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ANNUAL REPORT 2012

Chiesi

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OUR MISSION

Our aim is to be recognised as a research-focused international Group, able to develop and commercialise innovative pharmaceutical solutions to improve the quality of human life.
We want to maintain a high quality entrepreneurial team characterised by self-confidence and a collaborative spirit.
Our goal is to combine commitment to results with integrity, operating in a socially and environmentally responsible manner.

A CONSTANT GROW-UP OF THE GROUP IN 2012

In 2012, the Chiesi Group performed better than expected, achieving sales of 1,107 million euro (+ 4.7% on the previous year), and was extremely successful with the registration of new proprietary products and the acquisition of newly licensed-in products. It also continued with its development strategy by inaugurating its twenty-fifth affiliate in Mexico, a highly promising market undergoing rapid growth, and consolidating its presence in the US. These results mean that the Group can reasonably expect further development in the next few years.

The year's results are confirmation of the company's tendency to grow at a faster rate than that of the largest developed countries (Europe, the USA, Canada, Japan and South Korea), which is expected to fall to between 0 and 3% in the period 2012 – 2016.[1]

Low levels of market growth in developed countries are caused by phenomena which are all too evident: continued price containment policies implemented by health authorities, competition from generics for off-patent special care drugs, at times amplified by government decisions that penalise branded products, and the difficulties related to the registration of new special care drugs.

The market in developing countries, on the other hand, continues to expand rapidly (+11-14% in the period 2012 - 2016).[2] This represents another valid reason for the Group to move forward with its global development policy.

Chiesi's drugs for respiratory diseases, neonatology and cystic fibrosis continued to meet with the approval of GPs, specialists and patients.

The decentralised registration procedures for Foster NEXThaler were successfully completed in October, and as a result the product has now been approved in 14 European countries. The product is designed for use with an innovative dry powder inhaler and from a clinical point of view is equivalent to Foster pMDI (metered dose inhaler), which has already been on the company's product list for some time.

In November Foster was also approved for the MART indication (Maintenance and Reliever Therapy) in 26 European countries, thus confirming its efficacy both for maintenance and "as-needed" therapy.
Distributed in over 35 countries, Foster has made a significant contribution to the company's development and is a candidate for new potential indications for chronic obstructive Pulmonary Disease COPD, severe asthma and paediatric use, as well as registration in new markets.
Market figures indicate that Foster is the biggest-selling product resulting from Italian research in the world.
In October, the registration application for Bramitob, under the local brand name Bethkis, was approved by the US Food & Drug Administration. This tobramycin formulation is already being successfully marketed in 29 countries and is indicated for the treatment of cystic fibrosis patients suffering from *Pseudomonas aeruginosa* infections. The FDA's approval confirms the success of this drug and consolidates the company's leading position in the special care field.
Curosurf, the Group's most widely available drug, also maintains its position as worldwide standard for the treatment of respiratory distress syndrome in premature neonates. In February its synthetic equivalent (CHF 5633) was awarded the *Orphan Drug Designation* by the EMA for the treatment of respiratory distress syndrome in premature neonates with a gestational age of less than 37 weeks. CHF 5633 is more resistant to inactivation compared to natural surfactants, and this favours its use even in particularly critical conditions.
Research & Development remains the focal point for the Group's sustainable growth projects. In 2012 expenditures and amortisations in R&D reached 198 million euro (+16.9% compared to 2011), reaching 17.9% of revenues; a commitment which puts us among top Italian pharmaceutical companies and twelfth at European level according to recent rankings issued by the European Commission.[3]
Within the context of Business Development, an agreement was reached with Danish company Veloxis Pharmaceuticals for the exclusive distribution of the immunosuppressive LCP-TACRO in Europe, the CIS and

Turkey. A second long-term agreement was signed with Kamada, an Israeli pharmaceutical company, for the exclusive distribution of inhaled AAT in the same countries. The drug is indicated in the treatment of Alpha 1-Antitrypsin (AATD-IH) deficiency and is currently in clinical phase III.
In May the US affiliate Cornerstone took over EKR Therapeutics, a pharmaceutical company which commercialises special care products used for hospital therapy in the acute phase, such as Cardene, indicated for the short-term therapy of acute hypertension for cases where oral drugs prove ineffective.
A recent agreement to set up a joint venture based in Shanghai, between Chiesi China and Eddingpharm Ltd, represents a further step forward in the internationalisation programme in the most important emerging market for the continued development of the Group's respiratory product line.
All of the Group's managers and collaborators have once again demonstrated professionalism, spirit of initiative and passion in their work, overcoming a number of difficulties resulting from the development and completion of delicate and complex projects and the need to exercise careful control on processes and their rate of efficiency. Their commitment has helped create the company's sustainable growth in a collaborative atmosphere, where the desire for constant improvement and total respect of the company's values and social responsibility go hand in hand. Our sincere thanks go to everyone.

Alberto Chiesi
Chairman

Paolo Chiesi
Vice Chairman
R&D Director

1 *IMS Market Prognosis, Sept. 2012.*
2 *Ibidem.*
3 *Innovation Union Scoreboard 2013 (http://ec.europa.eu/enterprise/policies/innovation/facts-figures-analysis/innovation-scoreboard/).*

A DEVELOPMENT projected IN THE FUTURE

2012 results

2012 was a year characterised by the complete overhaul of the company's organisational model, with the aim of placing the Group in the ideal conditions to ensure there is the right level of focus on growth. The process of regionalisation, which has created three macro-regions (Southern Europe, Northern Europe and the non-EU countries), has helped bring the company closer to the business and make it more flexible so as to be able to meet different market needs. The overhaul of the governance system, also facilitated by the implementation of SAP and the renewal of some IT systems in Research & Development, has enabled the Group to rationalise and make the processes of innovation, production, distribution and commercialisation of its products more efficient.

All these activities have benefited from the constructive commitment of the people who make up the company and combine to support the Group's long-term development project, which is based on innovation, a targeted increase in international presence and a process of 'managerialisation', which will continue to ensure that the outstanding skills and professional enthusiasm needed for the sustainable long-term development of the business are available.

Concerning the Group's operative results, consolidated sales (1,107 million euro) have enabled the company to increase its growth rate by 4.7% compared to 2011, which is significantly higher than that of the main European markets. The results achieved in the UK, Germany, Austria and the Eastern European countries, the Netherlands, Turkey, Russia, Brazil, Pakistan and China allow the Group to counteract the crisis, which has had a particular impact on some of the Southern European affiliates.

Export sales for the year once again exceeded the levels forecast. Operations which were begun in Norway, Sweden and Denmark in 2010 and those more recently for Chiesi Mexico have started to make a significant contribution to the company's turnover.

Cornerstone Therapeutics has performed beyond expectations and has further consolidated its position in the US hospital market, partly due to the acquisition of EKR's products.

The share of turnover of sales generated outside the domestic market has reached almost 74%, further consolidating the Group's international profile.

Corporate products, which are those resulting from internal development, represent over 65% of the turnover, thus enhancing the value of growth and contributing to improve the

company's image. Foster (over 25% of sales), Clenil (14.4%) and Curosurf (13.1%) provide the largest contribution to both turnover and global development.
Measures introduced for continual improvement involving the Group's key processes have enabled it to further reduce the share represented by the cost of goods, thus helping to maintain gross and net operating margins at a satisfactory level. As already mentioned, the SAP Enterprise Resource Planning system was implemented during the course of the year and became operative as of January 2nd 2013.
Research contributions and incentives coming from outside the Group were once again cut back and the current political-economic developments leave little hope for significant improvement on this front, in Italy at least.
A process for the complete upgrade of the Group's production plants was begun in 2012, which involves transferring the Curosurf line to the San Leonardo site, creating a production line for Foster NEXThaler at the Blois plant (France) and reorganising the liquids line in Santana de Parnaìba (Brazil). Overall, investments in production and research facilities totalled 30.7 million euro.

Production at the Parma plant reached 52.2 million units, a figure which is up by 5.8% on the previous year. The total distribution of our products worldwide stood at nearly 91 million units, confirming the international success of Chiesi's drugs.

Prospects for 2013

Thanks to its pipeline which includes some of the most promising molecules for the treatment of respiratory diseases and several rare diseases, the Chiesi Group is confident of being able to continue his development in the future. Business partnerships and geographic development represent two further key components of the programme.
The primary driver of growth for 2013 will be Foster NEXThaler, which was first launched in Germany in March. Other countries are expected to follow in the course of this and next year, rapidly making a significant contribution to the sales of the product.
Investments in R&D will continue to grow, mainly focussing on respiratory diseases, neonatology, cystic fibrosis and regenerative medicine. Further commitment to joint initia-

tives with international academic centres and other companies will help generate new R&D projects and stimulate the ability to innovate.

Ugo di Francesco
Chief Executive Officer

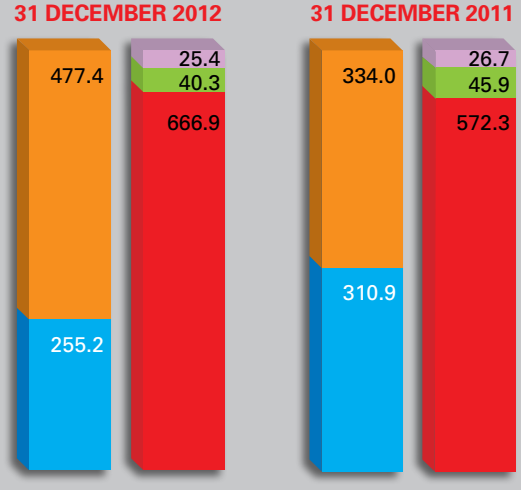
2012 Group financial highlights
(Value in Eur/000)

Operating results	2012	2011
Sales & Revenues	**1,106,808**	1,056,932
Growth	*4.7%*	*4.1%*
EBITDA	**247,120**	225,008
% on sales and revenues	*22.3%*	*21.3%*
Net income	**130,971**	120,850
% on sales and revenues	*11.8%*	*11.4%*

Other information	2012	2011
R&D costs	**197,981**	169,377
% on sales and revenues	*17.9%*	*16.0%*
Capital Expenditure:	**220,202**	72,155
- Merger and Acquisitions	160,214	1,427
- Tangible and Intangibles assets	59,988	70,728
of which R&D Investments	*12,285*	*38,985*
Number of employees	**3,830**	3,814
Number of Interim employees	276	390

Ratios	2012	2011
ROE (Net Income / Shareholders' equity)	**19.6%**	21.1%
ROCE (EBIT / Net Invested Capital)	**38.2%**	53.8%

Balance sheet structure (value in M/Eur))



(*)net of owned Shares

THE PHARMACEUTICAL SCENARIO: OLD AND NEW PLAYERS

Robert Galbraith
APM reporter (Agence de Presse Médicale) Health Europe

The largest pharmaceutical companies are at a crossroads and in the unaccustomed position of not knowing which is the best direction to go.
A successful and profitable industry is threatened by forces largely beyond its control.

