Francisco Ballester, head of marketing and sales at Novartis Spain, looked at Gonzalo Rodriguez, head of sales of the mass market division, “We are at a unique moment but the Novartis global situation will be challenging. We will have to defend/ an offensive commercial strategy. We need to re-invent our commercial operations”.

Francisco Ballester had previously worked at various Novartis subsidiaries in North and South America before coming back to Spain and knew that the reorganization of commercial operations would be critical to tackle the very specific situation of Novartis Spain.

Novartis Spain is one of the leading Novartis subsidiaries in the world with the best commercial performance in Europe. The Spanish subsidiary plans to launch seven products in the ethical segments (drugs delivered under physician’s prescription) within 18 months, starting in 2008.

At the same time Novartis Corporation is struggling with various issues that are directly affecting revenue, particularly in the US which accounts for 40% of the Novartis’ global sales revenue:

- Big earning Novartis brands are hard hit by generics, particularly in the anti-hypertensive and anti-infective markets with the consequent loss of revenue. It is anticipated that generic competition would dramatically reduce the sales of these brand medications by an amount of US$ 1.6M.
- Withdrawal from the market of an American brand which treats irritable colitis and loss of revenue totals US$ 600-700M.
- Delayed launch of an innovative anti-diabetic drug. The FDA approval of Galvus® (diabetes market) is delayed and at the same time the direct competitor has just been granted FDA approval.

As a consequence of this loss of revenue and sales drop (US$ 2.5 billion versus previous year), Novartis has decided to drastically reduce costs and all subsidiaries will have to contribute in maintaining IBT (Income Before Taxes). The re-engineering is based on a headcount reduction (i.e. 2,000 employees in the USA) and rationalization of therapeutic franchises.

In Spain there is no direct impact on the global re-engineering as the Spanish subsidiary has been growing steadily in previous years, the organization is considered adequate and there is no need for adjustment as the headcount matches the subsidiary’s global sales. However, there is a dual challenge: One how to launch seven brands in 18 months? Two how to obtain the suitable means for launching in such a situation of internal cost-containment and re-engineering?
A team is created with marketing, sales and business planning analysts to devise a commercial strategy that will enable the company to launch all the brands, and particularly new and innovative Novartis medications, in the anti-hypertensive and diabetes markets.

THE PHARMACEUTICAL INDUSTRY IN EUROPE AND IN SPAIN

People from other industrial sectors tend to assume that marketing medicines should be easy because of a built-in demand for cutting-edge products that extend life or enhance quality of life. In fact, nearly the opposite is true. The pharmaceutical firms have to face many challenges: high R&D investments, a very long time to market, tight price and reimbursement controls and increasing health cost-containment in Europe. In the ethical segment the market access is complex and varies from country to country in Europe.

PHARMACEUTICAL SECTOR BACKGROUND

The pharmaceutical industry is a top performing high technology sector and currently sells a variety of products and therapeutic healthcare packages that include drugs, diagnostic tests and devices as well as a wide range patient support services. The pharmaceutical industry is the top ranking sector with the highest share in R&D investment of the 36 European sectors: 19.2% (See Exhibit 1) of the total worldwide R&D business. The pharmaceutical industry is also the sector with the highest ratio of R&D investment to net sales.

By the time a medicinal product reaches the market, an average of 12-13 years will have elapsed since the first synthesis of the new active substance.

FIGURE 1
STAGES OF CLINICAL DRUG TESTING: TIME OF PRODUCT DEVELOPMENT

The cost of researching and developing a new chemical or biological entity was estimated at € 1,059 million in 2006. On average, only one or two of every 10,000 substances synthesized will successfully pass all the stages to become marketable medicines and the attrition rate of compounds is increasing.

In 2007, the pharmaceutical industry invested about € 26,000 million in R&D in Europe. In comparison with the North American and Asian regions, Europe is still seen as a less attractive R&D investment location in terms of market size and incentives for the creation of new innovative biotech companies.

Drug discovery and the cost of bringing a new chemical entity onto the market has dramatically increased over time (US$ Million): 138 in 1975, 318 in 1987, 802 in 2001 and 1,318 in 2006. Costs have been relatively stable in the pre-clinical phase but have increased both in terms of direct costs and in the time required for completing the clinical trials.

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In 2007, North America accounted for 45.9% of world pharmaceutical sales compared with 31.1% for Europe. According to data from IMS Health\(^3\), 66% of sales of new medicines launched during the period 2004-2008 were in the US market, compared with 26% in the European market.

Innovation is at the heart of the challenge faced by the pharmaceutical industry with a large cost of innovation both in terms of investments and time for making a new product ready for the market. Innovation is usually classified into three levels, according to the added therapeutic value and benefits for patients: first, incremental benefits, this is the case with new formulations and new dosage forms; second, stepwise innovation in the case of different molecules of a same family offering different properties such as indication, tolerability and drug metabolism and third by breakthrough innovation with a genuine new approach to the disease or a new chemical entity.

Patents provide an essential economic incentive for research that would otherwise not take place and are essential for rewarding innovation. Patent protection of medicines is rather short as drug discovery and drug testing are a long lasting process.

The European law ensures a patent protection of twenty years for pharmaceutical products. However, due to the long duration of clinical trials, the effective duration of patent-protection after marketing a drug is around ten years. This European regulation is applied in Spain to drugs marketed after October 1992. Prior to this date, the protection was restricted to the manufacturing process and copies were flourishing. A recent European law (Bolar clause) allows pharmacological and clinical studies before the end of patent protection and generic drugs can be launched as soon as the patent ends.

Patent expiration most often means that the revenue produced by a drug has finished. According to the European Commission, in the period between 2000 and 2007, the initial price of generics entering the market was on average 25 per cent lower than the price set by originator companies prior to loss of exclusivity. Additionally, prices for both drugs fall over time starting from the point of generic entry. The average delay during this period was found to be “about seven months” although for the most valuable products this figure drops to four months. Biologic medicines are often complicated by various additional issues and the patent is extended to include particular methods of industrial protection.

REGISTRATION OF MEDICINES AND REGULATORY ASPECTS OF PROMOTING ETHICAL DRUGS

There is probably no other sector as strictly regulated as the research based healthcare sector.

The European Medicines Agency is the European Union body responsible for coordinating the existing scientific resources put at its disposal by Member States for evaluation, supervision and pharma-covigilance of medicinal products. National drug authorities require registration of any drug in order to make it available to patients. The drug sponsor files a marketing application which demonstrates that the new drug has the sufficient quality and an acceptable efficacy ratio – safety / tolerability when used according to product labeling. In Europe, an applicant can choose between different registration procedures that involve just some or all of the EU countries, depending on the type and scope of the product. For new chemical entities, authorization is granted by the European Medicines Agency – EMEA - which is responsible for the scientific evaluation of applications for European marketing authorization of medicinal products (centralized procedure). Under the centralized procedure, companies submit a single marketing authorization application to the EMEA. Once granted by the European Commission, a centralized (or ‘Community’) marketing authorization is valid in all European Union (EU) and EEA-EFTA states (Iceland, Liechtenstein and Norway).

