries. The future poses many challenges and much work for our co-operation partners and us when striving towards capturing new markets.

I express my sincere gratitude to Biohit's personnel in Finland and abroad, to the over 4,000 shareholders and other interest groups for the trust you have demonstrated towards Biohit. We are engaged in valuable and successful co-operation for the benefit of both research and human well-being.

Helsinki, February 22, 2002

Yours sincerely,



Osmo Suovaniemi, M.D., Ph.D.  
President & CEO

19 Suovaniemi O. U.S. -patents 3,855,868, 4,058,370 and 4,215,092 have expired and are currently in general use.

20 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. Suovaniemi O.: Canadian patent 1,031,183, U.K. -patent 1,486,210 and U.S. -patents 4,144,030 and 4,290,997 have expired and are currently in general use.

21 Biohit's U.S. -patent 5,308,584: *Cuvette Matrix Tray*.

22 High Throughput Screening (HTS) refers to the study of large amounts of samples especially in gene and medical research.

23 Polymerase Chain Reaction (PCR) -technique is used for the amplification of small amounts of DNA. Kary Mullis received the Nobe prize in 1993 for inventing the PCR-technique in 1982.

24 Inventions by Osmo Suovaniemi in the 1960-1970s: the adjustable single- and multichannel mechanical pipette (Finnpipette) and the vertical measurement principle together with its numerous applications (e.g. Multiskan). Finnpipette and Multiskan are trademarks of Labsystems Oy. Applications of Biohit's electronic pipettors are used, e.g., by Becton Dickinson, bioMérieux, Eppendorf, Johnson & Johnson and 3M.

25 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.

26 TEKES (2001). *Paving the Way for Evidence-Based Medicine: Diagnostics 2000*.



## BIOHIT GROUP

### Biohit's Competence

Biohit's present management and certain key persons developed and commercialized successfully two inventions made by Dr. Osmo Suovaniemi in the 1970s. The inventions were the single- and multichannel, adjustable, mechanical pipettes (Finnpipettes<sup>27</sup>) and vertical light path photometry together with its instrument applications (e.g. Multiskan<sup>28</sup>).

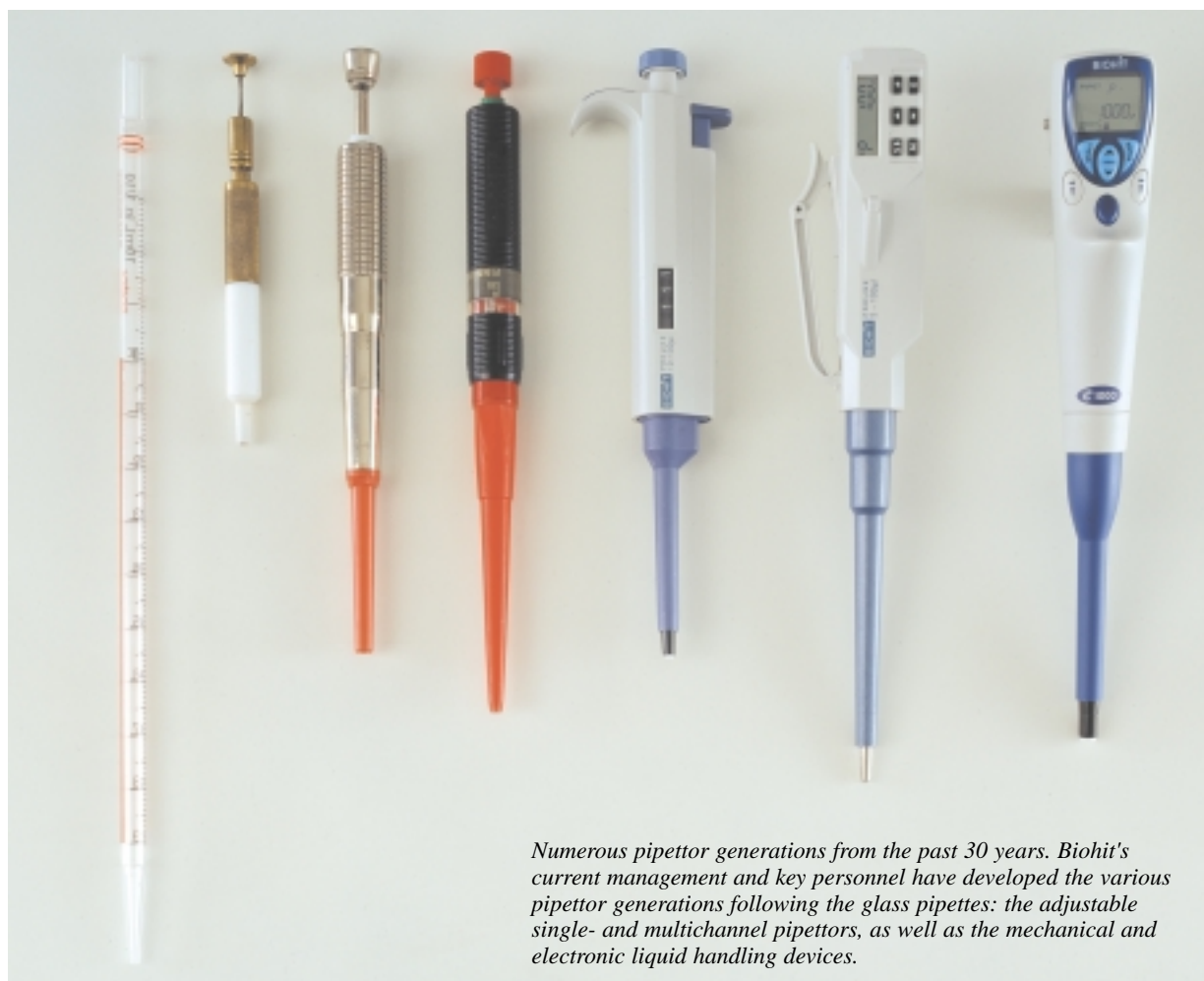
These inventions have been utilized so extensively that they can justifiably be called global industrial standards. The liquid handling instruments and systems based on these inventions served as the foundation for Labsystems and joint venture Eflab, the companies founded by Dr. Suovaniemi in the 1970s, and subsequently for the global business of numerous other companies. The value of the global business for products based on the above inventions exceeds today USD 1.5 billion annually. 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."<sup>29</sup>

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.

### Biohit's Business Environment

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 products used in PCR-<sup>30</sup> and HTS<sup>31</sup>-applications. The Nobel prize winning production method of monoclonal



*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.*

27, 28 Finnpipette and Multiskan are trademarks of Labsystems.

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

30 The Polymerase Chain Reaction (PCR) technique is used for the amplification of small amounts of DNA.

31 High Through-Put Screening (HTS) refers to the study of large amounts of samples.

antibodies<sup>32</sup> and the PCR-technique<sup>33</sup> 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<sup>34</sup>.

### **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 collaboration with leading researchers at universities and research institutions. 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.



*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.*

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.

Biohit's first vision to develop into one of the leading manufacturers of liquid handling products in the world in the 1990s has been realized. Despite increasing competition Biohit's global market share for electronic liquid handling devices continues to be approx. 60%, and the liquid handling product range developed and manufactured by Biohit is currently the widest in the world. Biohit is also the leading manufacturer of electronic OEM-liquid handling devices. Biohit's diagnostic tests, which are based on biotechnology, have guided the development of the liquid handling products, instruments and related software into synergistic analyzing systems.

These systems as well as the majority of their parts are expected to become dominant designs and industrial standards on the global market. Parts of these systems, e.g., liquid handling products, instruments and microplates, are used in connection with PCR-methods and DNA-chip technologies. Biohit's aim is to gain a significant market position also in these rapidly growing areas.

Biohit has defined a new vision which extends until 2005. Its core idea is to actively broaden Biohit's business portfolio on the basis of the liquid handling products, which have developed into industrial standards and global market leaders, to new synergistic product areas. Biohit's objective is to transfer these system businesses from the R&D phase to the global business phase via its extensive network of specialists, co-operation partners and customer service units.

### **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,

32 Milstein and Köhler received the Nobel prize for inventing monoclonal antibodies in 1984.

33 The PCR-technique was invented in 1983 by Kary Mullis, who received the Nobel prize for it in 1993.

34 MeritaNordbanken Research 6.3.2000



*Biohit's research and development combines the expertise of various fields into integrated know-how.*

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 the area of liquid handling Biohit continued to invest in the development of new pipettor generations in 2001. This development work is based on Biohit's 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 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 ulcer 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 2001 Biohit's R&D expenditure totalled MEUR 2.1.

### 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.

The management and key personnel of Biohit have numerous patents and 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<sup>35,36</sup> and a few hundred abroad in the fields of medical diagnostics, optics and mechanics.

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. Also for this reason, the seven sales and marketing subsidiaries of Biohit have continued to grow and develop favorably. Likewise, the distributor network comprised of approx. 60 main distributors worldwide has increasingly invested in the sales and marketing of Biohit's products. Biohit will continue to pay special attention to the development and protection of its multidisciplinary immaterial assets also in the future.

At the end of 2001 Biohit possessed altogether 51 patents of which 26 were Finnish, 10 U.S., 4 European, 4 Japanese and 7 others. In the area of liquid handling Biohit was awarded the following Japanese patents: JP 3168296 (Procedure for Locking the Adjustment Means of a Pipette, and Pipette), JP 3215859 (Pipette), JP 3215860 (Procedure for Filling and Emptying a Pipette, and Pipette) and JP 3240374 (Pipette), and the following Finnish ones: FI 107025 (Suction Device with Means for Removing a Replaceable Tip), FI 107026 (Tip for a Suction Device), FI 107027 (Suspension Device) and FI 108281 (Suction Device). In the area of diagnostics Biohit was awarded the Finnish patent FI 107808 (Method for Identifying an Individual at Risk for Vascular and Cancer Diseases) and three foreign ones. In 2001 Biohit filed numerous Finnish and international patent applications.

### 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.

The new production premises for diagnostic tests were completed and taken into use in Helsinki in 2001. All Biohit's diagnostic tests are produced in these premises. The premises enable to move from the pilot production of diagnostics to their mass production.

<sup>35</sup> *Tekniikka ja Talous* (Technology and Economy) 8.2.2001: 11  
<sup>36</sup> *Keksintöuutiset* (Innovation News). (2001). 4-5: 7.

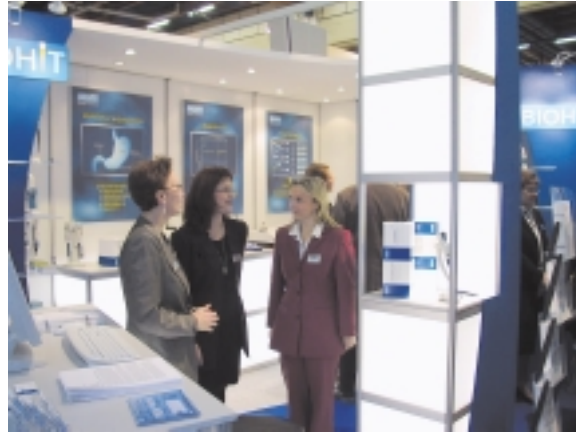
## International Sales and Marketing

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 2001 international sales accounted for approx. 96% of the overall MEUR 25.5 group net sales. The share of subsidiary sales of the group net sales was 75%. In 2001 51% of the net sales were generated in Europe, 25% in North America and the remaining 24% primarily in Asia. The net sales consisted primarily of the sales of liquid handling products.



*Biohit participates annually in numerous medical exhibitions. Biohit at the Finnish Medical Convention and Exhibition in January 2002.*



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

## LIQUID HANDLING



*Biohit is the leading manufacturer of electronic liquid handling devices in the world. In 2001 Biohit launched the new generation eLINE® -product range which was developed for most demanding liquid handling applications. The eLINE®-range received an honorary mention in the Pro Finnish Design 2001 -competition arranged by Design Forum Finland.*

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 slightly 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<sup>37</sup>- and CE<sup>38</sup>-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 for numerous Finnish 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.