A tougher regulatory environment has emerged where the focus is on a better risk-benefit ratio for new medicines, more clearly demonstrable outcomes and fewer side effects. At the same time, payers' drug budgets are being tightened by governments facing severe economic headwinds. Add in the impact of the patent cliff and it is easy to understand why there is such a bleak outlook.

Investors have become increasingly concerned about profitability of research-based drug companies. In particular they are concerned that R&D productivity for the industry as a whole is in decline and companies are finding it more difficult to recoup their costs.

As a result of these pressures, the pharmaceutical sector has entered a period of significant change.

Robert Galbraithis an English reporter working as a correspondent from Italy for APM Health Europe. ..... For over 20 years he has been dealing with economic journalism and, in particular, with the healthcare and pharmaceutical industries.

The blockbuster drug era is ending and a new one, in which specialised, smaller companies are likely to play a more important role, may be about to begin.

Much of the change is being driven by the glut of drugs going off-patent. Not surprisingly, the generics industry is growing fast and expected to start consolidating to exploit economies of scale and become more competitive.

Annual sales of generics in the global market could be as much as $230 billion by 2017. The impact is being felt most by the multinationals. Ernst & Young forecast last year that combined sales of the 13 largest drug companies would fall by 4% over the whole of 2012 compared to the previous year, largely as a result of generic competition.

Although there is considerable divergence in the strategies being employed to deal with the challenges, diversification has become a common watchword. Some groups have developed their own generics divisions while others see the over the counter market as an area in which brands will always have value.

Research-based companies are also looking to geographical expansion to offset the impact of the patent cliff, especially in new markets which have high potential growth rates. More than 70% of the world's population live in emerging markets and they generate 31% of its GDP.

An IMS Health study in 2012 estimated that these areas will account for 30% of international pharmaceutical spending by 2016. The most important are the so-called BRIC nations, Brazil, Russia, India and China. However, while offering obvious potential

rewards, these areas can also be problematic because they are so dissimilar to developed markets and even very different from each other.

On the other hand, their dissimilarities also provide opportunities not necessarily available in more developed markets. For example, the larger pharma companies are having considerable success with branded generics in emerging economies. They have higher margins and can generate loyalty in same way that OTC products do.

Perhaps, the biggest changes within the industry will result from efforts to improve R&D productivity. The focus has traditionally been on developing treatments for diseases with large patient populations because that is a way to be assured of a return on investment.

Yet, in the post-blockbuster era, attention is turning towards meeting unmet needs and developing personalised and targeted therapies. This aspect is reflected in new regulatory attitudes. Payments-by-results and cost-effectiveness agreements, designed to make pharmaceutical spending much more efficient, are increasingly being considered.

The growing interest in rare diseases is one aspect of this trend. It is by definition an area of unmet needs and specialisation. It is aimed at diseases that public health systems want to address because of the high impact on individual patients. It also has scientific benefits because the advances made in one rare disease may be applied in other fields.

It is an area which make business sense too. The returns on orphan drugs are significant. Clinical trials are small because of the reduced number of patients, therefore easier to organise and less costly. Commercial costs are similarly limited because there is no need for a large sales force. In addition, there is little threat from generics when the drugs go off patent because of the limited sales that they represent.

However, Big pharma has been slow to enter this market and many of the orphan drugs have been developed by mid-sized companies and biotechs. That may change as the major companies develop specific rare diseases divisions. But, for the time being, the approach to orphan drugs appears to demonstrate that smaller players in the industry can be more flexible and specialised.

The R&D productivity problem faced by larger groups does not seem to be affecting mid-sized companies and biotechs in the same way. Global R&D funding by drug companies is thought to have grown by about 5% last year. But some big groups were actually cutting R&D budgets in 2012, in an effort to make the pipeline more profitable, meaning that it was their smaller rivals who were investing more.

This aspect may have an impact on M&A strategies. It is questionable whether there is still an appetite for huge deals like those that saw Pfizer acquire Wyeth and Merck & Co capture Schering Plough. Few companies have the resources and it is debatable whether they create value or increase productivity. Instead more targeted acquisitions are expected, so-called "bolt-on deals" where a company is bought to be fitted in an existing area of the business.

More important perhaps, will be the development of partnerships and licensing agreements. This allows larger companies to benefit from early-stage research without taking on the risk of the project until it has been advanced. Pharma companies are also increasingly keen to become part of research networks, whether this be with academic institutors charitable foundations or biotechs and other pharmaceutical companies, in a shared approach to scientific study. There was a time when it was thought that the challenges facing the pharma industry would inevitably lead to a slowdown in the number of new drugs being developed. There were some who questioned where the new medicines would come from.

That does not seem to be case at all: the number of new drugs being developed has actually been gathering pace. In 2012, the Food and Drug Administration (FDA) approved 39 novel medicines, an increase of 30% on the previous year and the highest number for fifteen years. Oncology, with 11 new drugs approved, was the most important field.

This suggests that the changes are having an invigorating effect on an industry which had become complacent and too dependent on its blockbuster business model.

RESEARCH & DEVELOPMENT STRATEGY

Chiesi continues to be strongly committed to grow through innovation by internal research and development. In 2012 Chiesi dedicated 17.9% of revenues for a total of €198 mill (an increase of +16.9% on the previous year) to R&D and completed the investment related to the new R&D Centre which has been fully certified by the relevant Health Authority (AIFA) and received the 2012 Facility of the Year Award assigned by IPSE (International Society for Pharmaceutical Engineering).
The transfer of all R&D functions to the new site marks the transition of the organisation to the standards of the future and the implementation of its long-term strategy.
There are four main pillars to the Group's R&D strategy:

1. Product Focus and Productivity
2. Geographical Coverage
3. Development Model
4. Innovation

Chiesi plans to grow mainly from the strength of its core competences, which are focused on the respiratory area and drug delivery by inhalation. Research & Development in the respiratory therapy area represented 67% of total R&D spending.

Nevertheless, a significant portion of future growth is expected to come from development in the Special Care area. The latter implies focus on indications for neonatology and other diseases with high unmet medical needs managed by specialists in therapeutic areas or those related of the Company's business focus. The geographical scope of the clinical programmes will move from a focus on Europe to a broader scope, which will be global where possible, through partnerships for regions where Chiesi lacks capacity or capabilities. The model will adapt to this global scope and include the possibility of co-development especially for very demanding programmes such as respiratory projects for the US territory. Finally, Chiesi R&D is incrementally and efficiently implementing the shift from formulation and delivery innovation to a more visionary innovation in the research approach, exploring not only an increased number of new molecular entities, but also fields such as disease-modifying and regenerative medicine.
An indicator of this drive towards innovation is the positive trend in recent years in new patent filings. The Chiesi patent portfolio today comprises more than 1,400 patents in its therapeutic areas of interest.

Pipeline Progression

During 2012, the pre-clinical pipeline delivered a number of new compounds that have successfully progressed towards clinical development. New projects include single agents and fixed combinations. These molecules have potential for clinical applications in asthma, chronic obstructive pulmonary disease (COPD), cystic fibrosis and for the complications of prematurity. New classes of compounds such as PI3Ky/δ inhibitors and bi-functional molecules endowed with both bronchodilator and anti-inflammatory activity initiated the lead identification phase. Three new classes of compounds (MABA, p38 inhibitors and HNE inhibitors) progressed into lead optimisation and one new compound - a long-acting inhaled corticosteroid- initiated GLP -compliant pre-clinical development. Furthermore, 8 additional new drug targets were identified, which will be further explored in 2013.
21 new patents applications in 2012 confirm the growth trend of the last years.

Clinical Pipeline and Regulatory Status

Clinical development absorbed 59% of total R&D spending. In line with the Group strategy, investments in clinical development were directed primarily towards developing the respiratory pipeline. In 2012, 12 early development project and 17 full development project were active; in this contest, 22 clinical trials were ongoing, 10 of which were completed within the year.
New projects initiated clinical development reaching the stage of either first-in-man, first-in-patients or both within December 2012. A single agent NCE belonging to the class of Long-Acting Muscarinic Antagonists (LAMA) successfully completed the first-in-man study and initiated clinical development in COPD patients. A new potent and safe inhaled phosphodiesterase-4 (PDE4) inhibitor successfully completed first-in-man studies and is now being tested in asthma and COPD patients. Patient enrolment was also initiated for a new fully synthetic sur-

factant which, unlike existing surfactants contains two phospholipids and two peptide analogues of human surfactant proteins B and C. This distinctive feature is expected to achieve greater efficacy and better resistance to inactivation compared to products currently being marketed.

The Phase II programme for the triple fixed combination of a ICS-LABA-LAMA was successfully completed. The combination is now ready for Phase III pivotal studies.

The application for marketing authorisation of the new dry powder inhaler formulation of Foster (fixed combination of beclomethasone dipropionate and formoterol) was successfully completed.

Foster Nexthaler is now approved in Europe and the launch in various countries in 2013 will provide the asthma population with a very patient-friendly, easy-to-use, breath-activated device. Comparative studies performed during clinical development showed that the use of Foster Nexthaler is associated with a lower rate of errors in the use of the device compared to treatment delivered through other DPI inhalers.[1]

Foster pMDI was also approved in Europe for a new treatment regimen: the so-called Maintenance and Reliever Therapy (MART) for asthma after demonstration that the use of "as needed" Foster pMDI compared to "as needed" salbutamol significantly prolonged the time to first exacerbation resulting in a 36% reduction in exacerbation risk.[2]

The international registration plan for Foster pMDI continued successfully with a new submission in Israel and two additional approvals in Asian countries during 2012. Finally, the Foster pMDI COPD clinical programme was successfully completed, which will result in a marketing application for this new indication in 2013.

Another successful and significant regulatory milestone reached by Chiesi R&D was the approval of nebulised tobramycin by the FDA.

The Neonatology pipeline has progressed with a new synthetic surfactant reaching the clinical milestone "first study in patients", as noted above. Moreover, the Company plans to expand the pipeline in this therapeutic area through the acquisition and development of products designed to address complications of prematurity. Such acquisitions are targeted for the year 2013.
Consistent with its strategy to expand growth in the Special Care area, the Group has successfully concluded negotiations for the acquisition of two new products currently in phase III development.

- Alpha-1 Anti-trypsin (AAT) was licensed from Kamada, an Israeli Biopharmaceutical Company specialising in unique protein purification technology. The compound is the first inhaled AAT developed for the treatment of patients with emphysema caused by inherited AAT deficiency.
- LCP-Tacro, an innovative formulation of tacrolimus specifically designed to overcome the pharmacokinetic limitations of tacrolimus formulations currently on the market, was licensed from Veloxis. The compound is being developed for the prophylaxis of solid organ transplant rejection.

Both compounds are completing phase III programmes and have potential for expansion to additional indications.
Finally, in 2012 the Phase IIA development of CHF 5074 was completed, a microglial modulator with potential for the treatment of mild cognitive impairment and Alzheimer's Disease. The compound showed good safety and promising efficacy profiles. Chiesi is seeking a partner for future development and commercialisation of this promising compound.
In short, Chiesi remains fully committed to innovative R&D in its core areas of respiratory disease and neonatology, and to advancing and expanding the pipeline in these areas, as well as expanding R&D in other special care areas.