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\(^3\) IMS Health is a Market Research company specialized in collecting and analyzing pharmaceutical data.
Advertising and promotion are restricted to health professionals. Promotional guidelines strictly control the means and tools used to promote prescribed drugs. There is open debate on how much promotion influences doctors’ behavior. It seems that general practitioners in private practice, and who did their medical degree a long time ago, rely more on promotion as a source of drug information.

Any claim must be supported by clinical evidence and pertinent bibliographic references must support any promotional material.

The United States of America and New Zealand are the only developed countries where direct pharmaceutical to consumer advertising is allowed. The product information publicly available entails the following items: summary of product characteristics (SmPC), labeling and package leaflet - information provided in the medicine packaging which is part of the marketing authorization.

GET MARKET ACCESS

Setting the price of a new product is always a difficult task. Pharmaceutical companies have to weigh and balance more than just the traditional financial and market factors and consider such things as the value and societal economic importance of the drug, patient need, governmental tendency to control prices and fairness issues.

Pricing remains a central issue as European governments have a strong influence over corporate strategies and scope of competition. Pricing and reimbursement (P & R) has been made more consistent throughout Europe by the European Directive 89/102/CEE of December 21st 1988. Known as the transparency directive, it imposed a regulatory framework for price setting in European countries. These measures, for the most part, apply to regulators who must set out the criteria used to determine the price of drugs, adhere to deadlines and justify any price regulation decisions. Marketing authorization holders must provide adequate information for the regulator to make a decision. They must ensure that they comply with the general rule of free movement of goods. Reimbursement is a limiting factor and the decision generally reflects a trade-off between financial resources and a drug's quality and contribution to health.

Price and Reimbursement – P & R - are national procedures. After approval of a drug by the European Agency of Medicines, the new drug is filed on a country basis in order to be recognized by the national Health system and ensure payment for the drug. National regulations on pharmaceutical products reflect the underlying national attitudes towards the provision and financing of healthcare.

In all countries, reimbursement is negotiated on the basis of a variety of criteria. The therapeutic benefits of a product, vis-à-vis those of its competitors, are frequently cited. If a product is unquestionably superior in therapeutic terms, it will be reimbursed irrespective of the outcome of any health economic evaluation4. A number of European countries have started to incorporate health economic evaluations into the decision-making process, either as an additional tool to determine the reimbursement price (the Netherlands, Finland), or even as a mechanism to guide prescribers (NICE in the UK). More countries are adopting this stance and have set up working parties to draft pharmaco-economic guidelines to be used in the decision-making process (France, Italy).

National governments and their competent authorities have implemented a series of measures, both controls and incentives to influence supply of and demand for pharmaceuticals and ensure healthcare cost-containment. Some countries have given greater emphasis to supply others to demand. The supply-side controls are aimed at limiting the cost of reimbursed medicines to the

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4 Panos Kanavos LSE Health and Social Care, Overview of Pharmaceutical Pricing and Reimbursement regulations in Europe.
authorities, by controlling their price and/or reimbursement and by limiting their availability through the use of positive and negative lists. Additional measures of cost-containment include the regulation of demand via prescription restrictions (positive and negative lists of drugs), prescription guidelines, treatment protocols, generic substitution and incentives encouraging the physicians to prescribe cost-effective drugs.

**Market Access** usually refers to the conditions, tariff and non tariff measures agreed on by the European members for the entry of specific goods into their markets. However, the terminology of market access is also used in pharmaco-economics and refers to the process by which a company gets a drug onto market so that it becomes available to patients. Access is also defined as **patient access** or patient’s ability to obtain medical care. Ease of access is determined by such factors as availability of medical services, the accessibility at the patient’s health care facilities, transportation, hours of operation and costs of care.

Market access begins in 1999, in the UK, with the National Institute for Health and Clinical Excellence – NICE – and the emergence of cost effectiveness as a fourth hurdle in the regulatory approval of drugs. In the ethical segment (drugs under prescription) the drug has to successfully pass the conventional regulatory approvals: technical by EMEA, P & R by country.

More than only health economics, market access is a new philosophy which tries to optimize the commercialization of new drugs and to speed-up the uptake of new medicines.

Market access involves pricing and reimbursement and it would not make sense if the product did not get reimbursed. Without reimbursement, there is not really any product to market in the ethical segment. The concept of market access and the birth of the NICE totally changed the pharmaceutical perspective:

- The rationale has changed and focuses on health gain: how the product will add value, cut costs or achieve a particular payer-stakeholder goal.

- The customer basis has moved from the traditional customer, the gatekeeper to get access to the patient who was no longer the decision-maker, to the person who held the purse strings, this is the payer.

Drug manufacturers bear the risk of failing to commercialize a drug adequately after heavily investing in its development. Innovative risk-sharing schemes have emerged in response to payers increasingly denying reimbursement of novel and expensive drugs where, at launching, medical and cost-effectiveness of the drug has not been sufficiently established. These agreements are aimed to reduce the uncertainty about cost-effectiveness and/or budget impact in exchange for allowing the new drug market access. The types of agreements between payers and the European pharmaceutical laboratories depend on the country. The most stringent are usually applied in the UK and Northern countries. In order to facilitate Market access, these agreements are mainly implemented on two schemes defining how the reimbursed price or reimbursement conditions will be modified based on:

- The performance: at the population level, the reimbursement is conditioned by post-marketing evidence (observational clinical studies); at the patient level the scheme usually defines that the drug is funded only for patients who respond and in this case the clinical endpoints have been pre-agreed.

- Finance scheme: at the population level there is a price-volume agreement and the usage beyond this patient-volume is penalized financially; if the scheme is applied at the individual patient level: the drug is free or discounted beyond a specified number of doses or cumulative cost per patient.
SPANISH HEALTH SYSTEM

The Spanish health system is free, universal and a public health service for 45.9 million citizens. This is a constitutionally-guaranteed right and there are no out-of-pocket expenses, aside from medicines.

Universal, it covers 100% of the population. It is guaranteed and financed by the government through taxes. In 2001 the transfer of public health competencies to regional authorities was finalised. This means that the local governments finance, plan and deliver all health services; as a consequence, the seventeen local governments (one per region) ensure health care services. Each regional health body is managed by a health services director and a specific pharmacy department which is in charge of delivering health services, managing quality of care and controlling health expenditures. The regional health body is the “payer” the entity that includes a new drug on the regional list of drugs at the price granted by the Spanish Drug Agency, as pricing and reimbursement are national. However, control of drug usage is local and made by the regional governments.