<sup>37</sup> Geprüft Sicherheit (GS): A German product safety standard.

<sup>38</sup> Les Communautés Européennes (CE) -marking is a guarantee for authorities, importers and sellers that the product fulfils the requirements set by the European Union.

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 2002-2005 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. As a result, it has been estimated that the potential for the existing markets and new market segments will reach USD 1.5 billion.

### 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.



*The structure, ergonomical design and light weight of Biohit's electronic pipettors take much of the strain out of pipetting and, thus, reduce significantly and help to prevent the development of work-related upper limb disorders. Moreover, the microprocessor-controlled electronic pipettors contribute to minimizing human error 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<sup>39</sup> to 100 ml. They have opened up new dimensions in liquid handling technology in terms of precision, ergonomics and functionality. The ergonomic 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.<sup>40,41,42,43,44,45</sup> 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<sup>46</sup>.

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



*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.*

contamination and, as a result, the sample from carryover, e.g., in genetic studies<sup>47,48</sup>. 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.

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 ergonomic 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 ergonomic 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 1,000,000 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 ergonomic 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<sup>49,50</sup>.

<sup>39</sup> 1 µl = one millionth part of a liter.

<sup>40</sup> 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.

<sup>41</sup> Björkstén M.G., Almy B., Jansson E.S. (1994). Hand and Shoulder Ailments among Laboratory Technicians Using Modern Plunger-Operated Pipettes. *Applied Ergonomics* 25: 88-94.

<sup>42</sup> Fredriksson K. (1995). Laboratory Work with Automatic Pipettes: A Study on How Pipetting Affects the Thumb, *Ergonomics* 38 (5): 1067-1073.

<sup>43</sup> McGlothlin J.D., Hales T.R. (1995). NIOSH (National Institute of Occupational Safety and Health) *Health Hazard Evaluation Report*.

<sup>44</sup> Hodgson E. (1996). Work Related Upper Limb Disorders and the Laboratory. *World Directory of Environmental Testing, Monitoring and Treatment*.

<sup>45</sup> 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.

<sup>46</sup> 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.

<sup>47</sup> 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.

<sup>48</sup> Suovaniemi O. (2000). Finnish patent 104885: Filter.

<sup>49</sup> 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.

<sup>50</sup> 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.*

### Disposable Tips

The pipettors and injection molded plastic disposable tips manufactured by Biohit form together a reliable system<sup>51,52</sup>. 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.

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<sup>53</sup> 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 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
	1 000 µl	0.520 µl
	5 000 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.<sup>54</sup> The number of Biohit's accredited calibration laboratory is K041.

51 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.

52 Mannonen S., Tiusanen T., Suovaniemi O. (2000). Major Sources of Error of Air Displacement Pipettors. *International Labmate*, April.

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

**Liquid Handling in 2001**

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<sup>55,56</sup>.

In 2001 Biohit launched the single-channel models of the eLINE®-range, a new generation of electronic pipettors. The multichannel models will be launched in 2002. The eLINE® received an honorary mention on Feb. 1, 2001 in the Pro Finnish Design 2001 -competition arranged by Design Forum Finland.

The eLINE®-electronic pipettors offer the latest technology in the field of hand-held liquid handling. The range was designed to meet the most demanding pipetting applications offering, e.g., eleven liquid handling protocols for the various needs of today's laboratories. The micro-processor-controlled system and the novel construction of the eLINE®-pipettors enable maximum liquid handling performance with high levels of accuracy and precision. The ergonomical design of the eLINE® together with unique electronic tip ejection are examples of Biohit's continuous efforts to improve further the ergonomics and competitiveness of pipetting.

In the area of electronic liquid handling Biohit continued the development of OEM-products, which complement the product ranges and diagnostic systems of other companies. For example, Biohit developed for a Swiss company an application which is based on the eLINE®-concept. The application is connected to an instrument, and the system is used for measuring the factors affecting blood coagulation in operating rooms.

**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.



Biohit participated in the Digestive Disease Week Symposium in the U.S. in 2001. In the middle professor Barry Marshall who together with professor Robin Warren isolated the *H. pylori* in 1982. On the left professor Pentti Sipponen and on the right professor Matti Härkönen, who are both Biohit's co-operation partners and scientific advisors in the area of diagnostics.

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

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



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 aspirin. 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 (carcinogenicity 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<sup>57</sup>. 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%<sup>58</sup>. 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 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.

## GastroPanel and GastroSoft™

Biohit has developed a unique test panel (GastroPanel), which enables to determine from a blood sample whether the patient suffers from gastritis caused by *H. pylori* -infection, whether the gastritis is atrophic and in which part of the stomach the changes are located. This is done by measuring the levels of Pepsinogen I and Gastrin-17, and the *H. pylori* -antibodies from a blood sample. The test panel enables to identify those patients whose risk of gastric cancer and peptic ulcer have considerably increased and, as a result, need to be directed immediately to gastroscopy and the examination of biopsy samples.<sup>59,60,61</sup> The development of the test panel is based on, e.g., studies carried out during the past ten years<sup>62,63,64,65,66,67</sup> in which the prevalence of premalignant and malignant lesions in the stomach of ca. 22,000 males in Finland has been investigated<sup>68, 69,70,71</sup>.

The research carried out thus far has demonstrated that the results of the GastroPanel are in practice equally reliable as those received with gastroscopy and the

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- 70 Sipponen P., Marshall B.J. (2000). Gastritis and Gastric Cancer - Western Countries. *Gastroenterol. Clin. North. Am.* 29: 579-592.
- 71 Sande N., Nikulin M., Nilsson I., Wadström T., Laxén F., Härkönen M., Suovaniemi O., Sipponen P. (2001). Increased Risk of Developing Atrophic Gastritis in Patients Infected with CagA+ *Helicobacter pylori*. *Scand. J. Gastroenterol.* 9: 928-933.

57 Lim D. (1996). Microbiology, 2nd ed.: 522.

58 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.

examination of biopsy samples. This applies to cases when it is necessary to find out whether the mucosa of the stomach is healthy or whether it is inflamed or atrophic (atrophic gastritis). The research results support the argument that Biohit's test panel is suitable as an initial and easy method for examining dyspeptic patients. Nearly always a correct diagnosis is reached whether it is a case of a healthy, normally functioning mucosa or whether it is inflamed, atrophic and does not function normally.

Especially in case of younger patients over half of dyspeptic symptoms are functional (functional dyspepsia). These cases can be differentiated from organic symptoms by using Biohit's test panel. If the test panel demonstrates that the mucosa of the stomach is healthy this means that the symptoms are most likely functional and are not caused by a peptic ulcer. The risk of gastric cancer and peptic ulcer is very low, nearly nonexistent, if the stomach is healthy.

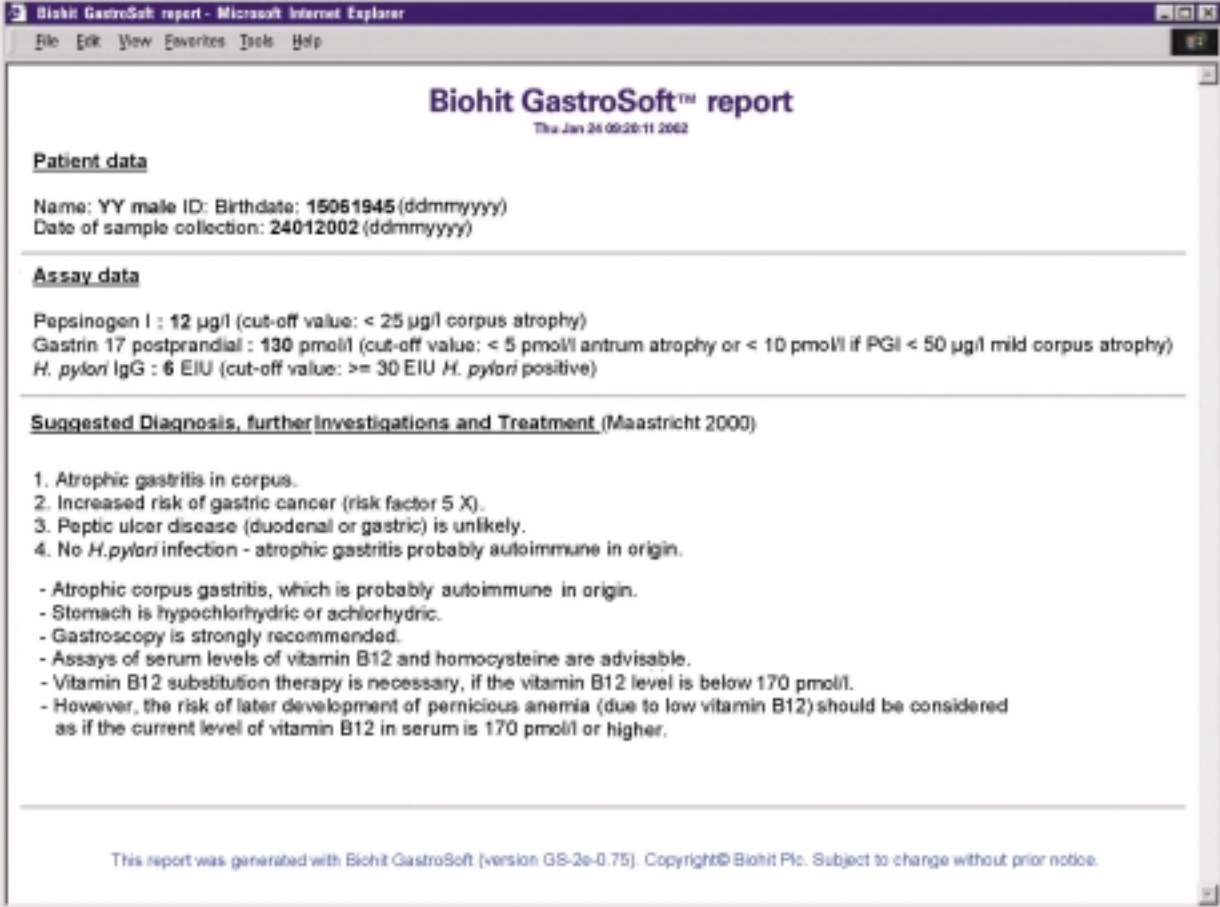
In 2001 altogether 292 patients suffering from dyspepsia were examined in a multicenter study carried out currently in Finland. The results of gastroscopy and examination of biopsy samples as well as Biohit's GastroPanel demonstrated that the mucosa of 149 patients was normal, and 30 patients suffered from advanced atrophic gastritis. The mucosa of the stomach of 80% of the patients examined was healthy or its surface was mildly inflamed (gastritis). There is no need for immediate

gastroscopy or the examination of biopsy samples for confirming the results of such patients if the patient does not suffer, e.g., from reflux disease, inflammation of the esophagus, use analgesics, have an exceptionally high cancer risk, or if the dyspeptic patient is not over 45 years. On the basis of the results 45 persons out of the 292, would have needed, on the basis of the results produced by the GastroPanel, gastroscopy and examination of the biopsy samples due to severe atrophic gastritis, related risks and possible diseases.

For the interpretation of the results produced by the GastroPanel Biohit has developed an easy-to-use computer program (GastroSoft). The laboratory results are entered into the program after which the program draws up a recommended diagnosis of possible *H. pylori* -infection and atrophic gastritis. Moreover, the program indicates the patient's risk of gastric cancer and peptic ulcer compared with normal population. The program further gives a recommendation based on the Maastricht 2000 -consensus whether eradication therapy of *H. pylori* -infection is necessary as well as an instruction whether gastroscopy, examination of biopsy samples and the measurement of the levels of vitamin B12 and homocysteine are necessary. The interpretation of the test results gained is normative; ultimately the doctor is responsible for additional examinations and the overall treatment of the patient. The program can be tried out at [www.biohit.com](http://www.biohit.com).