1 *P.G. Linnane, T. Voshaar, M. Spinola, A. Campanini, D. Lock, M. Scuri, B. Ronca, AS Melani. Usability evaluation of NEXThaler versus Diskus and Turbuhaler. European Resp. Society Annual Meeting, Vienna 2012, P1797:313s.*

2 *Papi A, Corradi M, Pigeon-Francisco C, Baronio R, Siergiejko Z, Petruzzelli S, LM Fabbri, Rabe KF. Beclomethasone-formoterol as maintenance and reliever treatment in patients with asthma: a double-blind, randomised controlled trial. Lancet Respir Med 2013; 1: 23-31.*

PHARMACOECONOMICS:
PAST, PRESENT AND FUTURE

Renato Dellamano
President of ValueVector and MME Europe, Milan, Italy

Pharmacoeconomics: what are we talking about?

When talking about a subject, caution should always be exercised to make sure all those involved in the conversation, even whilst using the same terminology, are actually talking about the same thing. This is particularly important when talking about pharmacoeconomics (PE) for two reasons: first of all, because too many people talk about it often only having a limited knowledge about it, typically the PE specialty area they are familiar with. Secondly, because, like all other sciences, PE is itself also a means rather than an end, i.e. it can be used for various purposes and from multiple perspectives.

Using one of the broadest and most popular definitions of PE – the one proposed by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), PE is "the scientific discipline that evaluates the clinical, economic and humanistic aspects of pharmaceutical products, services, and programmes, as well as other health care interventions, to provide health care decision makers, providers and patients with valuable information for optimal outcomes and the allocation of health care resources".[1]

While this is a pretty broad definition, it faithfully reflects the reality of what PE is used for, which is what really matters in practical terms.

A health economist and former professor of hospital management and – from 1996 to 2003 – global Director of Strategic Pricing at Roche, in Basel, Dr. Dellamano has built his reputation in the fields of pharmaceutical pricing, reimbursement and market access thanks to a solid methodological background with extensive global and local business experience, gained in more than 30 years in the pharma business.

Pharmacoeconomics: Its Present

At present there are two main areas of PE application:

- In healthcare systems, public and private payers use it to assess the merits of new medicinal products and make reimbursement and formulary coverage decisions
- In the pharmaceutical industry, it is primarily used to justify prices of the same products and support formulary listing, in the context of national and local (e.g., regional) pricing and reimbursement (P&R) procedures.

In particular, in some healthcare systems (e.g. in the United Kingdom and Australia), PE is used as the primary – if not the sole – criterion to make reimbursement decisions and, more recently, to negotiate discounts (e.g. "Patient Access Schemes" in the United Kingdom) with manufacturers; in other countries, PE is one among several tools used to evaluate medicinal products, with a broader range of factors and criteria used to reach a P&R decision.

In this context, on the one hand, pharmaceutical companies often use PE when it is too late, when clinical trials have already been completed and the final target indications and positioning of the new product have already been defined, for the good or bad. On the other hand, payers and formulary commissions often use PE instrumentally to justify pricing and reimbursement decisions that – in reality – are primarily driven by budget management considerations, in an effort to contain or reduce pharmaceutical expenditure.

For instance, this is perfectly illustrated by the application of PE in the context of the recent pharmaceutical pricing reform in Germany (the AMNOG), where it has been explicitly stated that: "The goal of the AMNOG is to contain the rapidly rising expenditure for medication…".[2]

The debate is now open in the very country that made PE the backbone of its health technology assessment (HTA) processes, i.e. the UK: "Value Based Pricing" (VBP) is supposed to come into force in less than a year from now, but little is known about what VBP will actually consist of; in the meantime, the role of the National Institute of Clinical Excellence (NICE) – the PE body that determines the fate of all new health technologies in England – is largely expected to remain crucial as is the use of PE thresholds to determine what should and should not be reimbursed on the National Health Service (NHS).

Pharmacoeconomics: Its Future

There is little doubt that PE is here to stay and more and more healthcare systems have declared that PE will play a greater role in HTA and P&R decisions (including France, Italy and – more recently – Spain).

The problem is how PE will be used. If PE is used to reduce the value of new drugs solely with the aim of meeting general budget control objectives, innovation will obviously suffer, especially if the way PE is used by payers in HTA and P&R decisions fails to become more transparent.

On the other hand, it provides an opportunity to enter into early discussions with national payers – an option already in existence in countries like Germany, Italy and the United Kingdom – on how clinical development programmes for their new products should be designed, what the appropriate comparators would be, outcomes and endpoints (e.g. quality of life) to best demonstrate the value of the new product.

This opportunity is particularly important for small and medium-sized pharmaceutical enterprises – which cannot afford the costly implications of negative HTAs and P&R failures that normally would only marginally affect larger corporations.

If PE is used to design clinical trials and development programmes more effectively, and to agree, in advance, on what methods and outcomes should be used to document a product's value, and how real-world use should be modelled both from a healthcare system and a drug manufacturer's perspective, then it will finally have fulfilled its purpose. To use Michael Drummond's words: "the future of pharmacoeconomics lies in developing both trial-based and modeling studies, improving their credibility and meeting the needs of decision makers"[3]. Interestingly, Michael Drummond's words date back to 1996: perhaps it is now the time to make this dream come true, for the common benefit of patients, healthcare systems and truly innovative pharmaceutical companies…

1 *From the Website of the ISPOR: http://www.ispor.org/terminology/default.asp, accessed on February 4, 2012.*

2 *Downloaded and translated from the Website of the German Ministry for Health: http://www.bmg.bund.de/krankenversicherung/arzneimittelversorgung/arzneimittelmarktneuordnung-sgesetz-amnog/das-gesetz-zu-neuordnung-des-arzneimittelmarktes-amnog.html, accessed on February 4, 2012.*

3 *Drummond MF, The future of pharmacoeconomics: bridging science and practice. Clin Ther. 1996 Sep-Oct;18(5):969-78; discussion 968.*

MAIN PRODUCTS

Foster

A fixed combination of beclomethasone dipropionate (corticosteroid) and formoterol fumarate (a long-acting β_2-agonist with rapid onset of effect) to be taken by inhalation. The drug is available as a pMDI (pressurised metered–dose inhaler) in solution. This formulation based on Modulite technology allows one or two inhalations twice daily. Foster's key feature is its extra-fine formulation, which guarantees uniform distribution and high drug deposition throughout the entire bronchial tree, including the small airways. Following its launch in Germany in October 2006, Foster is now sold in over 35 countries worldwide and further launches are planned throughout 2013.
The development of additional indications is underway, such as the treatment of chronic obstructive pulmonary disease (COPD), and the extension of Foster clinical use to include paediatric and adolescent patients. An innovative extra-fine dry powder inhaler formulation ("NEXThaler" DPI device) has been recently approved and is expected to be launched in Europe in 2013.

Brexin

Piroxicam β-cyclodextrin (PBC) is a successful example of the clinical application of "guest-host" technology, which has been awarded the Nobel prize. The guest is a starch derivative known as β-cyclodextrin, which solubilises the piroxicam host, a non-steroidal anti-inflammatory, thereby improving its pharmacological properties. Piroxicam β-cyclodextrin is mainly indicated for the treatment of painful and inflammatory con-

ditions in patients with rheumatic diseases such as rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. The drug is today sold in Europe, South America, Asia and Africa.

Clenil

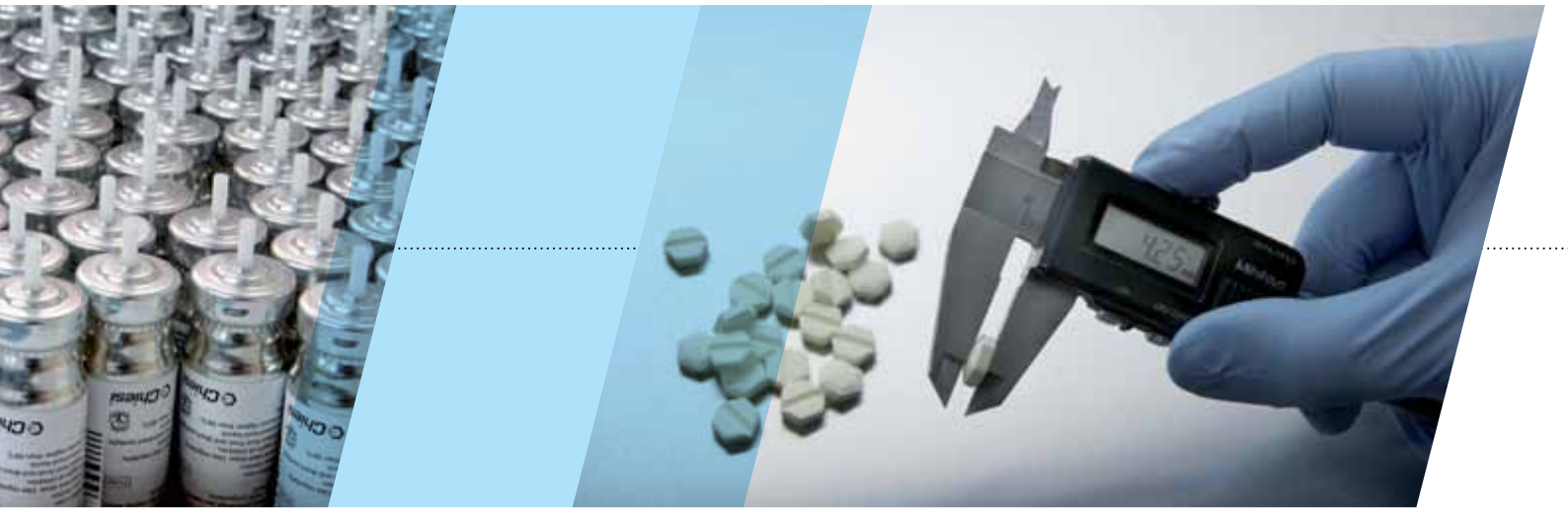
Clenil (beclomethasone dipropionate) is one of Chiesi's historical products and has become well established in the market since its launch in Italy in 1979. It is indicated for the treatment of asthma and other inflammatory and allergic conditions, and it comes in various formulations (pMDI, DPI and unit-dose vial for nebulisation). The pMDI formulation uses Chiesi patented Modulite technology. This has enabled the drug to achieve significant results in European countries, such as Italy and the United Kingdom, where sales and market share recorded constant growth last year.

Atimos

This is a formoterol fumarate pressurised inhalation solution (pMDI) based on Modulite technology and indicated for the long-term symptomatic treatment of asthma and chronic obstructive pulmonary disease (COPD). Thanks to its rapid onset and long-lasting therapeutic action (up to 12 hours), formoterol is considered to be one of the best β_2-agonists currently available on the market. Atimos ensures optimal distribution of this active ingredient throughout the entire bronchial tree, including the peripheral airways.
The drug is sold in all the main European markets and has proven to be well tolerated with respect to other DPI and pMDI formulations. The licensing of Modulite technology to Novartis confirms its efficacy.