Spain’s single payer health care system is ranked seventh best in the world by the World Health Organization. The main healthcare entities (See Exhibit 2) at the primary care level are the health clinics, which are manned by multi-disciplinary teams made up of family doctors, pediatricians, nursing staff and administrative personnel. They may also include social workers, midwives and physical therapists.

Specialized care is provided at specialty centers and hospitals, either in-patient or out-patient. Hospitals provide 24-hour emergency care to patients who have not been admitted.

Primary health care is based on primary care centers. The average time from patient’s home to Primary health center is around 15 minutes. Each center serves a registered population between 5,000 – 30,000 patients with an average of 20,000 patients per center; this works out to a list of 1,500 to 3,000 patients per general practitioner (GP). GPs work 6 to 7 hours a day with some off-duty rota work and are salaried. Specialist healthcare is made upon referral from the primary care centers.

Private health care insurance, around 15% of the population, is used either as a supplement or an alternative to public care. The private insurance companies have their own network of hospitals, clinics and laboratories. Policyholders usually do not have to wait as long for treatment. The only downside is that these companies can insist on patients only using doctors who are members of their group.

NOVARTIS – A GLOBAL PHARMACEUTICAL COMPANY – THE SPANISH SUBSIDIARY

In 1996, due to a need for future planning in a highly changing market (pharmaceutical industry concentration was starting and it was necessary to optimize R&D efforts), two veterans in the Swiss chemical and pharmaceutical industry, Ciba-Geigy and Sandoz, set in motion the most important corporate merger in the world up until that time. Novartis, which means new skills in Latin, was born as a result of that merger.

With the general headquarters in Basel, Novartis started its activity with 3 key life science areas: Health Care, Nutrition and Agribusiness. However, 3 years later, the company decided to disinvest all the resources in Agribusiness to focus its activity on Health Care.

Novartis started its activity with an initial investment of 3,500 million Swiss francs in R&D, one of the highest investments in the industry, and in less than 10 years, it became a leading company in
the research and development of new products for protecting and promoting health care and personal well-being.

With almost 100,000 employees, activities in 140 countries and $38,100 million in billing in 2007 (See Exhibit 3), Novartis took the 4th position of pharmaceutical corporations worldwide, with a growth of 10.7% in comparison with the previous year.

Novartis tackled this dynamic environment through 4 different divisions which complement each other, but work independently:

- **Pharma**: ethical Medicines (with medical prescription). The priority areas for research in this division are oncology, cardio-vascular, metabolic diseases, respiratory and infectious pathologies. The R&D efforts are very important, including new methods to speed up the identification processes of new molecules and increased focusing on molecules coming from the Novartis Institutes of Bio-Medicine Research (NIBR). In 2007, Novartis Pharma has 45 key medications commercialized, most of which are leaders in their respective therapeutic areas. The launching of innovative medicines and the concentration of all the company's efforts on certain areas, make Novartis one of the companies with the fastest growth in the industry in recent years. Since 2000, 17 new molecules from Novartis have been approved in USA, more than any other pharmaceutical company. Novartis stands out, and experts in the sector identify the company as one of the best combinations in the pharmaceutical industry of organic growth, development opportunities, and with low exposure to the risks related to patent expirations. Pharma division worldwide represented the 63% of the whole Novartis Corporation turnover.

- **Vaccines and diagnostics**: focused on the production of vaccines to protect against different viral and bacterial diseases that can be prevented through immunization and on the development of new methods for blood analyses. In this area, after the acquisition of Chiron in 2006, Novartis has become the 5th largest vaccine producer in the world. It is also the first pharmaceutical group that produces and commercializes vaccines on a large scale based on cell cultures for preventing seasonal flu, which is the most significant technological advance in the last half century. The product portfolio includes more than 20 vaccines for the prevention of most lethal viral and bacterial infections. The blood testing methods division of Chiron is dedicated to preventing the spread of infectious diseases by developing new methods of blood testing.

- **Sandoz**: is the worldwide division in charge of the development, production and marketing of generic products. Through Sandoz, Novartis is the only major pharmaceutical company that occupies a position of leadership in both patented prescription drugs and generic drugs, a segment of the pharmaceutical market that is experiencing strong growth. Considered the second largest generic company in the world in terms of sales (Novartis annual report 2007), Sandoz generic is not limited to traditional generics, but it also offers more value-added products using innovative technologies such as trans-dermal patches, inhalation devices and modified-release galenic forms. In addition, Sandoz is a pioneer in getting U.S. and European approvals for biosimilars. Within this division, Novartis has more than 950 active substances in more than 5,000 galenic forms, distributed in 30 countries. Among the most important groups of drugs are antibiotics, treatments for central nervous system disorders, gastrointestinal medicines, cardio-vascular treatments and hormone therapies.

- **Consumer Health**: deals with the creation, development and manufacturing of products without medical prescription. This division encompasses the activities of self-medication or OTC products (Over The Counter), Animal Health and CIBA Vision.

- **OTC**: this Novartis division is a world leader in research, development, production and marketing of products for self-medication available without prescription.
Novartis Animal Health: focuses on the welfare of pets and on improving health and productivity of farm animals. The product range offers solutions to prevent and treat various common animal diseases and parasitic infections. Many of these products are available with veterinary prescription.

CIBA Vision: is a world leader in research, development and manufacturing of optical products and services, especially contact lenses and lens maintenance products. CIBA Vision offers solutions that match the lifestyles, preferences and needs of consumers in over 70 countries.

**NOVARTIS IN SPAIN**

Novartis started operations in Spain on January 1, 1997, although its presence in the country goes back to 1917 with Ciba-Geigy, and to 1924 with the Sandoz group. Headquartered in Barcelona and with a team of more than 2,100 employees, in 2007 Novartis billed 1,080 million € (See Exhibit 4), and had a market share of 5.1% of the Spanish pharmaceutical market (Source: Novartis). In that year, over ten million people (1 in 4 in Spain), were treated with a medicine from Novartis.

It is also, with its three production facilities in the area of Catalonia, one of the largest pharmaceutical companies with manufacturing presence in Spain.

Novartis is represented in its four divisions through:

- Novartis Pharma, ethical products (prescription drugs).
- Chiron Iberia S.L. in Vaccines & Diagnostics.
- Sandoz Industrial Retail Generics and generic products in different therapeutic areas and raw materials for the manufacture of pharmaceuticals, respectively.
- Novartis Consumer Health, activities in units of OTC, Animal Health and CIBA Vision.