*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.*



**Biohit GastroSoft™ report**  
Thu Jan 24 09:28:11 2002

**Patient data**  
Name: YY male ID: Birthdate: 15061945 (ddmmyyyy)  
Date of sample collection: 24012002 (ddmmyyyy)

**Assay data**  
Pepsinogen I : 12 µg/l (cut-off value: < 25 µg/l corpus atrophy)  
Gastrin 17 postprandial : 130 pmol/l (cut-off value: < 5 pmol/l antrum atrophy or < 10 pmol/l if PGI < 50 µg/l mild corpus atrophy)  
H. pylori IgG : 6 EIU (cut-off value: >= 30 EIU H. pylori positive)

**Suggested Diagnosis, further investigations and Treatment (Maastricht 2000)**

1. Atrophic gastritis in corpus.
2. Increased risk of gastric cancer (risk factor 5 X).
3. Peptic ulcer disease (duodenal or gastric) is unlikely.
4. No H.pylori infection - atrophic gastritis probably autoimmune in origin.

- Atrophic corpus gastritis, which is probably autoimmune in origin.
- Stomach is hypochlorhydric or achlorhydric.
- Gastroscopy is strongly recommended.
- Assays of serum levels of vitamin B12 and homocysteine are advisable.
- Vitamin B12 substitution therapy is necessary, if the vitamin B12 level is below 170 pmol/l.
- However, the risk of later development of pernicious anemia (due to low vitamin B12) should be considered as if the current level of vitamin B12 in serum is 170 pmol/l or higher.

This report was generated with Biohit GastroSoft (version GS-2e-0.75). Copyright© Biohit Plc. Subject to change without prior notice.

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 gastric cancer and peptic ulcer. In addition, the program gives a recommendation based on the Maastricht 2 (2000) consensus on the treatment of *H. pylori* -infection.

## Vitamin B12 and Homocysteine

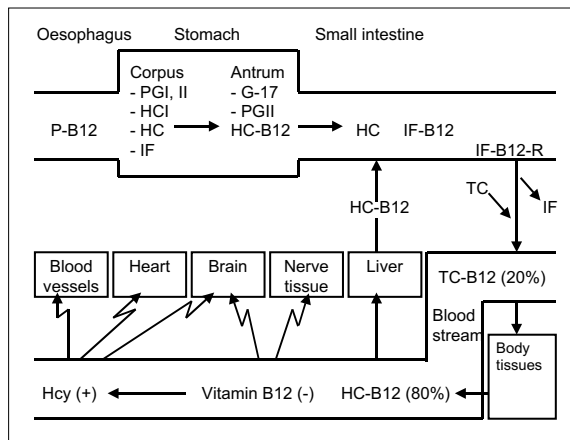
Atrophic gastritis of the corpus caused by *H. pylori* -infection or autoimmune disease results in the malabsorption of vitamin B12. The deficiency of vitamin B12 increases the level of homocysteine in the body. Homocysteine is an intermediate product of metabolism. The increased level of homocysteine in blood and tissues signal a serious disturbance of methionine metabolism in the cells. The deficiency of vitamin B12 is related, e.g., with dementia, depression, damages of the peripheral nervous system, and increases the risk of these diseases.<sup>72</sup> An elevated level of homocysteine in the body increases the risk of atherosclerosis and heart and brain strokes.<sup>73,74,75</sup>

<sup>72</sup> See <http://www.b12.com>.

<sup>73</sup> See <http://www.homocysteine.com>.

<sup>74</sup> Ranta P., Helske T., Kääriäinen I., Mäki T., Saarinen P., Kekäläinen L., Suovaniemi O., Härkönen M., Sipponen P. (2001). Serum Pepsinogen I Test Reveals Cases of Vitamin B12 Deficiency without Anemia in Patients with Gastric Corpus Atrophy. Presentation delivered at EUROMEDLAB 2001, Prague, Czech Republic, May 26-31.

<sup>75</sup> Härkönen M., Nikulin M., Sande N., Suovaniemi O., Sipponen P. (2001). Atrophic Corpus Gastritis Raises the Serum Levels of Homocysteine. Presentation delivered at the Digestive Disease Week, Atlanta, U.S.A., May 20-23.



**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.<sup>76</sup>

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. Approx. 5-20% of the elderly suffer from diseases caused by the lack of vitamin B12.

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.<sup>77</sup> 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<sup>78</sup>.

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, e.g., an injection of vitamin B12 at three months' intervals.

The deficiency of vitamin B12 in the body is an increasing health problem worldwide, especially concerning the elderly. Approx. 5-15% of the elderly suffer from diseases caused by the deficiency of vitamin B12. Available research results indicate that a significant part of the patients suffering from the deficiency of vitamin B12 are those whose deficiency has resulted from the malabsorption of vitamin B12 caused by atrophic gastritis. An observation, which needs to be taken seriously, is that the damages of the brain tissue and peripheral nervous system, e.g., dementia and depression, are irreversible and develop already years before the anemia caused by the deficiency of vitamin B12 occurs.

**Biohit's Test Panel Promotes Targeted Diagnoses and Treatment as well as Prevention of Diseases**

Biohit's GastroPanel and related GastroSoft are well suited for the use of general practitioners and specialists for diagnosing *H. pylori* -infection and atrophic gastritis as well as for screening the risk of gastric cancer and peptic ulcer from blood samples. Although atrophic gastritis is a serious disease it usually remains unnoticed and "underdiagnosed". One reason is, most likely, that the only reliable means so far to diagnose atrophic gastritis has been the histological (microscopic) examination of biopsy samples taken in connection with gastroscopy. The early diagnosis and correct treatment of atrophic gastritis prevents many of the diseases described above (evidence-based medicine).

The test panel enables to determine whether dementia, depression or heart or brain strokes are related with atrophic gastritis of the mucosa of the stomach. It is of utmost importance to identify this connection rapidly and at an early stage. The diseases related with the stomach can be treated, e.g., by eradication therapy of the *H. pylori* -infection. When also the levels of vitamin B12 and homocysteine are determined it is possible to assess the risks related with diseases of the nervous system and blood vessels. This, on its part, enables, e.g., to commence the vitamin B12 substitute treatment at a sufficiently early stage.

Approx. one third of the global population suffers from dyspepsia. Over half of the cases are functional and only a small part is related with organic diseases. The test panel is an economic and easy means to differentiate between cases of functional dyspepsia and more severe diseases caused by atrophic gastritis. Since over half of the world population are infected by *H. pylori*, and as half of these cases lead to atrophic gastritis, justified grounds exist to the routine use of the test panel in a similar manner as measuring blood pressure and cholesterol and analyzing blood count.

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

76 Holo-transcobalamin: The Physiologically Active Vitamin B12 Metabolite. *Clinical Laboratory International*, Vol. 24, No.8 (2000): 8.  
77 <http://www.b12.com>  
78 <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 pain and discomfort, and atrophic gastritis. Gastroscopy is relatively expensive, disliked by patients and cannot be performed on all occasions due to limited health care resources.*



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.

### **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<sup>79</sup>. The invention enables to trace gastric cancer or cancer of the large intestine by measuring the level of cellular fibronectin (cFn) in blood<sup>80</sup>.

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 complements the GastroPanel-examination. If the GastroSoft-program, which interprets the results of the test panel, indicates an increased risk of gastric cancer and the level of cFn is elevated, it is evident 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<sup>81</sup>.

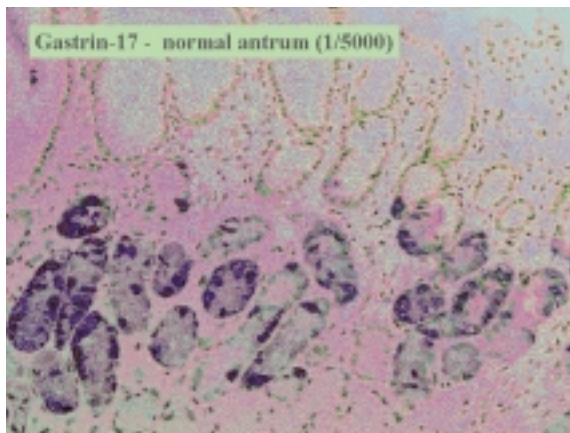
Biohit's cFn -test kit, which is protected by patents and patent applications, is based on a monoclonal antibody developed by Biohit and a hybridoma producing the antibody limitlessly. The markets for the cFn-test as a tumor marker can be considered large and even larger when combined with the GastroPanel 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<sup>82</sup>.

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

80 Ylätuupa S. (1996). *The Development of a Method for Quantification of Cellular Fibronectin EDACFn and Its Clinical Applications*, Ph.D. Thesis, University of Helsinki.

81 Suovaniemi O., Härkönen M., Sipponen P. (2001). Finnish patent application 20011908: *Method for Detecting Gastric Cancer.*

82 McGrath & Associates, Inc. (2002).



*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.*

### Monoclonal Antibodies

The different test kits of the gastric test panel are based on immunodiagnosics and on the use of Biohit's monoclonal antibodies (MAbs)<sup>83</sup> and microplates<sup>84</sup>, which can be used in vertical measurement applications<sup>85</sup>.

Biohit manufactures Pepsinogen I, Pepsinogen II and Gastrin-17 -antibodies which are related with the Gastro-Panel. 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 25 other MAbs, which are suited for immunohistochemistry and used in basic research as well as for classifying different types of cancer from tissue samples<sup>86,87,88,89</sup>. 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.

83 Milstein and Köhler invented monoclonal antibodies and received the Nobel Prize for this invention in 1984.

84 Vauramo, K. (1994). U.S. -patent 5,308,584: *Cuvette Matrix Tray*.

85 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.

86 Linnala A. (1998). *Tenascin, Fibronectin, Laminin and Their Integrin Receptors in Human Cell Cultures*, Ph.D. Thesis, University of Helsinki.

87 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.

88 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.

89 Ylä-tupa S. (1996). *The Development of a Method for Quantification of Cellular Fibronectin EDACFn and Its Clinical Applications*, Ph.D. Thesis, University of Helsinki.

### 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<sup>90,91</sup> enables, when

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

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



*Biohit's quick test for the determination of lactose intolerance from tissue samples taken in connection with gastroscopy.*

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.

### 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<sup>92</sup>.

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.<sup>93,94</sup> 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<sup>95</sup>.

The performance of the blood test for determining SLE has proven to be superior in clinical evaluations to the few competing tests. Recently the renowned researcher on rheumatic diseases and SLE, professor D.J. Wallace, together with his research team published positive results on the SLE-test<sup>96</sup>.

### 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 develops, 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.

Low concentrations of phytoestrogens may signal a risk for certain forms of cancer, e.g., large bowel, breast and

prostate<sup>97,98,99,100</sup>, as well as for ischemic heart disease<sup>101</sup>. In such cases the prevention of the diseases involves changes in diet to include more whole grain bread, berries, certain vegetables and soybean products<sup>102,103</sup>. People are more and more interested in nutrition and health. For this reason research work on phytoestrogens is undertaken very intensively worldwide.

### Market Potential and Marketing of the Test Kits

From Biohit's point of view the market potential for the test kits is nearly limitless, over USD 5.0 billion<sup>104</sup>. Since Biohit's test kits have been awarded patents and Biohit has actively filed new applications, the company's possibility to benefit from the potential through its subsidiaries, distributors and project exports seem promising.

However, when striving to benefit from this potential, Biohit and its co-operation parties face the challenge of rapidly increasing the awareness of doctors and patients of these products. As to the GastroPanel and GastroSoft the following means will be used:

- Congresses, exhibitions, testing and promotion by specialists. Biohit's global data base on gastroenterologists and researchers currently cover approx. 6,000 members in 50 different countries.
- Articles by researchers and popularized information disseminated by mass media to increase the awareness of patients to be correctly tested by a non-invasive method before treatment.
- The joint marketing of diagnostic tests and corresponding highly specific drugs, i.e., evidence-based medicine.
- Approval by authorities (e.g. in Europe, U.S. and Japan) before clinical use.
- Biohit's seven subsidiaries with their customer service networks.
- Biohit's distributors for liquid handling products most of whom have a customer service network and capability of selling diagnostics, instruments and analyzing systems.
- Biohit's multinational co-operation partners; possibilities with Beckman Coulter, Becton Dickinson, bioMérieux, Hoffmann-La Roche and Johnson & Johnson.
- New co-operation partners.
- Project exports (Asia, Near East, South America).