Clipper

An oral corticosteroid indicated for the treatment of mild to moderate ulcerative colitis in its active phase. The drug is available in prolonged-release gastro-resistant beclomethasone dipropionate tablets, to be administered once daily. The release design of the product ensures targeted delivery of the active ingredient in the mucosa of the distal ileum and the proximal colon, where the inflammatory process develops. The drug



exerts its anti-inflammatory effect locally and reduces the systemic adverse events normally associated with corticosteroids to a minimum. It is currently registered and sold in Italy, Belgium, Spain and the United Kingdom.

Curosurf

An animal-derived surfactant for endotracheal administration indicated in the prevention and treatment of neonatal respiratory distress syndrome in premature infants.
This disease is amongst the most common causes of neonatal death and is the result of lung immaturity in preterm newborns.
Its active ingredient is a natural surfactant mainly composed of polar lipids and proteins. Since its introduction in 1992, Curosurf has been used to treat approximately 2 million newborns. It is the world's leading surfactant, with a 68% market share, and is available in over 70 countries worldwide.

Bramitob

This new tobramycin formulation has been developed in a sterile inhalation solution for the treatment of chronic pulmonary infections caused by *Pseudomonas aeruginosa* in patients with cystic fibrosis (CF). The drug is available in mono-dose vials, to be administered twice daily in 28-day therapeutic cycles, alternating with a period of treatment suspension of the same duration. Bramitob showed improved lung function, reduced the need for and length of hospital stays, as well as the number of work and school days lost, and the need for intravenous antibiotics.
Bramitob is Chiesi's first product for cystic fibrosis and is registered and sold in 25 countries.
The USA launch, with the brand name "Bethkis", is planned for the next few months.

Hyaneb

This is a hypertonic solution for inhalation containing 7% sodium chloride and 0.1% sodium hyaluronate.
Hyaneb is a new formulation that makes it possible to fully benefit from the moisturising properties of hypertonic solution and at the same time minimise both the undesirable effects and unpleasant taste.

This result was achieved thanks to the addition of sodium hyaluronate, which, besides its specific properties, is also a macromolecule, and therefore does not modify the hypertonicity of the solution or its efficacy. The nebulisation of Hyaneb facilitates the mobilisation of the viscous secretions in the airways due to an osmotic mechanism. The high percentage of salt attracts water and facilitates the hydration of the mucus. Hyaneb is particularly indicated in patients with cystic fibrosis and in patients with bronchiectasis.

Iperten

This last generation dihydropyridine calcium antagonist (manidipine) is indicated for the treatment of mild to moderate hypertension. Unlike other traditional calcium antagonists and in addition to its antihypertensive action, manidipine also exerts specific effects aimed at reducing the total cardiovascular risk and improving the quality of life of hypertensive patients.
Today, manidipine is available in many countries under different brand names: Italy, France, Tunisia and Morocco (Iperten); Brazil (Manivasc); Greece and Germany (Manyper); Spain (Artedil).

Peyona

Peyona (caffeine citrate) is an orphan drug for hospital use only, registered in Europe through a centralised procedure and indicated for the treatment of primary apnoea of premature newborns. This pathology is characterised by the incomplete development of the brain centres which control respiration. Apnoea of prematurity is the manifestation of respiratory pauses, which reflect the immaturity of the breathing control systems. Caffeine stimulates the centres that control the central nervous system and has been shown to increase survival rate without neurological deficit, reducing respiratory support and the incidence of bronchopulmonary dysplasia.
The drug is marketed in Austria, Germany, the Czech Republic, Spain, Greece, Holland, Slovakia, the UK, Mexico, Poland, Hungary, Slovenia and Italy and was recently approved in China.

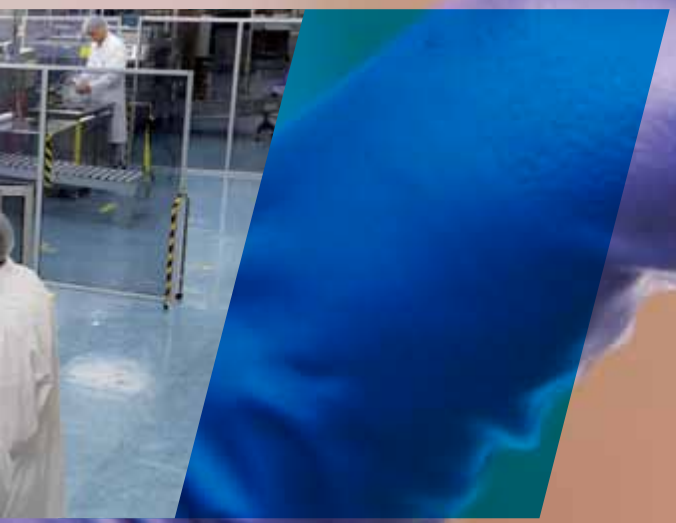
INDUSTRIAL OPERATIONS

Chiesi Group production takes place at three sites: the Parma production facilities (Italy), with 430 employees, who are split between the San Leonardo and via Palermo plants; the Blois-La Chaussée Saint Victor plant (France), which employs over 60 people; the Santana de Parnaìba plant (Brazil), which has over 100 employees.

Parma

The Group's most important production plant is also an international supply centre and exports to over 60 countries. The San Leonardo plant operates under the ISO 9001:2008 Quality Management System Certification and has passed many inspections carried out by the regulatory authorities of a number of countries, including the US Food and Drug Administration, the Canadian Therapeutic Products Program and the Agenzia Italiana del Farmaco.
A Health and Work Safety Management System complying with British Standard OHSAS 18001:2007 and an Environment Management system in accordance with ISO 14001:2004 have also been implemented and certified.
The proper application of international Good Manufacturing Practice standards, achieved using avant-garde technologies, represents the best way to guarantee worker safety and respect for the environment.

Annual production in Parma is over 52 million sales units.
The San Leonardo production facilities prepare solid form drugs: tablets and powders for DPIs (Dry Powder Inhalers); solutions and suspensions either for pressurised MDIs (Metered Dose Inhalers) with eco-friendly propellants (HFA) or sterile unit-dose vials (UDV) with Blow-Fill-Seal technology (BFS) for use with a nebuliser.
Current 3-shift production capacity for sterile UDV nebulisation polythene vials stands at 210 million units (vials) per annum. MDI double shift production capacity is in excess of 25 million canisters, with further successfully trialed potential capacity using a third shift.
The via Palermo production facilities prepare vials of sterile suspension for endotra-



cheal administration (Curosurf) and liquid form pharmaceuticals such as drops, syrups and nasal sprays. The 2006 expansions made in the Curosurf sterile suspension production department, which have been approved by European health authorities and the US FDA, along with those made at the plant supplying the active ingredient, have increased capacity to over 400,000 units. Due to growing sales of the product, plans have already been approved and begun for further significant expansion in new production departments, both for the active ingredient and the drug.
In addition, an automatic filling and assembly line for a new Dry Powder Inhaler (Nexthaler) is also ready and has already produced several hundred thousand units, which also includes the packaging line.
Production and support processes (Cleaning in Place, Sterilising in Place) are managed and monitored by approved IT systems. In order to further increase the level of automation, Manufacturing Execution System (MES) type IT architecture has been put in place. The IT dispensing system has been linked to this, whereas the electronic batch record, already operative in the sterile UDV and pMDI departments, is now being extended to the other departments.
The Engineering department in Parma has made a fundamental contribution to the creation of the new Research Centre and its approval from the various authorities concerned.

Blois

Production at the Blois facilities stands at over 6 million sales units, which are mainly destined for the other affiliates in the Group. The French production labs specialise in capsule and tablet blister packaging and also in the final assembly and production steps for MDIs, which can then be deposited in the ample refrigerated storage facilities at the plant.
The analytical transfer activities have been completed to authorise the Blois plant to check and release batches.
The plant is also equipped for direct distribution to the client for both the French and export markets.

Lastly, a new department is being created for the production, packaging, checking and storage of the new Nexthaler Powder Inhaler to assist the existing one in Parma.

Santana de Parnaìba

These facilities produce over 7 million sales units. The production lines prepare solid pharmaceutical forms (tablets), liquids and solutions and pressurised suspensions for inhalation (MDI), formulated for use with eco-friendly HFA propellant.
Aside from the local market, these products are destined for those of the Group's other affiliates, including Italy and the UK, as a result of AIFA approval (Italian Agency for Pharmaceuticals) following regular inspections on site, and for export to licensees and distributors.

Technological Support and Corporate Industrial Governance

The Corporate Manufacturing Technology, Corporate Engineering, Corporate Quality Operations, Corporate Logistics and Corporate HSE departments are able to support:

- Research and Development in scaling up developed products;
- production transfer between facilities inside or outside the Group;
- partners, when they produce directly using technologies patented by the Company.

In addition, they are able to support:

- the due diligence activities for Business Development;
- the technological lifecycle management of existing products

The Corporate Production function ensures that Lean techniques are made widely available throughout the Group's facilities to guarantee maximum productivity.
Lastly, Corporate Industrial Management Control oversees the Group's budget, product-costing and Industrial Reporting processes and also supports the economic assessment of the other corporate functions' activities, as well as managing production outsourcing.

STERIL-
OWN CROSS

THERAPEUTIC AREAS

Respiratory diseases

The company is fully committed to the treatment of pulmonary diseases. To this end, we have created drug delivery technologies and devices to ensure efficient active ingredient distribution in the lungs. Asthma is a chronic inflammatory disease affecting the entire bronchial tree.
Foster has been developed in order to provide innovative treatments for the respiratory field; its distinguishing feature is its extra-fine formulation based on Modulite technology.
The Modulite spray, which is able to release the active ingredient as extra-fine particles, guarantees the distribution of the drug throughout the entire bronchial tree, thus ensuring uniform treatment of inflammation and bronchoconstriction in the central and peripheral airways.
In addition to improving asthma treatment, the Group is currently engaged in identifying new effective treatments for chronic obstructive pulmonary disease (COPD), a condition which is characterised by a number of therapeutic needs that are as yet unmet. The pipeline mainly consists of projects designed to make significant advances in the treatment of asthma and COPD, thereby continuing to strive towards improving the quality of life of patients affected by these diseases.

Special care

Chiesi is also focussing its attention on the treatment and care of patients suffering from rare diseases, which can be potentially life threatening. The commitment in this area is considered strategic for the Group's future and potentially of great social impact. Aside from its longstanding commitment to the treatment of respiratory distress syndrome (RDS), a field in which the surfactant Curosurf has become the international gold standard, the company now also commercialises Peyona for the treatment of premature apnoea and is looking into other neonatal diseases, including bronchopulmonary dysplasia.
It wants to offer the medical and scientific communities new therapeutic options for the treatment of serious genetic diseases such as cystic fibrosis. There have been two initial steps in this direction: the first was the launch of Bramitob and the acquisition of Hyaneb for the treatment of cystic fibrosis patients, and the second was to set up a joint initiative with physicians and associations to improve the management of patients affected by this disease.

GLOBAL MARKETING

Sponsorship

The Chiesi Group supports many scientific activities and actively participates in some of the most important medical – scientific congresses in its therapeutic areas of interest.