The growth and good management of the Spanish subsidiary in recent years led to corporate recognition and in 2004, to the allocation of the management of the Intercontinental Region Emerging Markets (Emerging Markets Growth Region, EGM). The Intercontinental Region Emerging Markets extends over four continents, including more than 55 countries, and comprises China, India, Turkey, Russia, Australia, South Korea, Taiwan and other emerging countries in Asia Pacific, Middle East, Africa and Eastern Europe.

**NOVARTIS PHARMA DIVISION IN SPAIN**

The pharmaceutical division of Novartis in Spain offers to different groups various medical specialties in the following therapeutic areas: Cardio-vascular / Metabolism / Endocrinology, Dermatology, Infectious Diseases, Respiratory Diseases, Ophthalmology, Oncology / Haematology, Rheumatology / Inflammation / Bone Metabolism, Transplant / Immunology and Nervous System. The *vademecum* of the Pharma division in 2007 brought together 42 major products.

In 2007, net sales of the pharmacy division were € 687.2 million; representing 63.6% of total turnover of the corporation in Spain, and this meant a 7.7% improvement over the previous year. With a market share of 4.81%, the company ranked 4th in the ranking of pharmaceutical companies in Spain, behind Pfizer, Sanofi-Aventis and Almirall. Consolidated sales, including sales of licenses in Spain, reached the following figures: second company in sales by number of units, and second in value.

The pharmacy division in Spain has a staff of 1,359 employees and consists of two independent business units:
- Oncology: Novartis has a significant portfolio of oncology products that provides a variety of innovative therapies and practical solutions for cancer patients.
- Mass Market: with five therapeutic lines: (See Exhibit 5)
  - Cardio-vascular and Metabolism, the biggest earning therapeutic line: is the division devoted to cardio-metabolic diseases. It has a product portfolio that offers some of the best currently existing solutions to treat and protect patients in critical moments of cardio-metabolic diseases. The main products are indicated for the treatment of hypertension, hyperlipidemia, angina, heart failure and diabetes type II.
  - Other therapeutics franchises: CNS (Central Nervous System); Osteo-dermo-respiratory; IDTI (Infectious Diseases, Transplantation and Immunology); Ophthalmology.

**MARKETING AND SALES IN THE PHARMA INDUSTRY – COMMERCIAL ORGANIZATION**

**MARKETING IN THE PHARMACEUTICAL INDUSTRY**

The role of Marketing in Pharmaceutical firms encompasses a wide variety of activities driven by the stages of drug development:

**FIGURE 2
STAGES OF DRUG DEVELOPMENT**

**ROLE OF MARKETING**

- Provide background on market and product potential
- Define product profile needs
- Define comparators
- Define Outcomes Research needs
- Develop market
- Develop strategy
- Recommend development
- Input on product labeling
- Recommend filing strategy
- Define launch plan
- Develop positioning and branding
- Finalize strategy
- Finalize pricing
- Finalize promotion and branding
- Implement launch campaign
- Finalize field sales plans
- Monitor performance
- Adjust strategy and tactics
- Sequence promotion
- Manage product life cycle

Pharmaceutical marketing is strongly influenced by the attributes of the new drug and the assessment of key stakeholders. The involvement of marketing, from early phases of drug testing, is crucial for an in depth understanding of:

- The disease and competitors for creating a differentiated product profile and defining the needs in terms of research results in order to establish and demonstrate the clinical benefits before launching the new drug.
The customers and stakeholders who will be decisive in gaining market share and ensuring quick penetration.

General concepts are different in pharmaceutical marketing mainly because the customer and consumer are different and the consumers of ethical brands – under prescription – do not have their own choice.

**PHARMACEUTICAL MARKETING**

Planning and carrying out investment to address stakeholders by patient segment has become a key success factor of pharmaceutical firms in order to encourage the adoption of drugs and foster their use. As a consequence, marketers have a significant role in Market Access in order to effectively package and communicate the right information in the right way for the right customer at the right time, and particularly:

- Provide a wide range of information and data to local payers and their advisers so that they can evaluate a product's clinical benefits and economic effectiveness before making a decision about guidelines / recommendations and funding of medicines.
- Assess payer requirements in order to formulate a comprehensive strategy; the budget impact acceptance is the driver behind an optimal market access strategy and to collect appropriate data for developing comprehensive product value arguments.
- Connect a pure clinical message and a pure health economic message to reach all customers and communicate a common message. This marketing approach is about effectively packaging and communicating the right information in the right way for the right customer at the right time.

Physicians are probably the most important players in pharmaceutical sales. There are several channels by which a physician can be influenced including self influence through research (Individual research: Physician Desk References existing online; medical journals; medical websites; scholarly literature; conferences; pharmaceutical-branded websites), Peer Influence: Key Opinion Leaders (KOLs), colleagues, Direct Physician contact with Pharmaceutical Representatives.

**PRODUCT**

Traditionally, brand value in the pharmaceutical sector has been relatively simple. Blockbusters – driven by innovation, marketed on a science platform, supported by medical evidence, communicated through large sales forces and highly priced – have driven growth significantly for over a decade. The challenge is how these new products are going to be created as value-driven brands. It could be argued that value can only be driven from a clinical position. However, even in complex secondary care markets, such as oncology or diabetes management, prescription decisions are not made based on data alone, but on the powerful combination of data plus perceptions. The obvious functional benefits of a drug are efficacy, safety, convenience and cost-effectiveness. Brands add value to these, leading to differentiation from competition. In pharmaceutical firms, the intangible parts of the brand and the emotional and expressive benefits of the drugs are rarely promoted.

*Post market research and surveillance are often as active as in the pre-market phase.*

Drug safety is the primary public health reason why post-market research and surveillance is performed and sent periodically to the Health Agencies FDA or EMEA. Reasons for these programs are usually related to the fact that clinical research cannot precisely predict how a drug will behave once prescribed in usual conditions. The post-marketing surveillance or research is done voluntarily by the pharmaceutical companies in order to be able to market the drug more
knowledgeably and effectively. In addition to surveillance, pharmaceutical firms conduct or sponsor post-market drug research that will expand information in subgroup patients, assess the performance, the patient convenience and satisfaction of a new drug in pragmatic conditions.

Due to the specificities of the pharmaceutical sector regarding products in the ethical segment, the communication tools available are different to those that could be used in other markets (See Exhibit 6)

Some of the promotional and communication activities normally used in the sector are as follows:

- **Ad in specialized press**: Paid advertisements to be included in magazines, newsletters, journals and newspapers developed for physicians. Each media has its own periodicity and information regarding its audience.

- **Promotional material**: This includes brochures, information sheets and product factsheets that are given to physicians detailing the characteristics of the drug. Depending on the type of drug and on its phase in its life cycle, these materials are given to a larger or a smaller number of physicians; realistically this would be between 10% and 60% of the total number of physicians called.