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

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

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

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

96 Wallace D.J., Salonen E-M., Avaniiss-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.

97 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.

98 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.

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

100 Adlercreutz H., Mazur W., Kinzel J., van Reijnsen 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.

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

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

103 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.

104 MeritaNordbanken Research 25.8.1999.

This existing specialist, co-operation and customer service network has provided Biohit the unique advantage to commence the global testing, adoption and marketing of the new products on the largest and most important markets, i.e., the lead markets.

### **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



*In 2001 Biohit took into use new production premises for diagnostics and began to offer laboratory services.*



The results of the GastroPanel are analyzed with Biohit's GastroSoft-program ([www.biohit.com](http://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](http://www.biohit.com).

Instructions for taking samples and delivering the samples to the service laboratory can be ordered from Biohit Oyj, [lea.paloheimo@biohit.com](mailto:lea.paloheimo@biohit.com), fax: +358-9-773 86 200 or tel: +358-9-773 861/Lea Paloheimo.

### Diagnostics in 2001

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 ulcer from blood samples continued according to plans. Evaluations were carried out in Finland and on the most important market areas abroad by over twenty research and scientist groups. The results of the evaluations completed in 2001 were positive and supported the results of those completed previously.

The new production premises for diagnostic tests were completed and taken into use in Helsinki in 2001. The premises enable to enter from the pilot production of diagnostic tests to their mass production. All Biohit's diagnostic tests will be manufactured in the premises.

In March the ISO 9001 -quality system certification of Biohit Oyj was extended to cover also the area of diagnostics as a result of the audit conducted by Det Norske Veritas. In fall the certification was further extended, and currently the business area of diagnostics conforms also with the quality requirements set by the ISO 13485 -standard. This means that Biohit's diagnostic tests can be equipped with the CE-mark (IVD directive 98/97/EU) and the tests can, thus, be sold, in addition to research use, also for clinical use in the EU-area. In addition to the quality system certification, the diagnostic products were registered to the National Agency for Medicines in Finland.

In the U.S. the tests can be sold to service laboratories without the FDA-approval. It is estimated that Biohit will receive FDA-clearance for the GastroPanel in 2002. Work for obtaining equivalent approvals in Japan, China and Russia is in progress. Moreover, currently approx. 20 country evaluations are in progress on the basis of which local experts will recommend the use of Biohit's diagnostic tests. The results of evaluations finished so far have been positive. The goal of co-operation with the experts of medical companies, e.g., in Italy and Germany, is that especially the general practitioners would begin using the GastroPanel before subscribing medication for patients suffering from stomach pains and discomfort (evidence-based medicine). It has been estimated that, e.g., in Italy where the number of general practitioners exceeds 50,000, the annual need for the GastroPanel-examination is approx. 2.0 million.

In 2001 the marketing of the GastroPanel began for research use worldwide. In Canada authorities issued product licenses for the Pepsinogen I, Gastrin-17 and *Helicobacter pylori* -test kits of the GastroPanel. This enables Biohit to commence the marketing and sales of the GastroPanel also for clinical use in Canada. In 2001 United Clinical Laboratories commenced the marketing of the test panel for its clientele in Finland.

In the U.K. Immunology Quality Services evaluated with favourable results Biohit's anti-dsDNA ELISA -test kit for the diagnosis of systemic lupus erythematosus (SLE). The evaluation demonstrated that the sensitivity, specificity and precision of the test are good.

The European Commission granted Biohit an approx. MEUR 0.2 support for the development of monoclonal antibodies and test kits for phytoestrogens. The development work commenced in May 2001 and it will last until April 2004. The work is part of a Europe-wide project, the purpose of which is to study the role of dietary phytoestrogens in the prevention of certain types of cancer.<sup>105</sup>

In order to enhance the evaluation and adoption of its diagnostic test systems Biohit commenced to offer laboratory services targeted to researchers and the health care sector. The State Provincial Office of Southern Finland, Department for Social and Health Affairs, granted an authorization for the service laboratory on May 8, 2001. The service laboratory collects patient samples, e.g., from health care centers, occupational health service centers, other medical centers as well as regional and central hospitals. The laboratory analyses conducted aim to support basic research and promote correct diagnoses and related treatment.

<sup>105</sup> <http://www.phytoprevent.org>

## INSTRUMENTS

The business idea of Biohit is to offer its customer base also 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<sup>106</sup>), and vertical photometry and its instrument applications (e.g. Multiskan<sup>107</sup>). Biohit has researched and developed

<sup>106</sup> Finn pipette is a registered trademark of Lab systems Oy.  
<sup>107</sup> Multiskan is a registered trademark of Lab systems Oy.

further vertical measurement principles since the end of the 1980s<sup>108,109</sup>. 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<sup>110,111</sup>.

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 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%.

<sup>108</sup> 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.  
<sup>109</sup> Tiisanen T. (1992). *Inner-Filter Correction with a Fluorometer-Based Multifunctional Instrument*, Ph.D. Thesis, University of Helsinki.  
<sup>110</sup> McGrath & Associates, Inc. (1999).  
<sup>111</sup> 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.



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.

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.

#### **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.



*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.*

#### **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 increased by 5% in 2001 and totalled MEUR 25.5 (MEUR 24.2). If the effect of Wolf Laboratories Ltd., the company having specialized in commission business in the U.K. and which was sold at the end of 2000, is eliminated from the net sales of 2000, the growth of the Group net sales in 2001 is over 20%. The net sales continued to be generated primarily by the sales of liquid handling products and disposables.

Deviating from preliminary estimates, the significant investments made in 2001 and previous years in the research and development and establishment of a global co-operation and customer service network did not for the part of the diagnostic products generate a significant increase in the net sales. Although the market potential for Biohit's finished diagnostic products is great, gaining optimal benefit of this potential is time-consuming due to numerous evaluations and approvals by authorities which need to be obtained. In 2001 the investments made in the evaluations and marketing of the diagnostic products were covered by the profitable sales of liquid handling products.

Exports continued to account for approximately 96% of the net sales. 51 % of the net sales consisted of sales to European countries, 25% to North America and the remaining 24% mainly to Asia.

In 2001 the investments made in the evaluations and marketing of the diagnostic products were covered by the profitable sales of liquid handling products.

### Profit/Loss

The operating profit for the financial year totalled MEUR 0.2 (MEUR 0.5 loss in 2000). The operating profit before goodwill amortization totalled MEUR 1.2 (MEUR 0.5).

The Group fixed costs increased approx. 17% which was primarily due to investments in the international sales organization and the research, development and production of the diagnostic tests. Also the numerous evaluations and marketing of diagnostics had an effect on the fixed costs.

The net financial expenses totalled MEUR 0.2 (MEUR 0.1).

The profit before extraordinary items totalled MEUR 0.1 (MEUR 0.6 loss) and the loss for the financial year totalled MEUR 0.2 (MEUR 0.6 loss).

The earnings per share was MEUR -0.02 (MEUR -0.06).

### Balance Sheet

The business operations of Locus genex Oy, the subsidiary company specializing in diagnostic products, were transferred to Biohit Oyj on May 1, 2001. It has been calculated that the dissolution has a positive corporate tax impact of MEUR 0.7 on the Group, which is deferred in the consolidated financial statements over the remaining amortization period of 5 years of the goodwill relating to Locus genex Oy. With regard to the dissolution of Locus genex Oy, the balance sheet of December 31, 2001 includes a tax liability of MEUR 1.2 under short-term liabilities and a deferred tax receivable of MEUR 1.2 under receivables.

### Liquidity

The liquidity of the Biohit Group is good. The cash flow provided by operating activities was MEUR 1.9 positive (MEUR 0.9). The investments were financed primarily by cash flow from operating activities. MEUR 0.1 were withdrawn as research and development loans. MEUR 0.9 were paid off as long-term loans.

The equity ratio was on December 31, 2001 65.7% (66.9%).

### Investments

The gross investments totalled MEUR 2.2 (MEUR 7.1). The clean room unit enabling the mass production of diagnostic tests together with related equipment as well as machinery and equipment intended for increasing other production capacity constituted the major part of the investments.

The Group research and development expenditure totalled MEUR 2.1 (MEUR 1.7), i.e., 8.3% (7.0%) of the net sales.

### Administration and Personnel

During the financial year the following persons were members of the Board of Directors of Biohit Oyj.: Professor Reijo Luostarinen as the Chairman and docent Arto Alanko, Osmo Suovaniemi, M.D., Ph.D. and Professor Mårten Wikström as members.

SVH Pricewaterhouse Coopers Oy have acted as the auditors and Hannele Selesvuo as the responsible Authorized Public Accountant.

The number of personnel totalled on December 31, 2001 302 (266) of which 118 (114) worked at the subsidiary companies, 98 (86) at the Kajaani plant and 86 (66) at the Helsinki headquarters.

### Prospects for 2002

It is estimated that the net sales generated by liquid handling products increases approx. 15% and profitability will stay good in 2002. The sales of diagnostics is anticipated to develop favorably in 2002.

Biohit's ISO 9001 -quality system covers also the business area of diagnostics. In addition, Biohit diagnostics conforms with the quality requirements set by ISO 13485. This means that Biohit's diagnostic tests can be equipped with the CE-mark (IVD directive 98/97/EU) and the tests can, thus, be sold, in addition for research use, also for clinical use in the EU-area.

In the U.S. the tests can be sold to service laboratories without the FDA-approval. It is estimated that Biohit will receive FDA-clearance for the GastroPanel in 2002. Work for obtaining equivalent approvals in Japan, China and Russia is in progress. Moreover, currently approx. 20 country evaluations are in progress on the basis of which local experts will recommend Biohit's diagnostic tests to be used. The results of evaluations finished so far have been positive. The goal of co-operation with the experts of medical companies, e.g., in Italy and Germany, is that especially the general practitioners would begin using the GastroPanel before subscribing medication for patients suffering from stomach pains and discomfort (evidence-based medicine). It has been estimated that, e.g., in Italy where the number of general practitioners exceeds 50,000, the annual need for the GastroPanel-examination is approx. 2.0 million.