Respiratory

European Respiratory Society (ERS)

The ERS is the leading professional organisation in its field in Europe. Its scope covers both basic science and clinical medicine. Chiesi is one of the major sponsors of the ERS congress, a meeting hosting over 22,000 physicians interested in the respiratory field.

American Thoracic Society (ATS)

The ATS mission is to improve health worldwide by advancing research, clinical care and public health in respiratory disease, critical illness and sleep disorders. Chiesi is a sponsor of the ATS congress.

Cystic Fibrosis

European Cystic Fibrosis Society (ECFS)

The ECFS provides an international forum on all aspects of cystic fibrosis and fosters the best possible care for people with cystic fibrosis.

ECFS Patient registry

Chiesi is the sole pharmaceutical sponsor of the Patient Registry since 2009. The purpose of the ECFS is to measure, survey and compare aspects of cystic fibrosis and its treatment in participating countries, to provide data for epidemiological

research, and to identify special patient groups suitable for multi-centre trials.

Respiratory Distress Syndrome

Curosurf Family Meeting

The International Workshop on Surfactant Replacement can be considered one of the most important events sponsored by Chiesi. It is also commonly known as the "Curosurf Family Meeting" due the limited number of participants who attend only by invitation. The first edition of the Curosurf Family meeting was held in 1986; over the years, it has become a worldwide reference point for research into the surfactant field.

Recent Advances in Neonatal Medicine Congress

The Recent Advances in Neonatal Medicine Congress is organised every 3 years in Wurzburg by professor Christian P. Speer, with the support of the company as gold sponsor. The *Chiesi Excellence in Neonatology Prize* is awarded to the most important experts in the neonatology area.

European Society for Paediatric Research Congress (ESPR)

The European Society for Paediatric Research Congress is the most important European paediatric meeting with a focus on neonatology. The sponsorship agreement includes, alongside the ordinary congress activities, the Robertson Award for Neonatal Lung Research and the Neonatal Lung Symposium, both sponsored by an unrestricted educational grant.

European Society of Neonatologist Courses

Chiesi is the only sponsor of a two-day post-graduate course prior to the ESPR Congress, an interactive course with top level researchers, creating a partnership with the new generations of specialists.

Donorship

Cystic Fibrosis

Fondazione per la Ricerca sulla Fibrosi Cistica - onlus

The Fondazione per la Ricerca sulla Fibrosi Cistica – Onlus is a no-profit social utility

organisation, promoting and financing innovative research projects on cystic fibrosis. It also supports the training of young researchers and healthcare professionals, informing and updating them and the general public about the disease.

Respiratory Distress Syndrome
The Curosurf Team for the Children and Curosurf Family Meeting Community are supporting two projects in Central and South America:

BRAZIL: Como Gente Grande - Educate to fight Poverty – *"Project for People" Association – Milan, Italy*

The project, supported by the Curosurf Family Meeting Community, takes place in Valeria (Salvador de Bahia), a "Favela" of over 50,000 inhabitants. Its objective is to educate young girls (11-12 years old) to help reduce the high number of teenage pregnancies, often associated with obstetric complications, the sixth cause of mortality amongst Brazilian adolescent girls.

EL SALVADOR: The children's house *"Soleterre", Association Milan – Italy*

The project is aimed at preventing and reducing the number of school drop-outs and providing medical assistance for children and their mothers living in rural areas where poverty affects over 40% of the total population. 110 children are cared for and fed daily at the kindergarten and primary school.

High level donorship
Chiesi joins some of the most important global initiatives aimed at reducing the impact of major respiratory diseases on a global scale.

Global INitiative for Asthma (GINA)

The Global Initiative for Asthma (GINA) works with health care professionals and public health officials around the world to reduce asthma prevalence, morbidity and mortality.

Global Initiative for Chronic Obstructive Lung Disease (GOLD)

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) works with health care professionals and public health officials

to raise awareness and to improve the prevention and treatment of Chronic Obstructive Pulmonary Disease (COPD).

Global Alliance against Chronic Respiratory Diseases (GARD)

The Global Alliance against Chronic Respiratory Diseases (GARD) contributes to the WHO's global work to prevent and control chronic respiratory diseases. GARD is a voluntary alliance of national and international organisations, institutions and agencies from a range of countries working towards to reducing the global burden of chronic respiratory diseases.

Patient Organisations

Chiesi supports the following international organizations:

Respiratory

European Federation of Allergy and Airway Diseases Patient Association (EFA)

The EFA is a European network of patient organisations, prompted by the belief that an international organisation formed by European patient associations would be a more effective way of meeting the needs and safeguarding the rights of patients and their carers.

International Primary Care Respiratory Group (IPCRG)

The IPCRG provides a forum for its constituent national groups so that it may represent international primary care perspectives in respiratory medicine and raise the standards of care in individual countries and globally.

Cystic fibrosis

European Young Investigator Meeting

This meeting is organised by the European Cystic Fibrosis Patient Organisation together with the European Cystic Fibrosis Society. It aims to foster interaction between young scientists in order to create a long-term collaborative European network of CF investigators.

HUMAN RESOURCES

The most important and interesting event for the people in the Chiesi Group in 2012 was the *Voices* survey, a carefully designed tool providing an opportunity for everyone in the company to be heard and express their point of view on key issues concerning the climate in the workplace.
The survey, organised with the help of both the management and agency Towers Watson, which acted as guarantor for the methodology used, was launched in June. The results, which were released in October, highlighted that 86% of answers were supplied, a particularly high level coming well above the international benchmark.
The most revealing figure in the survey concerns people's level of *engagement*, which stood at 91%, once again above average in a comparison with that of other companies. Unusually high results were also achieved for enablement and organisational efficacy. Areas for improvement pinpointed by those taking part in the survey included company image, training and customer orientation. It was also particularly interesting to note the numerous additional comments from participants, highlighting the level of interest in the initiative.
Following the survey a series of focus groups were organised, which mainly concentrated on the areas for improvement emerging from the answers. The meetings generated a plan of action shared by all the affiliates and directly adopted by the company management and the CEO, who formally undertook to develop the measures for improvement resulting from the focus groups.

Organization

In 2012 the new Corporate Governance model was also implemented, with the aim of creating the ideal conditions for the Group to allow sufficient focus on growth. As part of this project, the regionalisation process was put into effect, with the result that three macro-regions were established (Southern Europe, Northern Europe, non-EU countries), designed to bring the company closer to business aspects and make it more flexible so as to be able to meet different market needs.
The new organisational development plan is fully operative and the delicate process leading up to its launch did not slow down normal scheduled activities.
Also of note was the change management process accompanying the implementation of the new information system SAP in Italy, which involved a well-structured communications and training programme, in addition to the organisational alignment concerning numerous departments.

Development

Regarding development activities, a Job posting platform was launched, and as a result several of the company's people have successfully applied for key international positions which they have already taken up. After taking part in the Top Employer ranking, Chiesi Farmaceutici Italia and its local companies in France, Spain, Germany and the United Kingdom have been awarded this important certification. This result means that the Group has been awarded the title of Top Employer Europe for the first time.
The second edition of the Chiesi Corporate Master, set up as a joint initiative with the SDA Bocconi, was successfully concluded. The course was greatly appreciated by participants, who confirmed the added value of the training programme on more than one occasion.

INFORMATION & COMMUNICATION TECHNOLOGY

Integrate, standardize and simplify

Business processes are increasingly becoming integrated and require reliable and timely information. A common language and a shared database are the essential prerequisites to be able to meet the needs generated by the Chiesi world.
CICT, in its role as technological business partner, has decided to base its initiatives in three guiding principles - *integration, standardisation and simplification* – enabling it to tackle the challenges of the business in the most effective and efficient way.
These principles are applied to both production and commercial processes, forming part of the SAP operative system, and to those in Research & Development, which need to combine long-term planning with an especially demanding need for flexibility.

SAPiens Project

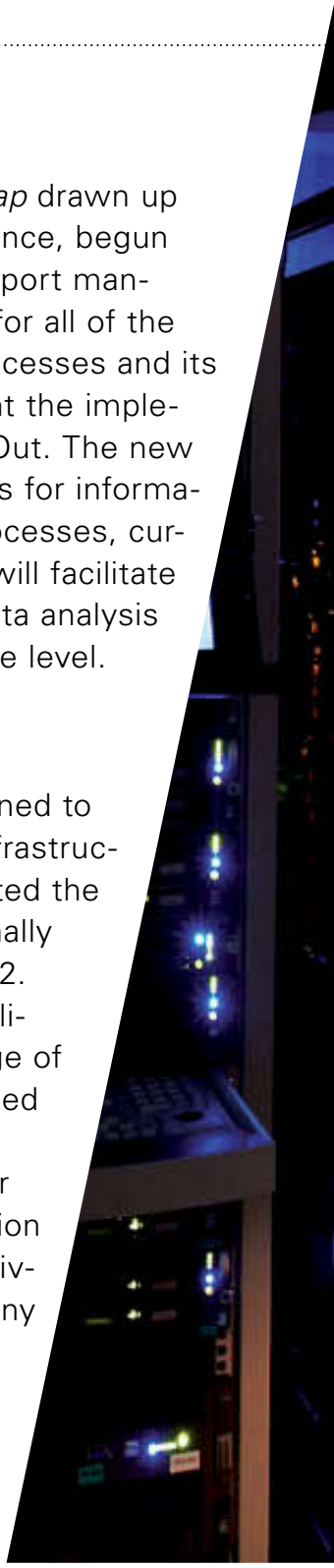
Since January SAP has been operating in line with the timeframes and procedures provided for in the project. The work done by the six business teams and six staff teams has ensured the successful launch of the system.
The next phase of the project (Roll Out) will see the launch of SAP in the Group's affiliates.

Business Intelligence

The objective of the *roadmap* drawn up to govern Business Intelligence, begun in 2012, is to standardise report management and its indicators for all of the company's fundamental processes and its affiliates, taking into account the implementation of the SAP Roll Out. The new access and distribution tools for information relating to business processes, currently being implemented, will facilitate and rationalise the entire data analysis system at Group and affiliate level.

Mercury Project

This project, which is designed to harmonise the Microsoft infrastructure at Group level, completed the programme for all the originally designated countries in 2012.
As a result, most of the affiliates can now take advantage of an advanced and standardised technological infrastructure which includes a single user database, shared collaboration tools, standardised connectivity across the whole company network and a single email domain name (chiesi.com).
In the course of 2013, Mercury will also be extended to Pakistan and the new affiliate in Mexico.



SOUTH EUROPE

Pharmaceutical Division Italy

For the seventh consecutive year the Pharmaceutical Division Italy performed at a higher level than that of the market, and was up by 0.3% (sell-in values) in the IMS Report confirming itself as leader within the respiratory market. This result was achieved despite the fact that 2012 represented a particularly negative year for the pharmaceutical market, with a drop in growth of 5.3% compared to the previous year.

The results achieved were dependent upon the therapeutic value of the company's products and the commitment of its various teams, as well as the image Chiesi has created for itself over time in its areas of focus: the respiratory, cardiovascular and special care fields.
Performance, which is defined as growth or a lower drop in growth rate compared to competitors, has been sustained by its brands: Foster, Clenil, Fluibron, Provisacor, Hirobriz, Clody, Sirio, Jumex, Xenazina, Clozapina, Asalex, Clipper and Peyona to mention the main products.