- **Key Opinion Leaders (KOL)**: These are physicians that are highly recognized in the sector. As their opinion is well respected by other doctors, it is very important that they support and employ the new pharmaceutical treatments. It is estimated that for this specialization in Spain there were about 250 KOL.

- **Scientific Conferences**: During the conferences physicians come to listen and exchange with other physicians and KOLs who are specialized in a particular subject such as new trends, new treatments, research and new drugs. In general the purpose is to update physicians on a specific field (i.e. cardiology or oncology).

- **Scientific Workshops**: These are similar to conferences but smaller, more local and can be initiated directly by the pharmaceutical laboratory.

*Mass Market brands* address large markets; they are primary care products for highly prevalent diseases such as high blood pressure. These mega brands target mainly the general practitioners and some specialists (i.e. cardiologists for high blood pressure). They are usually distributed through wholesalers and delivered under prescription in the retail pharmacies. Product communication of mass market drugs is a hybrid between medical evidence - communication based on the performance of the brand (efficacy, safety and tolerability) - and experience based messages for physician and consumer: convenient and easy to use, improvement in quality of life, educational programs; corporate reputation, disease related expertise, trust in the company and the sales rep relationships are critical success factors.

**DETAILED TO DOCTORS IN EUROPE- SALES FORCE MANAGEMENT**

Personal selling is a significant part of the promotional effort, and it is estimated that it represents from 26.4% to 42.6% of the promotional expenditures in the pharmaceutical industry5.

The representative is the primary point of regular contact between the company and the physician who will prescribe the product for the patient. The importance of medical representatives in achieving the strategic and tactical objectives is undeniable. Yet, the environment in which medical representatives are forced to operate is different in every country.

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The results of the study “Launch Excellence™: the imperatives for sales success” conducted by IMS Health identifies the following key-criteria for success in terms of detailing to doctors:

- Common points to all successful brands: the sales model is in-between; the launch has to be synergistic between primary and secondary/specialist care, taking into account that non-prescribing stakeholders are not a determinant for success.

- The main difference is that the impact of direct selling varies significantly according to the country in question. The percentage of contribution of detailing to doctors, at 2 years in primary care, varies from 59% in the USA to 50% and 46% respectively in Italy and Spain. In countries where health economic evaluation is mandatory, Canada and the UK, the impact of detailing is lower and respectively: 36% and 16%.

It is tempting for pharmaceutical companies to think of a continent as a single entity as far as promoting and selling their products is concerned. But while there are many similarities in the pharmaceutical markets in key European markets, many differences exist:

- Concentration of the markets and percentage share of the national European retail markets held by pharmaceutical companies.

- Ratio of doctors to representatives and average sales size of sales forces and company ranking in the sales league table in individual countries. The largest companies employ total non-hospital teams ranging from 140 (the smallest in the UK Top 10) to 550 (the largest in Italy’s top 10).

- The availability of doctors for promotional calls: in most European countries, evidence suggests that doctors have less time and are less willing to see representatives than in the past. Therefore, when a new drug is approved, no time can be lost in capitalizing on the asset.

- The length of time a representative spends with doctors in each of the five countries (See Exhibit 7).

The practice of operating with multiple sales forces is universal among leading pharmaceutical companies. Among the medium to smaller companies the sales forces required to maintain sufficient coverage of the national market is only slightly smaller, such a sales force size allows the company to contact around 70% of the GP population 3 to 4 times per year.

It is usual practice for companies to organize their field selling operations on a divisional structure. In some cases, rather than just employing a large number of sales people, companies introduced “specialist” divisions, concentrating on only one or two therapy classes by division. Alternatively, some simply deployed a second general force to promote a different range of products. Some use a therapeutic specialization (e.g. cardio-vascular or anti infective), others do not. In the case of Novartis, the Oncology division is a separate entity at the global, regional and local level.

The product/therapeutic specialization offers a significant advantage in terms of delivering a higher standard of information to the target doctor. The representatives are more highly trained in a limited number of products and a more restricted therapeutic and medical environment.

**DETAILING MIX**

The number of products mentioned during the selling interview will vary from company to company. Most usually a representative will present full information on two leading products, which are the company’s highest priorities at the time, together with a reminder about one or two additional brands.
The promotional impact is directly related to the position and the time spent on each brand during the interview with the prescriber.

For each cycle, the promotional grid for each sales force is defined. The promotional grid includes the brands which are promoted by each sales force and fixes the order in which the representative will conduct the promotional interview. For each position, the brand to be promoted is established, and the percentage of time to be spent on that promotion.

**FIGURE 3**

**EXAMPLE OF A PROMOTIONAL GRID**

<table>
<thead>
<tr>
<th>Brand</th>
<th>Position during the call</th>
<th>% of time spent during the call</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>60%</td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td>30%</td>
</tr>
<tr>
<td>C</td>
<td>3</td>
<td>5%</td>
</tr>
<tr>
<td>D</td>
<td>4</td>
<td>5%</td>
</tr>
</tbody>
</table>

The promotional grid is the basis of various metrics used for calculating the number of Reps needed for effectively and efficiently promoting a brand (Rep. Equivalent) and optimizing the brand P&L.

**SALES FORCE: SIZING**

*Determining the sales force size is critical and is based mainly on two indicators:*

- The Reach: Nº Doctors to be called / Total Nº of Doctors. The objective is to ensure optimal coverage according to the market potential, total number of scripts per market clients (See Exhibit 8).
- The concentration curve supporting the decision of how many physicians will be called. This curve is specific to each market and analyses, the number of physicians (GPs and specialists involved in prescribing this drug) and the expected Market Share (MS). It determines the efficiency floor over which the additional promotional effort is not effective at gaining MS (see also glossary at the end of the Exhibits).

In many cases profiling the doctors is a critical element for targeting and naming as a priority the prescribers who are the most susceptible to changes in their script. Doctor-profiling is a customer segmentation with classification of the physician and adaption of the promotion according to the grade of innovation - from slow movers/laggards to early adopters. This is particularly interesting at the moment of launching a new drug in order to maximize the call frequency on these target-doctors who can move rapidly and are likely to adopt faster the new drug.

**MANAGEMENT OF SALES FORCE**

Recruitment and selection of salespeople, training, compensation and performance evaluation are core tasks in organizing and implementing the marketing effort. Companies approach these tasks in different ways but certain questions are common for the effective management of these activities.

The sales manager/supervisor’s role in the pharmaceutical firms has changed to include more management and strategic thought, more decision-making and more delegation to the team which reports to him/her. The Electronic Management Systems (ETMS) have driven the change to higher
standards of managerial performance and behavior. As a consequence, the regional manager has become a key-player in company strategy implementation.