**INCOME AND CASH FLOW STATEMENTS**

<b>INCOME STATEMENT JANUARY 1- DECEMBER 31</b>		<b>Group</b>		<b>Parent company</b>	
<b>EUR 1 000</b>	<b>Note</b>	<b>2001</b>	<b>2000</b>	<b>2001</b>	<b>2000</b>
NET SALES	2.1.	25 545	24 247	15 525	13 494
Change in inventories of finished goods and work in progress		244	679	318	256
Other operating income		501	182	182	163
Materials and services	2.2.	-5 460	-7 661	-2 966	-2 560
Personnel expenses	2.3.	-9 883	-8 015	-5 904	-4 836
Depreciation and value adjustments	3.1.	-2 268	-2 395	-2 384	-1 222
Other operating expenses		<u>-8 442</u>	<u>-7 520</u>	<u>-4 591</u>	<u>-4 293</u>
OPERATING PROFIT/LOSS		237	- 483	180	1 002
Financial income and expenses	2.4.	<u>-182</u>	<u>-98</u>	<u>-309</u>	<u>-10</u>
PROFIT/LOSS BEFORE EXTRAORDINARY ITEMS		55	- 581	-129	992
Extraordinary items	2.5.	<u>0</u>	<u>239</u>	<u>0</u>	<u>-653</u>
PROFIT/LOSS BEFORE INCOME TAXES		55	- 342	-129	339
Untaxed reserves	2.6.	0	0	0	-359
Income taxes	2.7.	-273	- 247	22	-7
Minority interest		<u>-14</u>	<u>-27</u>	<u>0</u>	<u>0</u>
NET LOSS		-232	- 616	-107	-27

<b>CASH FLOW STATEMENT JANUARY 1 – DECEMBER 31</b>		<b>Group</b>		<b>Parent company</b>	
<b>EUR 1 000</b>		<b>2001</b>	<b>2000</b>	<b>2001</b>	<b>2000</b>
<b>CASH FLOWS FROM OPERATING ACTIVITIES</b>					
Profit/loss before extraordinary items		55	-580	- 128	991
Adjustments:					
Depreciations		2 268	2395	2 383	1 222
Provisions					
Financial income and expenses		182	98	309	10
Other adjustments		<u>24</u>	<u>-1</u>	<u>-38</u>	<u>0</u>
Cash flow before change in net working capital		2 529	1 912	2 526	2 222
<b>CHANGE IN NET WORKING CAPITAL</b>					
Increase (-)/decrease (+) in non-interest bearing receivables		424	1 185	-269	-599
Increase (-)/decrease (+) in inventories		- 468	-758	-401	-377
Increase (+)/decrease (-) in non-interest bearing liabilities		<u>-77</u>	<u>-1 124</u>	<u>243</u>	<u>152</u>
Funds generated before financial items and income taxes		2 408	1 215	2 099	1 398
Interests and other financial items paid		-442	-678	-321	-582
Interests received		153	297	148	286
Income taxes paid		<u>-243</u>	<u>-272</u>	<u>-75</u>	<u>-134</u>
Cash flow before extraordinary items		1 876	562	1 851	968
Extraordinary items paid		0	336	0	-316
Net cash flow from operating activities (A)		1 876	898	1 851	653
<b>NET CASH FLOW FROM INVESTING ACTIVITIES</b>					
Investments in tangible and intangible assets		-2 170	- 4815	- 1 904	-4 319
Proceeds from disposition of tangible and intangible assets		33	0	33	0
Loans given		0	0	-189	0
Grants received		425	0	425	0
Investments in subsidiaries		-42	-1 118	-129	-1 815
Disposition of subsidiary shares		0	- 76	0	0
Refund of advance payment		0	404	0	404
Repayments of loan receivables		0	0	82	56
Proceeds from disposition of other shares and holdings		0	57	0	57
Dividends received from investments		6	6	6	6
Net cash flow from investing activities (B)		-1 748	-5 542	-1 676	-5 611
<b>NET CASH FLOW FROM FINANCING ACTIVITIES</b>					
Proceeds from share issue		0	804	0	804
Increase in capital loan		111	22	111	22
Increase in long-term loans		73	824	64	824
Repayments of long-term loans		<u>-870</u>	<u>-1 208</u>	<u>-870</u>	<u>-1 126</u>
Net cash flow from financing activities (C)		-686	442	-695	524
Net increase (+)/decrease (-) in cash and cash equivalents (A+B+C)		-558	-4 202	-520	-4 434
Cash and cash equivalents at January 1		3 016	7 218	2 351	6 783
Cash and cash equivalents at December 31		2 458	3 016	1 831	2 349

## BALANCE SHEET DECEMBER 31

ASSETS EUR 1 000	Note	2001	Group 2000	2001	Parent company 2000
<b>FIXED ASSETS AND OTHER LONG-TERM INVESTMENTS</b>					
Intangible assets	3.1.1.	1 182	899	6 408	771
Goodwill	3.1.1.	3 671	4 621	0	0
Tangible assets	3.1.2.	6 370	5 645	5 724	4 969
Shares and holdings	3.2.	<u>216</u>	<u>205</u>	<u>6 074</u>	<u>8 107</u>
Total fixed assets and other long-term investments		11 439	11 370	18 206	13 847
<b>CURRENT ASSETS</b>					
Inventories	3.3.	4 253	3 785	2 167	1 690
Deferred tax receivables	3.7.	1 516	268	190	0
Long-term receivables	3.4.	0	0	186	172
Short-term receivables	3.4.	5 330	6 185	5 808	6 252
Cash at bank and in hand		<u>2 457</u>	<u>3 016</u>	<u>1 831</u>	<u>2 349</u>
Total current assets		13 556	13 254	10 182	10 463
<b>TOTAL ASSETS</b>		24 995	24 624	28 388	24 310
<b>SHAREHOLDERS' EQUITY AND LIABILITIES</b>					
EUR 1 000	Note	2001	Group 2000	2001	Parent company 2000
<b>SHAREHOLDERS' EQUITY</b>					
Share capital	3.5.1.	2 149	2 149	2 149	2 149
Share premium fund	3.5.1.	14 906	14 906	14 906	14 906
Accumulated profit/loss from prior years	3.5.1.	-600	-3	1 241	1 268
Net loss	3.5.1.	-232	-616	-107	-27
Capital loans	3.5.4.	<u>1 243</u>	<u>1 132</u>	<u>1 243</u>	<u>461</u>
Total shareholders' equity		17 466	17 568	19 432	18 757
<b>MINORITY INTEREST</b>		111	49	0	0
<b>APPROPRIATIONS</b>	3.6.	0	0	359	359
<b>LIABILITIES</b>					
Deferred tax liability	3.7.	104	109	0	0
Long-term liabilities	3.8.1.	2 080	2 790	1 998	2 730
Short-term liabilities	3.8.2.	<u>5 234</u>	<u>4 108</u>	<u>6 599</u>	<u>2 464</u>
Total liabilities		7 418	7 007	8 597	5 194
<b>TOTAL SHAREHOLDERS' EQUITY AND LIABILITIES</b>		24 995	24 624	28 388	24 310

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

The goodwill relating to Locus genex Oy will be amortized over 7 years. An exception has been made from the five year amortisation period because the investment is by nature long-term.

#### 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. R & D costs capitalized prior to 1998 were fully amortized in 2000.

#### 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. Exchange gains and losses are dealt with in the profit and loss account except for the unrealized exchange gain on non-current USD loan receivable from a subsidiary company which has been disclosed in the parent company's financial statements 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.

## 2. NOTES TO THE INCOME STATEMENT

<b>2.1. Net sales by Geographical Area</b> <b>EUR 1 000</b>	<b>2001</b>	<b>Group</b> <b>2000</b>	<b>2001</b>	<b>Parent company</b> <b>2000</b>
Finland	964	647	975	847
Scandinavia	817	686	817	593
Rest of Europe	11 228	11 628	7 187	6 625
America	6 368	4 620	3 945	3 010
Other countries	6 168	6 666	2 601	2 420
Total	25 545	24 247	15 525	13 494

<b>2.2. Materials and Services</b> <b>EUR 1 000</b>	<b>2001</b>	<b>Group</b> <b>2000</b>	<b>2001</b>	<b>Parent company</b> <b>2000</b>
Materials				
Purchases during the year	5 287	7 463	3 040	2 681
Change in inventories	-95	-140	-83	-121
Total materials	5 191	7323	2 957	2 560
External services	268	339	9	0
Total materials and services	5 460	7 661	2 966	2 560

<b>2.3. Personnel Expenses and Number of Personnel</b> <b>Personnel Expenses, EUR 1 000</b>	<b>2001</b>	<b>Group</b> <b>2000</b>	<b>2001</b>	<b>Parent company</b> <b>2000</b>
Salaries and wages	7 975	6 401	4 758	3 764
Pension expenses	1 067	894	737	622
Other personnel expenses	841	720	409	450
Total	9 883	8 015	5 904	4 836

### Salaries and Fees of the Management

The salaries of the Group's Presidents totalled TEUR 706 (TEUR 663 in 2000). The fees to the members of the Board of Directors were TEUR 67 (29) in the parent company and Group. No pension arrangements other than those laid down by law have been made with the Presidents of Group companies.

<b>Average Number of Personnel</b>	<b>2001</b>	<b>Group</b> <b>2000</b>	<b>2001</b>	<b>Parent company</b> <b>2000</b>
Office personnel	188	138	75	60
Factory personnel	101	84	101	84
Total	289	222	176	144

<b>2.4. Financial Income and Expenses</b> <b>EUR 1 000</b>	<b>2001</b>	<b>Group</b> <b>2000</b>	<b>2001</b>	<b>Parent company</b> <b>2000</b>
Dividend income from outside the Group	6	6	6	6
Interest income from long-term investments				
From companies within the Group	0	0	115	87
Other interest and financial income:				
From companies within the Group	0	0	25	64
From others	247	304	120	218
Total	247	304	260	369
Value adjustments of shares and holdings			-275	-82
Interest expense and other financial expenses:				
For companies within the Group	0	0	-1	-1
For others	-436	-408	-299	-302
Total financial income and expenses	-182	-98	-309	-10
Net foreign exchange gains/losses included in "Financial income and expenses"	-35	20	-37	44



<b>2.5. Extraordinary Items</b>		<b>Group</b>		<b>Parent company</b>
<b>EUR 1 000</b>	<b>2001</b>	<b>2000</b>	<b>2001</b>	<b>2000</b>
Extraordinary income	0	244	0	0
Extraordinary expenses	0	-5	0	-653
Total	0	239	0	-653

The extraordinary income in 2000 consisted primarily of the profit received from the sales of the shares of Wolf Laboratories Ltd and extraordinary expenses related to a Group contribution to a subsidiary.

<b>2.6. Untaxed reserves</b>		<b>Group</b>		<b>Parent company</b>
<b>EUR 1 000</b>	<b>2001</b>	<b>2000</b>	<b>2001</b>	<b>2000</b>
Accelerated depreciation	0	0	0	-359

<b>2.7. Income Taxes</b>		<b>Group</b>		<b>Parent company</b>
<b>EUR 1 000</b>	<b>2001</b>	<b>2000</b>	<b>2001</b>	<b>2000</b>
Current income taxes on extraordinary items	0	-80	0	189
Current income taxes on ordinary operations	-1 521	-145	-169	-196
Change in deferred income tax liability/receivable	1 248	-22	190	0
Total	-273	-247	21	-7

### 3. NOTES TO THE BALANCE SHEET

#### 3.1. Tangible and Intangible Assets

<b>3.1.1. Intangible Assets</b>	<b>Group</b>			
<b>EUR 1 000</b>	<b>Intangibles</b>	<b>Goodwill</b>	<b>Other capitalized expenses</b>	<b>Total</b>
Acquisition cost at beginning of year	817	6 488	685	7990
Additions	130	59	390	580
Acquisition cost at end of year	948	6 547	1 075	8 570
Accumulated depreciation and value adjustments at beginning of year	-274	-1 866	-328	-2 468
Depreciation for the year	-99	-1 009	-139	-1 247
Accumulated depreciation and value adjustments at end of the year	-373	-2 875	-467	-3 715
Net book value at end of year	574	3 671	608	4 853

<b>3.1.1. Intangible Assets</b>	<b>Parent company</b>			
<b>EUR 1 000</b>	<b>Intangibles</b>	<b>Goodwill</b>	<b>Other capitalized expenses</b>	<b>Total</b>
Acquisition cost at beginning of year	746	0	494	1 240
Additions	225	6 558	389	7 173
Acquisition cost at end of year	971	6 558	883	8 412
Accumulated depreciation and value adjustments at beginning of year	-308	0	-161	-469
Depreciation for the year	-89	-1 312	-136	-1 536
Accumulated depreciation and value adjustments at end of the year	-397	-1 312	-296	-2 005
Net book value at end of year	574	5 247	586	6 408

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).