Foster in particular performs much more successfully than its competitors, with a growth rate of almost 10 percentage points above that of the market. This achievement awards Foster a market share of 14.9% for the month of December. Clenil A continues to hold the absolute majority among aerosol corticosteroids with over 53% of the market share. In the cardiovascular area, Provisacor doubled its growth rate in 2012 compared to average rates for other statins.

Chiesi

In special care, in the muscular-skeletal area, sales of Clody are growing up by 5.4% in the injected bisphosphonates market, a result also due to the launch of the new Clody 200mg\4ml formulation.
Growth in the central nervous system area is higher than that of the related market for Sirio, and has gone into double figures with Jumex and Xenazina.
The Group's leadership in special care with Curosurf has been reinforced in neonatology with the addition of Peyona, which was used by most Italian neonatology departments in the course of 2012.
Commitment to the search for new opportunities has consolidated Chiesi's presence in the special care area with the launch of new formulations and brands from key acquisitions.
The therapy range for patients affected by thalassemia has been extended with the launch of the new Ferriprox 1000 mg formulation.
The acquisition of Hyaneb has instead added to the therapeutic options for cystic fibrosis sufferers, an area where Chiesi is already present with Bramitob.

Throughout the year various publications were released relating to projects being developed with the Regional Health Service on topics of appropriacy and resource consumption in the asthma field, which were designed to enhance the value of Foster and used for communications with the medical community and institutional representatives.

Internal audit results have certified the commitment of Chiesi's teams, and revealed that the company's strengths include its expertise regarding products, therapeutic areas and diseases, as well as the importance attached by the company to doctors and patients and its ethical approach to business.

Italy

Domestic direct Sales (K€)	263,353
Variation versus 2011	- 4.1%
Human resources	1,545
Commercial network	463

Chiesi France

In 2012, Chiesi SA achieved revenues of 106 million euro, which was a decrease on the previous year.
Chiesi SA felt the full impact of the negative evolution of the French pharmaceutical market for the first year. This was due, among other factors, to unusually drastic price cuts and changes to the measures for drug substitution by pharmacists.
Respiratory products, which represent more than half the Company's revenues, were all affected by price cuts; Cetornan 5g and Iperten suffered badly in this new context.
In spite of these difficulties, Chiesi SA effectively developed Innovair.
Rinoclenil, which was launched at the beginning of the year, reinforced the Group's presence in the respiratory and allergy fields. It was the launch of the year for the retail market and met with success.
At hospital level, Curosurf and Cetornan 10g had to face a context of uncertainty.
At the same time, the affiliate was overhauled to become a new, more customer-oriented organisation, and better-prepared for future challenges such as Special Care portfolio development. The management has promoted cross-functional teamwork by launching substantial projects including CRM (Customer Relationship Management) and CLM (Close Loop Marketing), implementing an innovative website, preparing for the NEXThaler launch, opinion surveys (VOICES and STEM) and continuing to look for partnerships and business alliances.
The Blois production site has begun with the plant extension so that NEXThaler project can be completed with the obtainment of the authorisation from the Health Authorities.
The new Quality Control laboratory dedicated to BDP and budesonide operations has been set up.
The ground preparation and transfer of external equipment for the Nexthaler project began in December.
In the meantime, routine plant activities and in particular the packaging of BDP bulk consignments from Brazil for Chiesi UK have been managed.

France

Domestic direct Sales (K€)	105,982
Variation versus 2011	-11.9%
Human resources	309
Commercial network (direct + interim)	160

Chiesi Spain

The Spanish pharmaceutical market has been affected by new harsh government measures introduced as a response to the economic crisis. In spite of these measures, Chiesi Spain total revenues reached €59.6 million. The Spanish affiliate distributed its sales force in three business units: Retail, focused on general practitioners and specialists; *Special Care*, focused on hospitals; and *Farma*, the new business unit created to focus on pharmacy sales.
2012 was a positive year for Foster sales, which despite a drop in growth of the respiratory market, grew by 21%. Vivace and Prevencor maintain Chiesi's presence in the cardiovascular area.
The Special Care unit focused its promotion activities on the hospital market with products including Clipper, Bramitob, Curosurf and Peyona. Sales of both Peyona and Bramitob grew significantly thanks to the efforts of the Special Care Team.
Due to market changes and the opportunity to promote Chiesi Spain OTC products, representing 25% of total sales, the Company decided to create a new business unit team to maximise the OTC/pharmacy market. This new business unit is intended to develop this market and ensure an increase in sales in the OTC field.
These changes will help the Spanish affiliate achieve its goals for 2013. Corporate products, mature products and new alliances with other companies will position the company as one of the best in the respiratory, cardiovascular and neonatology therapeutic areas.

Spain

Domestic direct Sales (K€)	54,672
Variation versus 2011	-13.5%
Human resources	236
Commercial network (direct + interim)	194

Chiesi Hellas

Global sales are up by 7.4% on the previous year. Despite this result 2012 was a really challenging year for Chiesi Hellas. The country continues to experience a recession (now almost 5 years), with a continuously decreasing GDP and a 25% rate of unemployment.

The pharmaceutical industry reacted negatively by reducing the number of jobs and investments. In this environment, Chiesi Hellas overhauled its management and organisation and took key business decisions including new co-promotion agreements. The expansion of the Company's business in Cyprus with the launch of Foster also consolidated the affiliate-s commercial presence there. Although 2013 continues to look challenging because of the lasting recession, Chiesi Hellas has already designed its strategy to further develop synergies and communicate effectively with the medical community. We are confident that Business Development & Licensing activities and acquisitions, together with the drug promotion action plans, will drive the company towards a new record sales year and make its reputation in the Country.

Greece

Domestic direct Sales (K€)	13,447
Variation versus 2011	7.4%
Human resources	60
Commercial network	40

Chiesi Belgium

The growth of the Belgian affiliate is mainly driven by Inuvair, which continues to gain market share, and achieved an important growth on last year. Furthermore, Chiesi Belgium has become an important player in the Belgian respiratory market and is greatly appreciated by healthcare professionals and specialists in particular.
An important priority was the relaunch of Brexine, a NSAID which had not been promoted in Belgium for some years. Early figures look very promising, and the affiliate is convinced that the production transfer to Chiesi Group will contribute to enhancing its current performance.
In Special Care, Curosurf further strengthened its market leader position and Clipper also made excellent progress in terms of market penetration. These results enabled the Company to move 6 places up the national company ranking to 46th place.
2013 will be a milestone for the Belgian affiliate: Inuvair Nexthaler will be launched, which will have a significant influence on the sales of Inuvair but also contribute to the innovative image of Chiesi as a respiratory partner in a country very prone to the use of DPI. The launch of Peyona will intensify Chiesi's presence and leadership in the neonatology area.

Belgium

Domestic direct Sales (K€)	13,038
Variation versus 2011	41.9%
Human resources	33
Commercial network	23

NORTH & CENTRAL EUROPE

Chiesi Ltd, United Kingdom

2012 saw the UK affiliate achieve a long held ambition achieving sales of £102.8 million. This achievement saw Chiesi climb to reach 18th position in the league table of UK pharmaceutical companies (IMS, BPI).

Clenil gained an all-time high peak market share of 74% with a sales level of £54 million whilst sales of Fostair reached a level close to £20 million, once again showing strong year-on-year growth rates.

Chiesi has now cemented its position as an important respiratory company within the UK marketplace whilst at the same time achieving significant growth within its special care product portfolio, particularly within the neonatology and cystic fibrosis therapeutic areas.

Contribution from local products was also maintained and there are plans to further invest within this segment.

During the year, the company successfully restructured the UK sales teams to create a commercial team which continued to meet the needs of the rapidly evolving NHS.

The new role of Head of Compliance was created and successfully filled as was the appointment of a new Medical Director.

The ambition of the UK affiliate for the subsequent year, in addition to further strengthening its presence in both the respiratory and special care areas, is to continue its success in collaboration with Corporate functions within the area of new business development where several interesting opportunities are currently being investigated.

United Kingdom

Domestic direct Sales (K€)	126,819
Variation versus 2011	19.6%
Human resources	183
Commercial network (direct + interim)	161

Chiesi Germany

In 2012, Chiesi Germany was able to further increase on the previous years' success: total sales were kept at a high level, reaching a total of 109.9 million euro, up by 8.3% compared to 2011, and therefore securing a top-five position in the German respiratory market.

Foster maintained its well-established lead as the key driver for growth, reaching 64.6 million euro and a market share of 22.4% in the fix-combo-market. Besides Foster, sales of which were up by 20.6% on 2011, Forair also went beyond expectations by reaching +13.3% versus 2011. Overall, the total sales of products promoted by the sales force account for 78% of total company turnover.

As of December 2012, Chiesi Germany is now headed by Dr. Kai Joachimsen, who took over from Thomas Gauch, assigned Head of North & Central Europe. The Company is prepared to focus on the successful launch of Foster NEXThaler DPI to ensure that growth continues and the company's position in the respiratory market is further strengthened.

Germany

Domestic direct Sales (K€)	97,703
Variation versus 2011	8.3%
Human resources	203
Commercial network (direct + interim)	198

Chiesi Central Eastern Europe

The Chiesi Central Eastern Europe Group with its headquarters in Vienna, Austria, is the regional structure representing the Chiesi corporation in most of the Eastern European Countries (except Poland and Russia) and the Countries within the Commonwealth of Independent States (CIS). The whole group is serviced in logistics, regulatory, medical und financial matters from Vienna. Besides Chiesi's corporate products in respiratory disorders, rheumatology and neonatology, the portfolio at regional level has a traditional

strength in anaesthesiology, intensive care and rare disease medicine and the treatment of addiction. The Chiesi Central Eastern Europe Group is actively looking for further in-licensing products, contributing to selected business areas.

Austria & CEEC

Sales in Austria and CEEC Market (K€)	54,375
Variation versus 2011	7.0%
Human resources	186
Commercial network (direct + interim)	104

Chiesi Austria
Chiesi Austria is managing the portfolio in Austria with two business units, in primary and in special care. The primary care unit has a strong focus on respiratory diseases with its flagship Foster as well as some products in CNS. The launch of our Formoterol MDI and a Montelukast generic are completing further the portfolio. The special care unit has a broad product range in intensive care medicine, including Curosurf for premature babies and Bramitob for cystic fibrosis. In license of Talecris (US) the product Prolastin offers an important treatment for a rare genetic pulmonary disease.

Chiesi Bulgaria
Activities started 2005; the company (Ltd.) was established beginning of 2008. In addition to Foster, Budiair and Curosurf, the in-licensed Ferriprox (Apopharm, Canada) is complementary in the special care segment. Flamexin was launched at the beginning of 2006 and is keeping a strong position in the antirheumatic treatment.