RECRUITMENT AND SELECTION

They have a direct impact on a company’s field marketing capabilities. The role of personal selling in the pharmaceutical industry determines recruitment and selection criteria which have evolved from a “vendor” profile, with top negotiating abilities, to a more technical and scientific profile with communication skills.

Communication has become a key factor of selection with the evolution of the promotional activities handled by a medical Rep. In past years, the most usual means to contact GPs, apart from at the clinic, was to provide them with a slideshow or a film containing a balance between educational material and product promotion. Today, the medical Reps organize meetings and select the audience and also provide a Key Opinion Leader who gives a talk on the disease for which the company’s products are indicated.

Among pharmaceutical sector specifications is the frequent selection of young professionals with double training: medical/scientific and business degrees. In Europe, it is not exceptional to find medical doctors sales departments including the primary care segment. The beginners, with double training, are future candidates to be promoted to the marketing staff department. Starting off in sales is considered as an essential step for knowing the customers in depth.

TRAINING

The pharmaceutical companies’ sales people are highly trained in the specifications and technologies of their products but also in the diseases for which the product is indicated, the available therapeutic alternatives and competitors and the care protocols already recommended by health authorities for the patients for whom their brands are aimed at.

Particularly in the ethical segment, they receive initial and refreshment training on the previous topics and also on pharma-covigilance and reporting adverse events and the application of promotional guidelines.

A significant training effort is spent on the demographics, buying processes and other relevant characteristics of their markets.

New sales recruits may receive a combination of training and orientation about company policies and procedures. The initial sales training usually encompasses: product, company, customer and disease knowledge, regulatory training and generic selling skills.

Effective sales training cannot be carried out as a one off event and periodic reinforcements are implemented.
FIGURE 4
MANAGEMENT OF SALES FORCE: MEASURING SALES FORCE ACTIVITY

Sales & Sales Force activity

- Call Rate
- Targeting
- Meetings
- Share of Voice
- Resource Level

Sales & SF Activity + SF Quality => SALES

<table>
<thead>
<tr>
<th>Prescriptions</th>
<th>Revenue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brick*</td>
<td>Actual TO</td>
</tr>
<tr>
<td>Territory*</td>
<td>Growth</td>
</tr>
<tr>
<td>Regional*</td>
<td>MS</td>
</tr>
<tr>
<td>National Regional*</td>
<td>MS growth</td>
</tr>
<tr>
<td>International</td>
<td>*ETMS: Electronic Territory Management System</td>
</tr>
</tbody>
</table>

The Share of Voice (SoV) measure of a brand comparatively expresses the weight of the brand with its direct competitors. SoV is a reliable measure of sales forces activity (See Exhibit 9). The most drastic example is the case of a decreasing SoV in a territory, something usual in cases of vacancy (territory where the Doctors are not called, because the positions are not covered).

The management of sales forces and monitoring of sales force activities has drastically changed with the Electronic Territory Management System (ETMS). This is an essential tool for territory distribution and it also includes a follow-up by medical reps of the calls, meetings and to cross-check the targeting in order to confirm coverage and frequency of calls.

MANAGEMENT OF SALES FORCES: MEASURING SALES FORCE EFFECTIVENESS

Rewarding sales people is the most visible and tangible aspect of sales management and, undoubtedly, the major factor affecting the salesperson’s performance.

Reward plans should direct the sales force toward activities that are consistent with overall marketing objectives.

However, the salesperson’s potential influence on the buying decision and the abilities required to exert this influence are major key issues affecting their performance. These issues are well known: lack of self-discipline, lack of objectives, priorities & deadlines, indecision and procrastination, attempting too much at once, leaving tasks unfinished and unclear communication.

IN SPAIN

The retail market accounts for 65 % of drugs purchased by prescription (ethical segment). However, hospitals are seen as vitally important for market-success, not only for the many products with significant within-hospital use, but also for the influence which they exert on GP prescriptions.

Target customer base of General Practitioners is: 47,300 in Primary Care out of a total of 54,600 registered physicians.
In terms of coverage the average Spanish Medical Rep is responsible for contacting a group of 250 to 300 GPs.

Company activity programs are organized in detailing cycles, usually three cycles per year. The number of cycles has dramatically decreased in the past 15 years from 4 to 5 cycles per year in Primary Care to the current situation of 3 per year. Each cycle means that new promotional material is produced for each brand, including the literature used by the Reps.

**NOVARTIS PHARMA THERAPEUTIC FRANCHISES**

At the end of 2007, Novartis Pharma Spain was organized into 6 therapeutic franchises for the promotion of various brands:

- Cardio-vascular and metabolism (CVM) therapeutic franchise with the following brands: Diovan® - valsartan family, Lescol® hypolipemic drug, selectively lowering blood cholesterol and Starlix® anti diabetic licensed-in drug. The cardio-vascular franchise represented 16 % of the total revenue of the Pharma Division (Diovan Family & CoDiovan 85.234 € Mil - 79% of the CVM franchise and Lescol® with 22.8 € Mil the other significant part of the CVM franchise).  
- Bone – Dermatology and respiratory drugs.  
- Central nervous system medicines.  
- Classical drugs with a long history in Novartis (i.e. Voltaren® diclofenac, anti inflammatory drug and pain killer).  
- Infectious diseases, bone marrow transplant and immunology.  
- Ophthalmology.

**NOVARTIS CARDIO VASCULAR FRANCHISE AND THE VALSARTAN / DIOVAN® FAMILY**

Novartis had launched its antihypertensive Diovan® in the United States in February 1997, as the second brand in a new class of antihypertensive drugs the ARA II class: the angiotensin receptor antagonists. Merck’s ARA II, Cozaar® - losartan had pioneered the therapeutic class in 1995.

The hypertension market was very large and growing. Growth started historically with the launch of the calcium channel inhibitors followed by the ARA II class and combinations of ARAs II with diuretics. The ARA II class was small and with various competitors; in 1997 and 1998 two other competitors were launched. Additionally a new forthcoming ARA II and a new category of antihypertensive medicines were expected to be launched soon. The ARA II class market share was rather small comparatively with other antihypertensive medicines: ARA II 8% in the US in 2001. The ARA II brands were perceived and used as a second line therapy when other alternatives had failed to control blood pressure.

In 2007 the hypertension market is the first market in value and the second in prescriptions of the total Spanish pharmaceutical market. Total sales account for billion € 1.1 (+4.8% 2007 vs. 2006) and for 118 million units. The ARA II class is the driver behind market growth. And, for first time in 2006, it is the leader in the high blood pressure market in value and units. Currently Novartis leads the high blood pressure market and maintains a top ranking position with valsartan ranking first in units for the hypertension market. However, many key molecules will be losing their patents in the very near future and will become generic. This is the case with losartan Cozaar®, in 2007.