<b>3.1.2. Tangible Assets</b>		<b>Group</b>		
<b>EUR 1 000</b>		<b>Buildings</b>	<b>Machinery and equipment</b>	<b>Total</b>
Acquisition cost at beginning of year		2 295	5 779	8 074
Additions		13	1 733	1 746
Disposals		<u>0</u>	<u>-62</u>	<u>-62</u>
Acquisition cost at end of year		2 309	7 450	9 758
Accumulated depreciation and value adjustments at beginning of year		-28	-2 400	-2 428
Accumulated depreciation on disposed assets		0	62	62
Depreciation during the year		<u>-115</u>	<u>-907</u>	<u>-1 022</u>
Accumulated depreciation and value adjustments at end of the year		-144	-3 245	-3 388
Net book value at end of year		2 165	4 205	6 370

<b>3.1.2. Tangible Assets</b>		<b>Parent company</b>		
<b>EUR 1 000</b>		<b>Buildings</b>	<b>Machinery and equipment</b>	<b>Total</b>
Acquisition cost at beginning of year		2 295	4 792	7 088
Additions		13	1 590	1 603
Disposals		<u>0</u>	<u>-62</u>	<u>-62</u>
Acquisition cost at end of year		2 309	6 320	8 629
Accumulated depreciation and value adjustments at beginning of year		-28	-2 091	-2 119
Accumulated depreciation on disposed assets		0	62	62
Depreciation during the year		<u>-115</u>	<u>-732</u>	<u>-848</u>
Accumulated depreciation and value adjustments at end of the year		-144	-2 761	-2 905
Net book value at end of year		2 165	3 559	5 724

Disposals consist mainly of fully depreciated assets which are no more used in the business operations. The book value of production machinery and equipment is TEUR 2 814.

### 3.2. Shares and Holdings

<b>Group</b>		
<b>EUR 1 000</b>		<b>Shares</b>
Book value at beginning of year		205
Translation difference		<u>11</u>
Book value at end of year		216

<b>Parent Company</b>					
<b>EUR 1 000</b>	<b>Shares Group companies</b>	<b>Shares other</b>	<b>Capital loans</b>	<b>Loans receivable from companies within the Group</b>	<b>Total</b>
Book value at beginning of year	6 043	148	480	1 436	8 107
Additions	129	14	0	92	235
Disposals	-1 513	0	-480	0	-1 993
Value adjustments	<u>-275</u>	<u>0</u>	<u>0</u>	<u>0</u>	<u>-275</u>
Book value at end of year	4 384	161	0	1 528	6 074

Disposals in shares in group companies and capital loans result from the recording of advance liquidation proceeds received in connection with the dissolution of Locus genex Oy. Other shares mainly consist of shares in Nordea and Elisa Communications, having a market value of TEUR 150 on 31 December 2001.

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%
Oy Finio Ab, Finland	100 %	100 %
Locus genex Oy, Finland	100 %	100 %
Vantaan Hienomekano Oy, Finland	100 %	100 %

Vantaan Hienomekano Oy and Biohit OOO did not have business operations in 2000 and 2001. During the financial year former Biohit Systems Inc. has been merged with its subsidiary company Vanguard International Inc., the name of which has subsequently been changed to Biohit Inc. Locus genex Oy was put into voluntary liquidation on December 14, 2000 and its business was transferred to Biohit Oyj on May 1, 2001.

### 3.3. Inventories

EUR 1 000	2001	Group 2000	2001	Parent company 2000
Materials	1 043	958	1 041	918
Work in progress	52	52	43	25
Finished products/goods	3 098	2 775	1 084	747
Advance payment	59	0	0	0
Total inventories	4 253	3 785	2 167	1 690

### 3.4. Receivables

EUR 1 000	2001	Group 2000	2001	Parent company 2000
<b>LONG-TERM RECEIVABLES</b>				
Receivables from Group companies				
Loans receivable	0	0	186	172
<b>SHORT-TERM RECEIVABLES</b>				
Receivables from companies within the Group				
Accounts receivable	0	0	3 864	3 666
Loans receivable	0	0	84	180
Other receivables	0	0	238	196
Receivables from other companies				
Accounts receivable	4 493	4 429	1 201	1 223
Loans receivable	8	41	8	8
Other receivables	334	735	174	232
Prepayments and accrued income	494	980	239	748
Total short-term receivables	5 330	6 185	5 808	6 252

### 3.5. Shareholders' Equity

3.5.1. Shareholders' Equity EUR 1 000	2001	Group 2000	2001	Parent company 2000
Share capital at beginning of year	2 149	2 085	2 149	2 085
Share issue	0	64	0	64
Share capital at end of year	2 149	2 149	2 149	2 149
Share premium fund at beginning of year	14 906	14 166	14 906	14 166
Premium from share issue	0	732	0	732
Adjustment to 1999 share issue expenses	0	8	0	8
Share premium fund at end of year	14 906	14 906	14 906	14 906
Profit/loss from prior years at beginning of year	-619	4	1 241	1 268
Translation difference	19	-7	0	0
Profit/loss from prior years at end of year	-600	-3	1 241	1 268
Loss for year	-232	-616	-107	-27
Capital loans at beginning of year	1 132	1 446	461	775
Increase	111	22	783	22
Decrease	0	-336	0	-336
Capital loans at end of year	1 243	1 132	1 243	461
Total shareholders' equity	17 466	17 568	19 432	18 757

In the parent company out of the total of the increase in the capital loan, TEUR 672, relates to the advance liquidation proceeds transferred to Biohit Oyj as a result of the dissolution of Locus genex Oy.

<b>3.5.2. Distributable equity at 31 December</b>			<b>Group</b>		
<b>EUR 1 000</b>	<b>2001</b>		<b>2000</b>	<b>2001</b>	<b>Parent company</b>
					<b>2000</b>
Profit/loss from prior years	-600		-3	1 241	1 268
Loss for the year	-232		-616	-107	-27
Unrecorded interest on capital loans	-421		-360	-421	-39
Accelerated depreciation recorded in shareholders' equity	<u>-255</u>		<u>-255</u>	<u>0</u>	<u>0</u>
Total	-1 508		-1 234	713	1 202

<b>3.5.3. Share capital of the parent company</b>						
	<b>2001</b>		<b>2001</b>		<b>2000</b>	
	<b>No. of shares</b>	<b>EUR</b>	<b>% of shares</b>	<b>% of votes</b>	<b>No. of shares</b>	<b>EUR</b>
A-shares (20 votes per share)	3 875 500	658 835	30.65	89.84	3 875 500	658 835
B-shares (1 vote per share)	<u>8 767 877</u>	<u>1 490 539</u>	<u>69.35</u>	<u>10.16</u>	<u>8 767 877</u>	<u>1 490 539</u>
Total	12 643 377	2 149 374	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.

<b>3.6. Appropriations</b>			<b>Parent company</b>
<b>EUR 1 000</b>			<b>2001</b>
			<b>2000</b>
Untaxed reserves			359
			359

The appropriations derive from the accelerated depreciation.

<b>3.7. Deferred income tax liabilities and receivables</b>			<b>Group</b>		
<b>EUR 1 000</b>			<b>2001</b>	<b>2001</b>	<b>Parent company</b>
					<b>2000</b>
Deferred income tax receivables					
From consolidation entries	1 327		268		
From temporary differences	190		0	190	0
Deferred income tax liabilities					
From temporary differences	104		109	0	0
Net	1 413		159	190	0

In the group an amount of TEUR 970, included in the deferred income tax receivables resulting from consolidation entries, related to taxes payable by Locus genex Oy as a result of its dissolution. This has been deferred in the group accounts over the remaining amortization period of the goodwill relating to this company.

The deferred income tax receivables in the parent company result 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.

#### 3.8. Liabilities

<b>3.8.1. Long-term Liabilities</b>			<b>Group</b>		
<b>EUR 1 000</b>	<b>2001</b>		<b>2000</b>	<b>2001</b>	<b>Parent company</b>
					<b>2000</b>
Loans from financial institutions	1 291		1 990	1 241	1 973
Other long-term debt	<u>789</u>		<u>800</u>	<u>757</u>	<u>757</u>
Total long-term liabilities	2 080		2 790	1 998	2 730
Debts falling due in more than five years					
Loans from financial institutions	33		34	33	34
Other long-term debt	<u>378</u>		<u>473</u>	<u>378</u>	<u>473</u>

<b>3.8.2. Short-term Liabilities</b>			<b>Group</b>		
<b>EUR 1 000</b>	<b>2001</b>		<b>2000</b>	<b>2001</b>	<b>Parent company</b>
					<b>2000</b>
Loans from financial institutions	796		883	796	870
Advances received	148		284	58	0
Accounts payable	1 246		971	717	493
Other liabilities	727		908	2738	216
Accrued liabilities	2 317		1 062	2 279	873
Liabilities from Group companies					
Accounts payable	<u>0</u>		<u>0</u>	<u>10</u>	<u>10</u>
Total short-term liabilities	5 234		4 108	6 599	2 464

Accrued liabilities consist mainly of a tax liability related with Locus genex (TEUR 1 212) and holiday pay and related social security accruals.

## 4. OTHER NOTES

### 4.1. Pledges given, Commitments and Contingencies

<b>Pledges given EUR 1 000</b>	<b>2001</b>	<b>Group 2000</b>	<b>2001</b>	<b>Parent company 2000</b>
<b>Loans for which mortgages and pledges have been given</b>				
Loans from financial institutions	1 906	2 776	1 906	2 776
Corporate mortgages	3 389	3 389	3 389	3 389
Other long-term liabilities	757	757	757	757
Mortgages on real estate	757	757	757	757

The parent company has given pledges of EUR 0.2 million on behalf of Group companies.

<b>Leasing commitments EUR 1 000</b>	<b>2001</b>	<b>Group 2000</b>	<b>2001</b>	<b>Parent company 2000</b>
Due for payment in the following year	1 190	963	575	462
Due for payment at a later date	2 855	3 278	1 906	1 999
Total	4 045	4 241	2 481	2 461

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

### Other commitments

On December 31, 2001, the social security payment commitments related with the unused personnel options of the parent company totalled to TEUR 15.

### Interest on capital loans

On December 31, 2001, accumulated, unrecorded interest on capital loans was TEUR 421 (TEUR 39) for the parent company and TEUR 421 (TEUR 360) for the Group.

### Derivative contracts

The group has no off-balance sheet financial instruments.