Chiesi Czech Republic
Especially the hospital products represent an important basis in the portfolio (Sufentanil, Midazolam, Fentanyl) in Czech Republic. Bramitob was launched in 2008 and is adding to the special care products like Curosurf. The respiratory products give a lot of potential for further growth, especially Foster under the brand Combair which was launched in 2011.

Chiesi Romania
2012 was still a difficult year for the pharmaceutical industry due to very unfavourable

changes and a strong shortage in liquidity in the health care system. Chiesi Romania successfully managed to develop our position, especially with Curosurf and Flamexin. For 2013 a couple of new launches will further stimulate the development of the portfolio and the organisation.

Chiesi Slovakia
The subsidiary, operational since 2004, has always been successful all over the years. Since the launch of Foster in 2007 Chiesi is enjoying a high market share.

Chiesi Slovenia
Our well established affiliate (since 1998) has its most important area of activities in respiratory with Foster and Atimos. Further ReVia (anti addiction drug) and "Midazolam Torrex" are main contributors to the position in Slovenia.

Chiesi Hungary
In spite of the difficult pharmaeconomical situation in Hungary the business was successfully developed in 2012, mainly based on the sales in respiratory (Foster, Atimos), but also in the segment of antirheumatics (Piroxicam-betacyclodextrin, Brexin) with a traditional strong position in intensive care (Curosurf, Bramitob, Midazolam, etc.).

Chiesi Pharmaceuticals Export Area
The areas managed by the export division are the former Yugoslavian Countries, the Baltics and the CIS (including Mongolia). Local partner companies are providing service for registration, marketing and distribution.
This area represents currently some 20% of the total revenues for Chiesi Pharmaceuticals in the territory, and is considered for the future a major source of dynamic development.

Chiesi Netherlands

It has been a record-breaking year for this young affiliate, celebrating its 5 year anniversary in 2012. In times of economic turmoil, Chiesi Netherlands has been showing ambitious growth rates despite the downtrend in the healthcare market segments. Revenues have been growing by 62.2% compared to the previous year to exceed 15 million euro.
This achievement saw the Dutch affiliate break

into the top 35 pharmaceutical companies in the Netherlands. The results have been driven by convincing growth rates for the major brands in the respiratory (Foster, Atimos) and neonatal (Curosurf, Peyona) therapeutic brands. In 2013 the affiliate will continue to focus on increasing its sales by expanding its current portfolio and by launching Foster NEXThaler.
Building the Chiesi brand in The Netherlands, by corporate social responsibility activities and added-value services and -programs (Chiesi College) for all relevant stakeholders, will contribute to the reputation and acceptance of the company and its current and future brands.

The Netherlands

Domestic direct Sales (K€)	15,146
Variation versus 2011	62.2%
Human resources	47
Commercial network	28

Chiesi Poland

The Polish affiliate was established at the beginning of 2005. The initial focus was to develop the position of hospital products (Curosurf, and the anaesthetic portfolio). Bramitob has been added to the special care product range. Since 2009 pulmonary products, starting with Budiair, followed in 2010 by Atimos and Fostex, have boosted the development of the Polish organization. Currently, Foster is the main driver of Chiesi Poland business with the contribution of 69.5% to Total Sales.
At the beginning of 2012 the Government introduced a new Reimbursment Law which resulted in price pressure, fixed margins, pay back, risk sharing agreements. It has generated negative financial impact on the whole Polish Pharmaceutical Industry. In spite of this difficult pharmaco-economic situation in 2012 the Polish Organization achieved a very good performance with an 13.1 % growth rate in value and was ranked in the TOP10 fastest growing companies on the Polish market.

Poland

Domestic direct Sales (K€)	15,115
Variation versus 2011	13.1%
Human resources	112
Commercial network (direct + interim)	107

EMERGING COUNTRIES & INTERNATIONAL COMMERCIAL OPERATIONS

Chiesi Russia

Russian pharmaceutical market continuously growing in value despite the difficult economic environment +12% Vs 2011; Chiesi Russia sales growth driven mainly by Curosurf which represent > 60% of local turnover. 2nd leading brand is Vasobral with 5 mln Euro turnover, shortly followed by Respiratory Franchise and Bramitob.
Despite the fact that Foster is not covered with National reimbursement 2012 was the 1st year when we nearly achieved 1 mln Euro Foster sales in Russia. Successfully started cooperation with biggest National manufacturer Pharmstandard on Foster, Atimos and Clenil local packaging to meet the Russian government objectives to localize products which are already reimbursement and may be included in future reimbursement.
To meet the changing pharmaceutical market environment in terms of regionalization and decentralization of decision making process it was established new structure of Market Access Managers responsible for each of 8th Federal Areas with its own healthcare peculiarities and different financing capabilities.
Main objective of newly created structure is to include our Respiratory Franchise products – Foster in particular in local reimbursement programs and protect Curosurf market share.
Among the the main targets of 2013: continue double digit sales growth development; succeed with inclusion of Foster in National treatment guidelines; further development of Curosurf; start fully operational local legal entity.

Russia

Domestic direct Sales (K€)	28,926
Variation versus 2011	45.1%
Human resources	96
Commercial network (direct + interim)	74

Chiesi Mexico

In June 2012 Chiesi opened its 25th affiliate. Chiesi Mexico will firstly focus on the Specialty Care sector with Curosurf and then extend commercial activities to drugs for respiratory diseases launching Innovair by the end of 2013 which represents a key milestone of the program of growth in the Country.
Chiesi was present in Mexico since 2007 having sales only with Curosurfthrough a local partner, today it has 15 employees and expanding for the new launch of the Respiratory Line. Curosurf has been growing in double digit numbers year by year. Peyona was launched in October 2012 and expected to be a key product for the subsidiary.
Mexico is the 15th most important pharmaceutical market in the world and the second in Latin America after Brazil estimated to be worth $14 Bn USD.

Mexico

Domestic direct Sales (K€)	3,820
Variation versus 2011	N/A
Human resources	15
Commercial network	9

Chiesi Brazil

Chiesi Brazil surpass the Brazilian pharmaceutical market growing 13% in sales in local currency this year.
The event of the year for the affiliate was the introduction of the Clenil Family in the "Farmacia Popular". This program is the first national initiative to have a fully reiumbursement system for some diseases, such as asthma.
The introduction of Clenil and some other products in this program will be making possible for the country to reach and treat a great number of patients.

Brazil

Domestic direct Sales (K€)	63,796
Variation versus 2011	2.5%
Human resources	297
Commercial network	136

Chiesi Pakistan

Year 2012, witnessed the creation of another milestone: 25 years of successful operation during which it ensured and established highest level of efficiency standards and leadership in the Pakistan Pharmaceutical Market.

In 2012, despite the natural disasters and the uncertain political situation, Chiesi Pakistan has achieved growth above the market by focusing on its flagship Foster. Specific programs were developed to promote the brand and the product in order to increase market share, that reached 10.3%.

Brexin is still the leading product of the subsidiary: an increase of 23% it represents 34% of total sales. Curosurf has posted a growth of 31.3% compared to 2011. The two generic branded Pulmikast (montelukast) and Esotone (esomeprazole) achieved significant growth. Other products such as corporate Clenil Aerosol, Aerosol Clenil Compositum, Atem nebulized solution and Rinoclenil increased over the previous year.

In 2013, Chiesi Pakistan, which moved its headquarters in one of the fastest growing commercial areas of Lahore, will continue to focus on enhancing sales through the expansion of its products in all therapeutic areas and the launch of two new products in the respiratory and neonatology.

Pakistan

Domestic direct Sales (K€)	10,834
Variation versus 2011	16.2%
Human resources	168
Commercial network	129

Chiesi Turkey

In 2012, Chiesi Turkey continued to strengthen its position in its sixth year in the Turkish pharma market, achieving 26 millions € in line with the previous year despite the ongoing difficulties due to: average price reduction of 15% and a tremendous attack from competitors (6 new products) in the R03F1 market (associations beta2 stimulants / CSI).
In this difficult environment, the major products had developped a good performance. Foster has succeeded to become the only original product in the Respiratory Market that has a positive unit growth vs 2011. This success has rendered Chiesi Ilaç as one of the most important companies in the respiratory field.
In addition to its core products, Chiesi Turkey has succesfully managed the UCB products, Xyzal & Cirrus, and achieved a 40% unit sales increase.
In special care area, Curosurf has continued its growth in market share, units and value thanks to a continous expansion in the number of hospitals and that of customers.

National Symposium on Surfactant Replacement was organized for the first time in Turkey with a great success and the highest number of participants.
Special Care has achieved 25% of the Chiesi Turkey total turnover in 2012 .

Turkey

Domestic direct Sales (K€)	26,002
Variation versus 2011	0.2%
Human resources	146
Commercial network	118

Chiesi China

2012 was another important year for Chiesi China, not only another year with solid results with Curosurf – over 23% growth in local currency in sales, but also the opportunity to add new products to its portfolio.
The leadership of Curosurf has become even more a strategic priority for the subsidiary.
Thanks to its presence in all the major neonatology congresses, the Company has continued to enhance its reputation.
Chiesi China has expanded its presence in the areas of the country where the health care reform being led to an improvement of hospital facilities and skills, such as the central and western provinces. This has contributed to increase the turnover of the subsidiary, today aware to be the # 1 in the Chinese market for surfactants.
The process of registering other imported corporate products, such as Foster and Clenil UDV, has reached the final stage of approval. The launch of these new products is planned at the end of 2013. For this purpose a joint venture was established with the Chinese pharmaceutical company Eddingpharm. The joint efforts of the two companies will facilitate the local promotion of the two products, especially in the initial period of market penetration. In the meantime, Chiesi China plans to continue to expand its portfolio, through the approval of other imported products.

China

Primary Sales (K€)	20,977
Variation versus 2011	21.9%
Human resources	77
Commercial network	57

International Commercial Operations (ICO): Egypt, Maghreb, Nordic Countries

Last year International Commercial Operations achieve the following key objectives:

- the creation of Chiesi Mexico (June 2012);
- the consolidation of the organisation in Scandinavia and entry into Finland (October 2012);

- the setting-up of a Joint-Venture in China for the commercial development of Foster and Clenil UDV (December 2012).

Revenues were in excess of 53 million euros with a growth rate of over +10% on those generated in the same territories in the previous year; this result was achieved thanks to the contribution of several non-EU markets (Algeria, Colombia, South Korea, the United Arab Emirates, Jordan, South Africa, Taiwan, Tunisia and Vietnam) and business expansion in new markets (Finland, Libya, Malta, Norway and Sweden).
Curosurf, with a 48% share of the turnover, is the top product for International Commercial Operations and continues to grow; in 2012 the product achieved excellent results in Colombia, South Korea, Iran, South Africa and Vietnam in particular.
Foster still has a limited share of the turnover (10%), although geographically it is expanding rapidly as is its growth rate (Albania, South Korea, Denmark, the United Arab Emirates, Finland, Jordan, Lebanon, Libya, Malaysia, Malta, Norway, Sweden, Taiwan and Tunisia).
Brexin/Cycladol and Clenil, established products within the export portfolio, continue to represent a significant part of ICO revenues (18%).
Other products, such as Cetornan, Rinoclenil and Liometacen also continue to generate substantial revenues, underlining their strong competitiveness in various markets.