Novartis decided to differentiate Diovan® from other ARAs II on efficacy and selectivity, competing for first line use, and developing new indications, dosages and combination products. The management of the cardio-vascular franchise and the creation of the Diovan® family have been remarkable at creating long-term value for the CVM portfolio.
Diversification through line extensions ensured Diovan® value protection and extended brand life. The patent of Diovan® and CoDiovan will finish in some years, due to this Novartis started an extensive program of line extensions:

- New indications, expanding the market base and supporting product growth, included congestive heart failure and high-risk hypertension.
- Expanding the brand scope through new formulations with a starting dose of 320 mg to enhance efficacy as well as other strengths and combination products. These reformulations offer long term revenue protection and in the case of Diovan they maximize clinical benefits.

To succeed in franchise management, Novartis supported these strategic goals with an extensive clinical trial program and by increasing share of voice in medical publications. Novartis started an ambitious phase IV program of clinical studies as cardiologists focus on clinical evidence. Repositioning alone would not have been sufficient to improve Diovan®’s market share. The growth of the Valsartan / Diovan® family has been impressive and shows an excellent brand lifecycle management (See Exhibit 10).

**NEXT LAUNCHES IN NOVARTIS PHARMA SPAIN**

At the end of 2007 Novartis Spain wants to launch Exforge®, a combination of Valsartan and Amlodipine. Amlodipine is already a generic drug and is used in monotherapy, which is effective at decreasing high blood pressure. The combination of Valsartan and Amlodipine maximizes efficacy for controlling blood pressure. Additionally, it provides more patient convenience as the combination of these two molecules with complementary mechanisms of action decreases the frequency of the adverse effect related to the use of the ARA II class: ankle edema. The improvement of the compliance related with better tolerability optimizes the ratio efficacy – safety versus other competitors.

Exforge® brand is a line extension of Valsartan / Diovan®. However, two positions were evaluated when launching Exforge®: A Diovan line extension or standing alone and positioning it as a product to limit cannibalization of the other Diovan® brands.

Marketing raises various critical issues for success:

- Promote Exforge as a new and distinct drug with clear and emotional messages.
- Play operational synergies between the brands of the CVM franchise and build-up a strong category call.
- Focus on high potential customers.

In the coming months and within a timeframe of 18 months, three other brands are planned to be launched by Novartis Spain in the CVM franchise: an innovative anti hypertensive medicine and a product for treating diabetes mellitus (often referred to simply as diabetes).

Diabetes is a syndrome characterized by metabolism disorder and abnormally high blood sugar (hyperglycemia). Diabetes is a chronic and progressive disease that has an impact upon almost every aspect of life. There is evidence that good control of blood glucose levels can substantially reduce the risk of developing complications and delay the progression of the disease. The management of high blood pressure and raised blood lipids are equally important. With the launch of these brands, Novartis consolidates their leading position in the cardio-vascular market and covers the main metabolic disorders responsible for disease and mortality in developed countries.

**Rasilez® - aliskiren** is a new chemical entity for treating high blood pressure, first in a new therapeutic class, the rennin inhibitors. It acts directly on rennin, the protein secreted by the kidney
and where the increase in blood pressure originates (See Exhibit 11). The innovative mechanism of action of the aliskiren molecule ensures 24h control of blood pressure.

Novartis started an extensive clinical trial program and established that, by acting on the origin of hypertension, the intermediate clinical outcomes of cardio-vascular disease improve. Rasilez® - aliskiren should reduce complications caused by high blood pressure and atherosclerosis such as cardiac failure, kidney insufficiency or stroke.

Novartis initiates a new franchise in a new category for treating type 2 diabetes. **Galvus® vidagliptin and Eucreas®**, a combination of vidagliptin and metformin that is indicated for diabetes type 2, also known as adult onset diabetes.

Galvus® vidagliptin is a new chemical entity of a new category, the Dipeptidyl peptidase IV (DPP-IV). Galvus is the second comer to a new class of oral antidiabetic agents which reduce blood glucose in a dose dependent manner and enhance the function of the pancreatic cells which secrete the hormone (insulin) responsible for controlling blood glucose. They promote satiety, decrease food intake and weight loss is observed.

Eucreas® is the combination of vidagliptin with another anti-diabetes agent metformin; this molecule is the generic of reference for first line treatment of diabetes type 2 when non-therapeutic management - combination of diet, exercise, and weight loss – has failed. The majority of patients start with metformin (90% of patients in Spain).

Galvus® should logically be combined with metformin when monotherapy does not control blood glucose and Eucreas® is the fixed combination for uncontrolled patients on metformin alone.

Direct competitor Merck’s Januvia®, sitagliptin launched in the US in October 2006 and in Europe in April 2007 as the first DPP-4 inhibitor. The European Commission approved Galvus® and Eucreas® in January 2008.

The diabetes market is rapidly growing. The epidemiology of diabetes is as follows: nearly 6% of adults in the world have diabetes, 246 million people worldwide. Prevalence is rising rapidly, particularly in developing countries. Worldwide prevalence is expected to increase to 7.1%, totaling 380 million people by 2025. Incidence is high with estimates as follows: India (40.9 million), the US (19.2 million), Russia (9.6 million) and Germany (7.4 million). Diabetes related global sales were US$12.8 billion in 2007. Novartis, with innovative brands in a fast growing market, has a big opportunity, maximized by the fact that the most prescribed oral antidiabetic drugs have restrictions on use.

**GETTING READY FOR LAUNCHING**

In order to successfully launch so many brands in such a short timeframe and optimally reorganize the Spanish commercial operations, Francisco Ballester designated a task-force dedicated to address the following critical issues: be ready with various scenarios according to the uncertain time schedule for granting P&R, optimize category management for maximizing promotion efficiency.

At the end of 2007, in Novartis Spain the sales force was organized as follows (see exhibits 12 & 13):

- “Mirror Sales Force (SF) lines”: three Primary Care lines promoting the same brands in each territory. However, the promotional grid can vary according to each SF line since the order and time spent for each brand is allocated differently in each line. Spain is split into 78 geographical territories and the 78 territories are similar for the 3 SF lines.
- 1 cardio-vascular SF line calling on hospital specialists and representatives are 28.
• 1 Bone & Joint line with 23 Medical Reps.
• 1 Respiratory & Dermatology (RED) line of 29 Medical Reps.

Each regional manager is responsible for: 2 cardio-vascular reps, 1 RED representative and 3 Primary Care territories (9 medical representatives), managing in total 12 medical representatives.

The starting point is that the SF lines should be increased and the performance for each line must also grow. In relation with these two objectives, the direct selling organization has to be re-engineered.

An additional challenge was that the date when Price & Reimbursement was granted by the Spanish Agency of Medicines was uncertain.