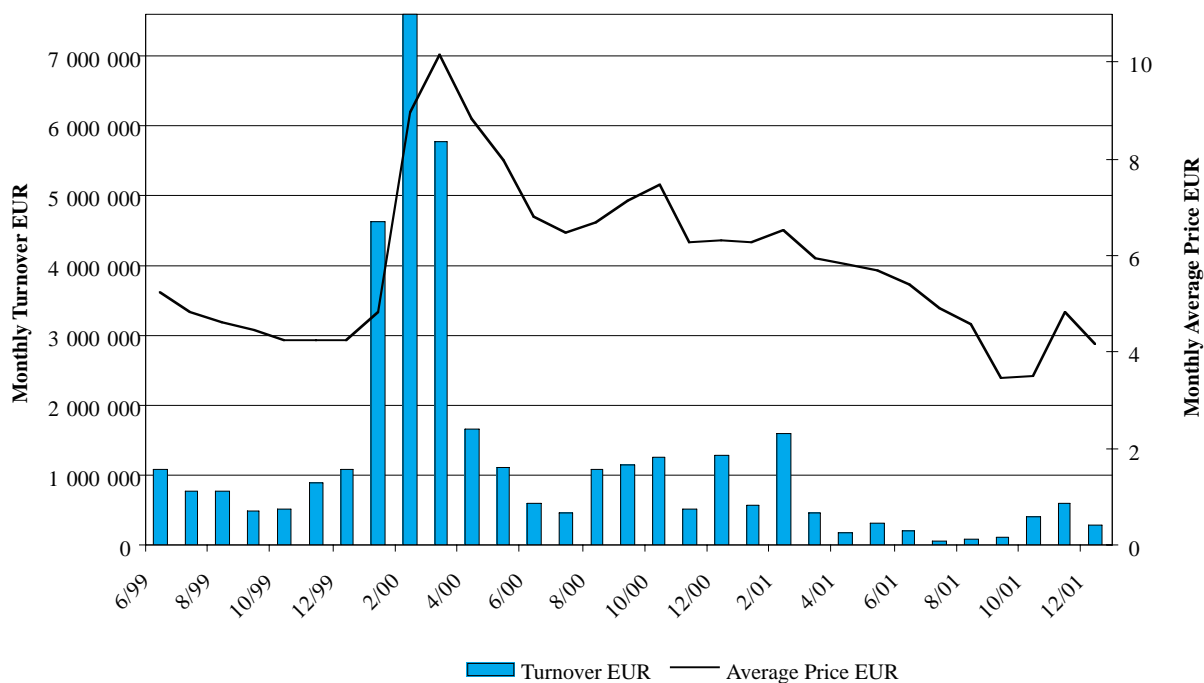
### 4.2 Ratios

<b>Financial ratios</b>	<b>1997</b>	<b>1998</b>	<b>1999</b>	<b>2000</b>	<b>2001</b>
Net sales	14 481	16 881	20 551	24 247	25 545
Increase in net sales %	14.6 %	16.6 %	21.7 %	18.0 %	5.4 %
Operating profit/loss	414	1 387	1 332	-482	237
% of net sales	2.9 %	8.2 %	6.5 %	-2.0 %	0.9 %
Profit/loss before extraordinary items and income taxes	176	451	825	-580	55
% of net sales	1.2 %	2.7 %	4.0 %	-2.4 %	0.2 %
Profit/loss before voluntary provisions and taxes	158	1 141	1 162	-341	55
% of net sales	1.1 %	6.8 %	5.7 %	-1.4 %	0.2 %
Return on equity, %	*)	12.1 %	3.8 %	-4.6 %	-1.3 %
Return on investment, %	10.8 %	12.2 %	8.5 %	-0.8 %	2.0 %
Equity ratio, %	-5.1 %	38.8 %	66.0 %	66.9 %	65.7 %
Investments in fixed assets	867	1 392	1 271	6 208	2 212
% of net sales	6.0 %	8.2 %	6.2 %	25.6 %	8.7 %
Research and development	622	740	1 270	1 698	2 114
% of net sales	4.3 %	4.4 %	6.2 %	7.0 %	8.3 %
Total assets	12 415	18 435	24 699	24 626	24 996
Personnel, average	154	164	184	222	289

\*) Shareholders' equity negative in 1997.

Ratios per share	1997	1998	1999	2000	2001
Earnings per share, EUR	0.03	0.06	0.04	-0.06	-0.02
- earnings per share, adjusted for dilution of options	-	-	0.04	-0.06	-0.02
Equity per share, EUR	-0.11	0.69	1.33	1.30	1.28
Price/earnings (P/E)	-	-	102	-101	-233
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
- lowest price	-	-	3.75	4.20	3.00
- highest price	-	-	6.00	13.50	7.20
- price on December 31, 2001	-	-	4.13	6.20	4.28
Market price for B-shares					
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
Development of exchange of B-shares, pcs 1 000	-	-	1 240	3 647	909
- % of total amount of shares	-	-	16.58 %	41.93 %	10.36 %
Average number of shares, adjusted for share issues	6 215 181	6 264 526	11 354 957	12 573 123	12 643 377
- adjusted for dilution of options	-	-	12 066 730	13 275 579	13 220 400
Number of shares at the balance sheet date, adjusted for share issues	6 253 537	10 264 537	12 264 537	12 643 377	12 643 377
- adjusted for dilution of options	-	-	12 976 310	13 345 833	13 220 400

### Turnover and Average Price of Share 18.6.1999–28.12.2001



### 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	2001		2001		2000	
	No. of shares	EUR	% of shares	% of votes	No. of shares	EUR
A-shares (20 votes per share)	3 875 500	658 835	30.65	89.84	3 875 500	658 835
B-shares (1 vote per share)	<u>8 767 877</u>	<u>1 490 539</u>	<u>69.35</u>	<u>10.16</u>	<u>8 767 877</u>	<u>1 490 539</u>
Total	12 643 377	2 149 374	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.

#### Ownership of shares by sector on Dec. 28, 2001

A-Shares	No. of shareholders		pieces	No. of shares %
	pieces	%		
1. Companies	3	30.00	919 990	23.74
2. Households	7	70.00	2 955 510	76.26
Total	10	100.00	3 875 500	100.00

B-Shares	No. of shareholders		pieces	No. of shares %
	pieces	%		
1. Companies	205	4.91	1 948 702	22.23
2. Households	8	0.19	244 952	2.79
3. Public organizations	2	0.05	519 600	5.93
4. Non-profit organizations	21	0.50	90 030	1.02
5. Households	3 911	93.65	5 662 231	64.58
6. Foreign	29	0.69	296 770	3.38
Shares which are not entered into the book-entry system			5 592	0.06
Total	4 176	100.00	8 767 877	100.00
Nominee-registered shares	5		195 130	2.23

#### Ownership according to the number of shares owned on December 28, 2001

A-Shares	No. of shareholders		pieces	No. of shares %
	pieces	%		
1-1 000	1	10.00	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	10.00	19 990	0.52
Over 50 000	8	80.00	3 855 500	99.49
Total	10	100.00	3 875 500	100.00

B-Shares	No. of shareholders		pieces	No. of shares %
	pieces	%		
1-1 000	3 700	88.50	1 230 300	14.02
1 001-5 000	382	9.14	794 403	9.06
5 001-10 000	48	1.15	374 580	4.27
10 001-50 000	32	0.77	595 888	6.8
Over 50 000	19	0.45	5 767 114	65.78
Total	4 181	100.00	8 762 285	99.93
Shares which are not entered into the book-entry system			5 592	0.06
Total			8 767 877	100.00

**Major shareholders on December 28, 2001**

10 major shareholders according to number of shares	A-shares	B-shares	Total no. of shares	%
Suovaniemi, Osmo	2 285 340	967 207	3 252 547	25.73
Biocosmos Oy		734 869	734 869	5.81
Erja-Yhtymä Oy	700 000		700 000	5.54
Interlab Oy		610 996	610 996	4.83
Suovaniemi, Ville	208 280	371 300	579 580	4.58
Suovaniemi, Joel	208 280	345 100	553 380	4.38
Härkönen, Matti	57 200	449 300	506 500	4.01
Suovaniemi, Oili	121 600	322 935	444 535	3.52
Suovaniemi, Vesa	74 800	293 117	367 917	2.91
LEL Työeläkekassa		361 600	361 600	2.86

10 major shareholders according to number of votes	A-shares	B-shares	Total no. of votes	%
Suovaniemi, Osmo	45 706 800	967 207	46 674 007	54.10
Erja-Yhtymä Oy	14 000 000		14 000 000	16.22
Suovaniemi, Ville	4 165 600	371 300	4 536 900	5.26
Suovaniemi, Joel	4 165 600	345 100	4 510 700	5.23
Erja-kiinteistöt Oy	4 000 000		4 000 000	4.63
Suovaniemi, Oili	2 432 000	322 935	2 754 935	3.19
Suovaniemi, Vesa	1 496 000	293 117	1 789 117	2.07
Härkönen, Matti	1 144 000	449 300	1 593 300	1.84
Biocosmos Oy		734 869	734 869	0.85
Interlab Oy		610 996	610 996	0.71



### Ownership by management on December 28, 2001

The members of the Board and the President of the Company owned a total of 2 285 340 A-shares and 2 378 072 B-shares on December 28, 2001. This in total stands for 36.88% of all shares and 55.73% of the votes in the Company. Additionally, their unused rights of options unsubscribed stand for 8.75% of the issued option rights for personnel, which is 0.28% of the share capital and 0.04% of the votes.

### Personnel and other option rights

The personnel options of the second stage entitle to subscribe altogether 400 000 pieces of Biohit's B-shares between January 1, 2002 – April 1, 2002 for a price of EUR 3.36.

The 625 000 rights of option subscribed by Martin John Anthony Williams and Robert Erwin Williams, the owners of Jencons Scientific Ltd. Acting as the distributor for Biohit's products, entitle to subscribe 625 000 B-shares of Biohit for a price of EUR 1.68 between April 26, 1999 – September 30, 2002.

### Formulas used in calculating key ratios

Return on equity, %	$\frac{\text{Profit before extraordinary items} - \text{income taxes for the period} \times 100}{\text{Shareholders' equity} - \text{capital loans} + \text{minority interest (average over the year)}}$
Return on capital employed, %	$\frac{\text{Profit before extraordinary items} + \text{interest and other financial expenses} \times 100}{\text{Total assets} - \text{non-interest-bearing liabilities (average over the year)}}$
Equity ratio, %	$\frac{\text{Shareholders' equity} - \text{capital loans} + \text{minority interest} \times 100}{\text{Total assets} - \text{advance payments received}}$
Earnings per share, EUR	$\frac{\text{Profit before extraordinary items} - \text{income taxes for the period} - \text{minority interest}}{\text{Average number of shares, adjusted for share issue}}$
Equity per share, EUR	$\frac{\text{Shareholders' equity} - \text{capital loans}}{\text{Number of shares at the balance sheet date, adjusted for share issues}}$
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, %	$\frac{\text{Dividend/share} \times 100}{\text{Earnings per share}}$
Effective dividend yield, %	$\frac{\text{Dividend, adjusted for share issue/share} \times 100}{\text{Stock exchange price on December 31, adjusted for share issues}}$
Price/earnings, (P/E)	$\frac{\text{Stock exchange price on December 31, adjusted for share issues}}{\text{Earnings per share}}$

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## PROPOSAL OF THE BOARD OF DIRECTORS AND AUDITORS' REPORT

### Proposal for the handling of the loss

The distributable earnings of the Parent Company are EUR 712 163.45. The Group does not have distributable earnings. The Board of Directors proposes that no dividends be paid and that the loss for the period of EUR 107 381.11 be transferred to the retained profit/loss account from previous years.

Helsinki, February 15, 2002

Reijo Luostarinen  
Chairman of the Board  
of Directors

Osmo Suovaniemi  
Member of the Board  
of Directors,  
President & CEO

Mårten Wikström  
Member of the Board  
of Directors

Arto Alanko  
Member of the Board  
of Directors

### Auditor's 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 year 1.1. – 31.12.2001. The financial statements, which include the report of the Board of Directors, the income statement, balance sheet and notes to the financial statements of the Group and parent company, 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.

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 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 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 year audited by us. The proposal by the Board of Directors regarding the handling of the loss for the financial year is in compliance with the Companies' Act.

Helsinki, February 28, 2002

SVH PricewaterhouseCoopers Oy  
Authorized Public Accountants

Hannele Seesvuo  
Authorized 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. Board member of certain scientific foundations. Chairman of four international academic conferences. Senior advisor of international business for different U.N.-organizations, some governments and ministries. Owner of 2 consulting firms, chairman and shareholder of 3 companies and board member of altogether 10 companies in 1980-1997. Member of the Board of Lapponia House Oy. Author of 15 books, chapters in 5 books, editor of 2 books and author of 70 articles, working papers and research papers. Editorial board member of 5 international scientific journals. International operations and global business strategy expert in companies located in different countries. Holdings in Biohit on December 28, 2001: 65,000 B-shares and rights of option for 25,000 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. 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 Federation (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 28, 2001: No shares and no rights of option.



*Osmo Suovaniemi, M.D., Ph.D. 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 Institute of Management (LIFIM) in 1982. In 1976 he was awarded by the Finnish Foundation of Inventors for the single- and multichannel Finnipette 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 most patents in Finland (58 pcs) and a few hundred worldwide, mainly in the fields of medical diagnostics, optics and mechanics. Holdings in Biohit on December 28, 2001: 2,285,340 A-shares and 967,207 B-shares, no rights of option.



*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 Scientiarum 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. Holdings in Biohit on December 28, 2001: No shares, rights of option for 10,000 shares.