Egypt
The company has consolidated its local presence via a commercial network dedicated to promoting and commercialising its own products in the muscular-skeletal area.
Despite the problems affecting the country during 2012, local turnover has remained stable as a result of Brexin sales in particular.

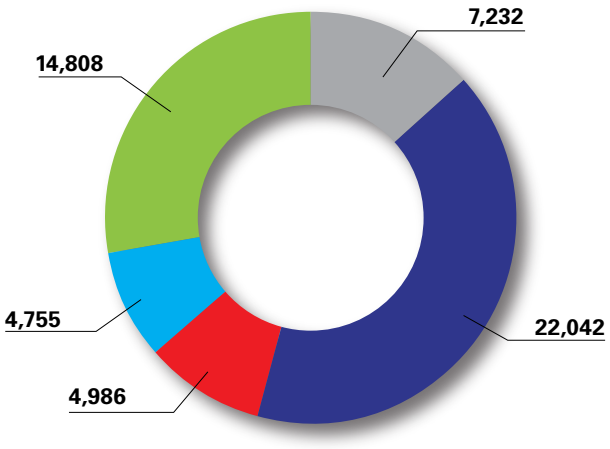
Maghreb
In Algeria the company has an established commercial network dedicated exclusively to its own products and continues to achieve excellent results, mainly thanks to products such as Clenil, Cetornan and Cycladol, and local sales in 2012 once again show positive growth (+21.1%) on the previous year.

Business in Tunisia also continues to do extremely well, and sales in 2012 were up by 48.1% placing Chiesi among the first twenty international companies in the country.

Nordic Countries

Over the course of 2011 ICO decided to manage promotional activities for Foster in Norway and Sweden directly, taking on staff and creating a compact sales network managed via a services company. 2012 was therefore the first full year's work: efforts were concentrated on consolidating the organisation, on the productivity of the network and its expansion with the aim of covering Finland (October 2012).

International Commercial Operations Sales 2012



- **North Africa**
- **Europe**
- **Far East***
- **Middle East**
- **Southern Hemisphere**

** China not included*

Chiesi Pharma USA

The US subsidiary, Chiesi Pharmaceuticals Inc., provides both local and global product development to Chiesi Group. The company headquarters are in Rockville, MD, not far from the headquarters of the US Food and Drug Administration (FDA).
In 2012, the primary achievement of Chiesi Pharmaceuticals Inc. was the approval of a US New Drug Application (NDA) for tobramycin inhalation solution intended for the treatment of *Pseudomonas aeruginosa* infections associated with Cystic Fibrosis with the local brand of Bethkis. In addition, Chiesi Pharmaceuticals Inc. is responsible for the global clinical program leadership for the tobramycin project, and the oversight for manufacturing in the US.
The US subsidiary also continues to be responsible for the conduct of the Phase 1 and Phase 2 clinical studies of CHF 5074, a potential new drug to treat Alzheimer's disease.

Cornerstone Therapeutics (USA)

Cornerstone Therapeutics is a specialty pharmaceutical company, owned in majority by the Chiesi Group, focused on commercializing products for the hospital and related specialty markets. We are actively seeking to expand our portfolio of products for these markets through the acquisition of companies and/or products and internal development.
In June 2012, the Company acquired EKR Holdings, Inc. and its wholly owned subsidiary, EKR Therapeutics, Inc., a specialty pharmaceutical company focused on serving the acute-care hospital setting. As part of the transaction, the Company acquired the

product rights to cardiovascular products, Cardene I.V. and Retavase. The elimination of duplicative administrative functions following the integration into the existing operations produced significant cost synergies. The combined sales force has significantly expanded its reach in the U.S. hospital market and expanded the commercial infrastructure providing the capability to adapt efficiently upon launch of new hospital products and react quickly to the market changes.

The currently marketed products and/or approved products include: Cardene i.v., Curosurf, Zyflo CR, Bethkis, and an antitussive/antihistamine combination product The commercialization is expected in 2013.

In addition to the commercial products, the Company is focused on developing some other products:

- Retavase, a recombinant plasminogen activator, approved for the use in the management of acute myocardial infarction;
- Lixar, an investigational, orally-active, vasopressin receptor 2 antagonist targeting the treatment of hyponatremia.

Leveraging upon the management expertise and expanded sales infrastructure the Company will focus on the following priorities during 2013:

- Integrating new products into the hospital market more efficiently;
- Launching Bethkis pursuant to license agreement with Chiesi;
- Launching our HP/CP ER Suspension product;
- Securing FDA approval for a new active pharmaceutical ingredient, or API, supplier and certain manufacturing process changes to allow for re-launch of Retavase.

USA (Cornerstone Therapeutics Inc.)

Domestic direct Sales (K€)	91,444
Variation versus 2011	20.9%
Human resources	108
Commercial network	49

Business Development and Strategic Alliances

The Chiesi Group has set itself the objective of increasing the percentage sales of special care products from 17% (2012) to over 30%.
Two important licensing agreements were already signed in 2012, with the aim of strengthening the Group presence in the Special Care area:

1) An exclusive distribution agreement with Kamada for the commercialisation of nebulised Alpha 1-Antitrypsin (A1AT) for the treatment of A1AT deficiency in Europe, Turkey and the CIS.
2) An exclusive distribution agreement with Veloxis Pharmaceuticals for the commercialisation of the immunosuppressive drug LCP-Tacro in Europe, Turkey and the CIS.

LCP-Tacro is a new formulation of tacrolimus indicated in the prevention of organ rejection for kidney transplant patients. The product was filed in the first half of 2013.

Chiesi's special care pipeline now has two new products thanks to these agreements. A1AT consolidates the Group's position in the respiratory field and LCP- Tacro opens up a therapeutic area of immunosuppression to control the risk of rejection in transplant patients. These agreements provide very promising prospects with regard to both company growth and improved compliance for patients, who will be able to follow their treatment programme more easily.

Chiesi has also finalised the acquisition of Eupharma, strengthening this cystic fibrosis area by commercialising Hyaneb.

In the course of 2012 the affiliate Cornerstone took over EKR Therapeutics – a US company which targets the hospital business. EKR commercialises Cardene (a calcium antagonist approved for the treatment of acute hypertension) and is working towards a relaunch of Retavase (a fibrinolytic agent for the treatment of acute myocardial infarction in adults). Chiesi has contributed to the process by adequately financing Cornerstone.

A series of local agreements were also reached in China, Spain and Greece in 2012.

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Alessandro Chiesi
Andrea Chiesi
Maria Paola Chiesi
Giacomo Chiesi
Ugo Di Francesco
Carlo Salvatori

Board of Auditors

Giuseppe Piroli
Paolo Alinovi
Vincenzo Simonazzi

Executive Committee

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Vice-Chairman and R&D Director	Paolo Chiesi
Chief Executive Officer	Ugo Di Francesco
R&D Planning and Control Director	Andrea Chiesi
Strategic Planning Director	Maria Paola Chiesi
Corporate Human Resources & Organisation Director	Ugo Bettini
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THE MOST IMPORTANT EVENTS IN 2012

- Foster Nexthaler Approval in 17 European Countries.
- Bramitob approved in the U.S. with the local brand Bethkis.
- European approval of the MART posology Foster.
- Mexico: opening of the 25th Group subsidiary.
- Clinical trials for the triple combination in COPD, for the PDE4 inhibitor via inhalation and for the synthetic surfactant.
- China: joint-venture agreement for the launch of Foster and Clenil.
- USA: acquisition of EKR, company active in the hospital sector, by the subsidiary Cornerstone.

GLOSSARY

Beclomethasone dipropionate (BDP): synthetic glucocorticoid with potent anti-inflammatory action. When taken through inhalation, this drug reaches the lungs directly where it exerts its effect. Its low level of absorption in the rest of the body ensures negligible systemic side effects.

Chronic Obstructive Pulmonary Disease (COPD): term used to indicate two related lung diseases – chronic bronchitis and emphysema. Both diseases are characterised by chronic and progressive obstruction of the airways making it difficult to breathe.

Cystic Fibrosis (CF): chronic hereditary disease of the lungs and the digestive system, which currently affects roughly 70,000 people worldwide. A mutated gene creates a protein that causes production of a thick viscous mucus that accumulates and renders breathing difficult. This in turn makes it easier for secretions to build up and consequently promotes the development of dangerous infections. In the digestive system the mucus tends to block ducts in the pancreas and prevents digestive enzymes from working in the intestines, which leads to malabsorption of food and stunted growth.

Dry Powder Inhaler (DPI): a device for administering drugs in the treatment or control of respiratory diseases and conditions.

Generally Accepted Accounting Principles (GAAP): term used to refer to the standard framework of guidelines for financial accounting used in any given jurisdiction; generally known as Accounting Standards. GAAP includes the standards, conventions, and rules accountants follow in recording and summarizing transactions, and in the preparation of financial statements.

Hydrofluoroalkanes (HFA): innovative propellants used in some inhalers for the management of asthma. They do not damage the ozone layer. A propellant is a gas which facilitates the diffusion of an inhalant drug in the lungs.

Long-acting Beta-agonists (LABA): drugs which open peripheral and central airways and keep them unobstructed by relaxing bronchial smooth muscle. LABAs are often administered with steroids in inhalation form as a long-term bronchodilation treatment for patients with moderate to severe asthma or other chronic lung diseases.

Manufacturing Execution Systems (MES): it solutions that support the primary production processes in a production plant. These applications close the gap between ERP systems and production equipment control or SCADA (Supervisory Control And Data Acquisition) applications. MES applications have become essential to support both real-time production control as well as the data collection and reporting ("manufacturing intelligence") necessary to improve production performance.

Piroxicam β-cyclodextrin (PBC): a successful example of "host-guest" technology, whereby the host, a starch derivative known as β-cyclodextrin, solubilises the guest, an anti-inflammatory drug known as piroxicam, thus enhancing the pharmacological properties of its active ingredient.

Pressurised Metered-Dose Inhalers (pMDI): A device which ensures that a specific quantity of drug is delivered to the lungs. Widely used by the Chiesi Group for its products, it is commonly employed in the treatment of asthma, Chronic Obstructive Pulmonary Disease (COPD), and other respiratory conditions.

Respiratory Distress Syndrome (RDS): Disease typically affecting premature neonates caused by insufficient production of endogenous surfactant and immature lungs. The condition may also be due to a genetic problem linked to the production of proteins associated with the surfactant. RDS affects 1% of neonates and is the main cause of mortality in premature infants.

Unit-Dose Vials (UDV): non-reusable sterile containers containing a single dose of drug. Pharmaceutical products packaged in vial or mono-dose bottles are easily recognisable and simple to use.

Ulcerative Colitis (UC): inflammatory bowel disease (IBD) which causes lesions known as ulcers to develop in the lining of the colon and rectum. Ulcers form where the inflammatory process destroys the cells which normally line the colon, causing in bleeding and pus. The inflammation may also result in frequent bowel movements, and therefore diarrhoea.

Spacer: is a type of add-on device used by asthmatics to increase the efficacy of the inhaler.

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