**Management Team**

*Osmo Suovaniemi. President & CEO.*



*Pertti Ekholm. Product Design.* With Biohit since 1988. Mr. Ekholm has worked, e.g., for ITT, Nokia Electronics, Outokumpu and Kone Instruments. In 1973 he joined Labsystems as Chief Instrument Designer, where he was responsible for the design of key instrumentation such as vertical light path analyzers and mechanical Finnpiptetors. He has been inventor in numerous patents both in Finland and abroad.



*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 after which she continued her studies at HSE and 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.



*Elisa Johansson. Financial Management.* B.Sc. (Econ., Accounting and Finance). With Biohit since 2001. Mrs. Johansson graduated from the Helsinki School of Economics in 1979. She has acted as Financial Manager of Kontram-Yhtiöt Oyj between 1987-2001, as Operation Planner at the Technical Research Center of Finland between 1984-1987, as Office Manager at Kanthal Oy between 1982-1984 and in office duties at the Embassy of Finland in Washington D.C. between 1979-1981.



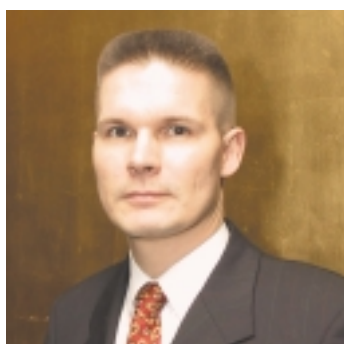
*Ritva Kara. Domestic Sales and Marketing.* B.Sc. (Engineering, Measurement and Adjustment). With Biohit since 1988. In addition to having received a B.Sc. from the Helsinki Institute of Technology in 1979, Mrs. Kara is a qualified laboratory technician. She has also completed a study program at the Institute of Marketing, Helsinki, in 1990. Before joining Biohit, she worked as Service Engineer and Product Specialist at Labsystems Oy in 1980-1988, as medical laboratory technician at the Central Hospital of Vaasa between 1979-1980 and 1969-1976 and between 1965-1969 as laboratory technician at Rikkihappo Oy, which today belongs to the multinational Kemira Group.



*Sari Mannonen (née Ylätupa). International 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 also 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 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 1955-2000. He has also experience o business-to-business e-Business systems.



*Oili Suovaniemi. Financing and Payments.* With Biohit since 1988. Mrs. Suovaniemi has completed the JOKO Executive Education study program at the Helsinki School of Economics between 1977-1978. In 1969 she graduated as a registered nurse. Between 1970-1986 she worked for Labsystems Oy and Eflab Oy in duties related to general and financial administration.

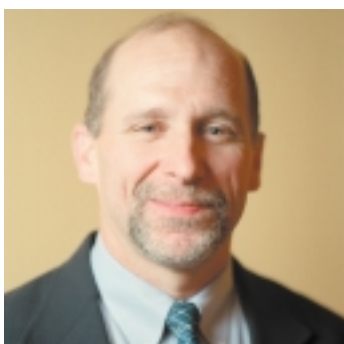


*Erkki Vesanen. Research and Development.* M.Sc. (Engineering, Electronics). With Biohit since 1989. Mr. Vesanen has acted as Managing Director of Innomedia between 1986-1989 and between 1976-1986 at Labsystems Oy in several duties related to product development, production, marketing and international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

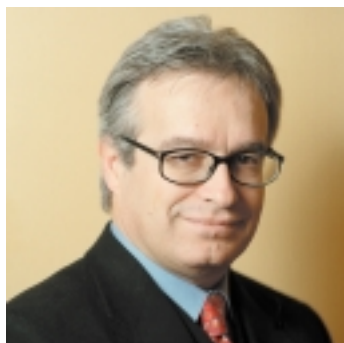
**Managing Directors of Subsidiaries**



*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.



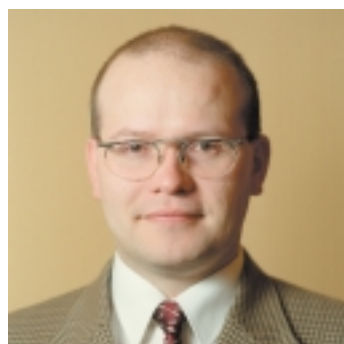
*Robert P. Gearty. U.S.* Managing Director of Biohit Inc. since April 2000. Mr. Gearty earned a B.A. in Biology from St. Michael's College in Winooski, Vermont in 1977. After graduation, Mr. Gearty was employed by Rossignol Ski Company, Williston, Vermont. In 1979, he joined Vanguard International, Inc., 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 Vanguard's U.S. introduction and subsequent distribution of the Biohit line of liquid handling products. At Vanguard 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 Vanguard 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.



*Peter Messner. Germany.* Managing Director of Biohit Deutschland GmbH since July 2001. M.Sc. (Engineering). Mr. Messner received his M.Sc. from the Technical High School TGM of Vienna in 1963. Upon graduation he joined the Finnish shipyard Rauma-Repola Oy and was in charge for the development of deck machinery for icebreakers. Between 1970-1978 he acted as Export Manager for Sanitary Equipment/Eastern Europe and Conveying Systems/Global for the Finnish group Huhtamäki Oy. He specialized in logistics, and between 1978-1980 he planned the overall bakery distribution handling for Fazer Oy in Finland. In 1980 he joined Labsystems Oy first as International Project Manager and later as Export Manager for Eastern Europe. In 1987 he commenced his own environmental consulting activities first in Finland and since 1991 in Germany.



*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 French and 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 background 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., Helsinki University Central Hospital HD 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 Department of Public Health 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 SVH Pricewaterhouse Coopers Oy, Hannele Seesvuo, 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 43.

The Board convened 18 times during 2001.

The total remuneration for the members of the Board totalled EUR 7,400.28. In addition, the members of the Board received separate consulting fees EUR 27.452,52 for duties which were not related with Board membership but instead with the members acting as scientific advisors.

#### **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 44.

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 46.

#### *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 2001 SVH Pricewaterhouse Coopers 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.

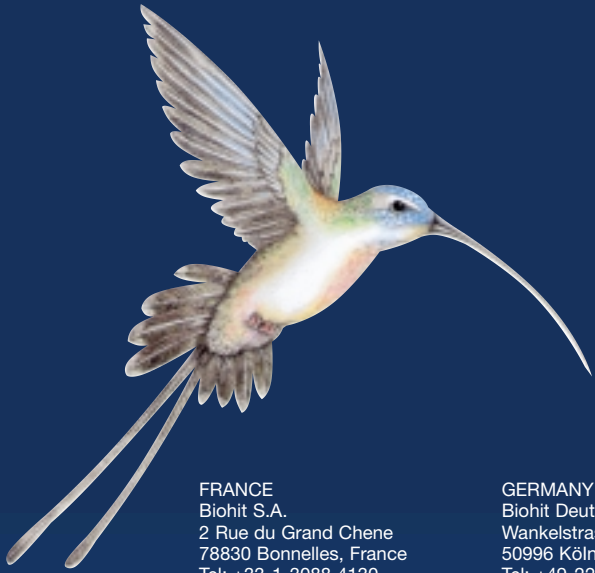
## MAJOR EVENTS IN BIOHIT'S HISTORY

Year	Events	Net Sales EUR 1 000
1988	<ul style="list-style-type: none"> <li>– Establishment of Biohit Oy</li> <li>– Basic research and market surveys</li> <li>– Electronic pipettor development</li> <li>– Establishment of Locus genex Oy</li> </ul>	
1989	<ul style="list-style-type: none"> <li>– TEKES<sup>112</sup> funding for the development of the electronic and mechanical pipettors, pipettor tips as well as microplates</li> </ul>	125
1990	<ul style="list-style-type: none"> <li>– Worldwide introduction of the electronic pipettor</li> <li>– Assembling of pipettors and injection moulding begins in Kajaani</li> <li>– Introduction of the first monoclonal antibodies</li> </ul>	491
1991	<ul style="list-style-type: none"> <li>– TEKES funding for the development of mechanical pipettors</li> <li>– First deliveries of electronic pipettors</li> <li>– Establishment of the first subsidiary in France</li> <li>– Introduction of new monoclonal antibodies</li> </ul>	2 143
1992	<ul style="list-style-type: none"> <li>– Launch of the mechanical pipettor</li> <li>– Launch of the multichannel electronic pipettor</li> <li>– Establishment of subsidiaries in Italy and the U.K.</li> <li>– Ph.D. Thesis of Tapani Tiusanen: An application invention of vertical measurement; the self-correcting, multiparameter measuring instrument</li> </ul>	4 244
1993	<ul style="list-style-type: none"> <li>– Launch of the multichannel mechanical pipettor</li> <li>– Co-operation with Eppendorf and bioMérieux begins</li> </ul>	6 419
1994	<ul style="list-style-type: none"> <li>– Development of the renewed electronic pipettor</li> <li>– Co-operation with Ortho Diagnostic Systems of Johnson &amp; Johnson begins</li> <li>– Establishment of joint venture in Japan</li> <li>– Ph.D. Thesis of Osmo Suovaniemi: The vertical measurement invention, its applications and the invention of electronic liquid handling devices</li> </ul>	8 425
1995	<ul style="list-style-type: none"> <li>– Launch of several new liquid handling products</li> <li>– Establishment of subsidiary in Germany</li> <li>– Co-operation with Eastman Kodak Co. Clinical Diagnostic Systems, later acquired by Johnson &amp; Johnson begins</li> </ul>	10 550
1996	<ul style="list-style-type: none"> <li>– Reinforcement of international sales and marketing</li> <li>– Improvement of the cost structure and quality of products</li> <li>– The GastroPanel program begins</li> <li>– Ph.D. Thesis of Sari Yläupa: An application invention of vertical measurement and immunoassays; the determination of cFn from blood samples and its importance in cancer diagnostics</li> </ul>	12 638
1997	<ul style="list-style-type: none"> <li>– Moving into new facilities in Helsinki</li> <li>– ISO 9001 -quality system certification</li> <li>– Co-operation with Becton Dickinson and 3M begins</li> <li>– Receiving EUREKA<sup>113</sup> status on the basis of which TEKES funding received for the gastric test panel program</li> </ul>	14 481

<sup>112</sup> TEKES = The National Technology Agency of Finland.

<sup>113</sup> 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.

<b>Year</b>	<b>Events</b>	<b>Net Sales EUR 1 000</b>
1998	<ul style="list-style-type: none"> <li>– Production and injection moulding in Helsinki</li> <li>– Locus genex Oy and Biohit Systems, Inc. become Biohit Group companies</li> <li>– External evaluation of the first test kit (Pepsinogen I) in the GastroPanel-program</li> <li>– Ph.D. Thesis of Auli Linnala: Basic research on Biohit's monoclonal antibodies (cFn and tenascin), which are related with cancer diagnostics</li> </ul>	16 881
1999	<ul style="list-style-type: none"> <li>– Listing on the New Market -list of the Helsinki Exchanges</li> <li>– Continuation of aggressive patenting policy</li> </ul>	20 551
2000	<ul style="list-style-type: none"> <li>– Completion of new production premises in Kajaani</li> <li>– Accreditation of the calibration laboratory for liquid handling products</li> <li>– Preparation to commence the global marketing and sales of diagnostic tests and analyzing systems</li> <li>– Commencement of the sales of instruments</li> <li>– Reinforcement of international collaboration and customer service organization through acquisitions in the U.S. and Russia</li> </ul>	24 247
2001	<ul style="list-style-type: none"> <li>– Clinical evaluations carried out in various countries for assessing the reliability of the following diagnostic tests: GastroPanel for diagnosing <i>Helicobacter pylori</i> -infection and atrophic gastritis, as well as for screening the risk of gastric cancer and peptic ulcer, and tests for diagnosing lactose intolerance and SLE.</li> <li>– Marketing of the GastroPanel began for research use</li> <li>– Development of test kit for cellular fibronectin (cFn)</li> <li>– Completion of new production premises for diagnostics in Helsinki</li> <li>– Service laboratory taken into use</li> </ul>	25 545



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