The work team was made up of marketing and sales managers of the CVM therapeutic franchise, the business planning manager and the product managers in charge of cardio-vascular and diabetes brands. The objectives assigned to the team by Francisco Ballester were clear:

• How to produce innovative commercial plans in order to launch with the same intensity all the brands?
• How to optimize customer segmentation and profiling?
• How to maximize sales force performances taking into account that the number of customers is increasing?
EXHIBIT 1

RANKING OF INDUSTRIAL SECTORS BY AGGREGATE R&D FROM THE WORLD’S TOP 1,402 COMPANIES ON THE 2008 EU SCOREBOARD- 2007

<table>
<thead>
<tr>
<th>Sector</th>
<th>Share in R&amp;D investment (%) according to ICB (36 sectors)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmaceutical &amp; Biotechnology</td>
<td>19.2</td>
</tr>
<tr>
<td>Technology hardware &amp; equipments</td>
<td>18.3</td>
</tr>
<tr>
<td>Automobiles &amp; parts</td>
<td>17</td>
</tr>
<tr>
<td>Software &amp; computer services</td>
<td>7.1</td>
</tr>
<tr>
<td>Electronic &amp; electrical Equipment</td>
<td>7</td>
</tr>
<tr>
<td>Chemicals</td>
<td>4.4</td>
</tr>
<tr>
<td>Leisure, goods</td>
<td>3.7</td>
</tr>
</tbody>
</table>

ICB: Industrial Classification Benchmark set up by FTSE (Financial Times Stock Exchange) & Dow Jones

EXHIBIT 2

HEALTH/ MEDICAL CENTERS IN SPAIN

<table>
<thead>
<tr>
<th>SPAIN - HEALTH CENTERS, 2008</th>
<th>Control</th>
<th>Centers</th>
<th>Beds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Care Centers</td>
<td>Public</td>
<td>2,879</td>
<td>-</td>
</tr>
<tr>
<td>Hospitals</td>
<td>Public Civic Hospitals</td>
<td>313</td>
<td>104,689</td>
</tr>
<tr>
<td></td>
<td>Ministry of Defence</td>
<td>4</td>
<td>995</td>
</tr>
<tr>
<td></td>
<td>Industrial Accident and Occupational disease Mutual Funds</td>
<td>20</td>
<td>1,468</td>
</tr>
<tr>
<td></td>
<td>Private - non profit</td>
<td>120</td>
<td>19,925</td>
</tr>
<tr>
<td></td>
<td>Private for profit</td>
<td>345</td>
<td>33,088</td>
</tr>
<tr>
<td></td>
<td>Others</td>
<td>2</td>
<td>816</td>
</tr>
<tr>
<td>TOTAL HOSPITALS</td>
<td>804</td>
<td>160,981</td>
<td></td>
</tr>
</tbody>
</table>

Source: Ministry of Health and Consumer Affairs.
EXHIBIT 3

**NOVARTIS CORPORATION 2007 REVENUE SPLIT PER DIVISION**

Source: Novartis Annual Report

EXHIBIT 4

**NOVARTIS SPAIN 2007 SALES REVENUE SPLIT PER DIVISION**

Source: Spanish Brochure 2008
EXHIBIT 5

NOVARTIS PHARMA MAIN BRANDS CLASSIFIED BY THERAPEUTIC FRANCHISE

- Cardiovascular and Metabolic diseases
- Osteo-Dermo Respiratory
- Central Nervous System
- Classic Products
- Infectious Diseases, Transplantation and Immunology
- Ophthalmology

EXHIBIT 6

MARKETING COMMUNICATION TOOLS - PHARMACEUTICAL ETHICAL SEGMENT

<table>
<thead>
<tr>
<th>Tools Marketing Communication</th>
<th>Activities</th>
<th>Medicines Delivered Under Prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADVERTISING</td>
<td>Directed exclusively to Health Care</td>
<td>Brand communication to HCP</td>
</tr>
</tbody>
</table>
| PROMOTION DETAILING           | Material and promotional activities or events managed by Medical Reps:  
                                 | - Visual aids, folders, Product Monograph and any information which is not a scientific publication.  
                                 | - Meetings and conferences of HCP.  
                                 | The Summary of Product characteristics (SmPC) edited by the Registration Body must be handed out during five years after launch. | Any promotional material is reviewed internally in order to cross-check that the information matches with the SmPC. Each promotional documentation is submitted to the Health Authorities and they can react and fine if the content is not appropriate and does not fit the SmPC. |
| SALES PROMOTION               | Promotional activities in order to foster short term selling are restricted. | In case of a new drug, the Medical Rep can give samples to the physicians during the two years following launch. |
| PUBLIC RELATIONS              | The message is information but not commercial communication. It is not paid for by the sponsor and should be considered as news by the journalist. Impersonal stimulation of demand through general media: press release, press conference, prizes, etc. | Corporate communication is identical to other sectors. Brand communication focuses on the environment of the disease (epidemiology, burden of the disease, mortality) in the unsatisfied medical needs and expected patient benefits. |
| DIRECT MARKETING              | Direct marketing is limited to HCP. | Direct To Consumer (DTC) is not allowed in Europe. |

* European Promotional Guidelines
EXHIBIT 7

KEY FIGURES: METRICS IN EUROPE

<table>
<thead>
<tr>
<th>EUROPE</th>
<th>GP Avg N Rep Calls per Day</th>
<th>Duration Interview (minutes)</th>
<th>Cost Containment through control of Sales Forces Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>3</td>
<td>Avg: 5-7, Max: 20-30</td>
<td>Latest restrictions (ABPI Code of practice – 2007). No more than 3 unsolicited calls may be made on each prescriber by an individual Rep in each year, including “call backs”.</td>
</tr>
<tr>
<td>FRANCE</td>
<td>5.3 – 5.5</td>
<td>Avg: 5-10, Max: 10-15</td>
<td>Good Promotional Practices (Social Security &amp; Leem - 2005) aimed at limiting the impact of detailing by fixing &amp; controlling the activity of Medical Reps (content)</td>
</tr>
<tr>
<td>SPAIN</td>
<td>12 - 14</td>
<td>Avg: 2-5, Max: 10</td>
<td>Access to the Health Centers (Primary care) is regulated by Regional Governments: previous appointment.</td>
</tr>
</tbody>
</table>

Source: Carried out by authors.

EXHIBIT 8

SALES FORCE EFFECTIVENESS: MARKET SHARE ACCORDING TO THE NUMBER OF CALLS IN A DEFINED MARKET

Source: Carried out by authors based on Novartis data.
EXHIBIT 9
SOV MEASURE OF THE NEGATIVE IMPACT OF A VACANCY IN A TERRITORY

MONTHLY SALES (UNITS) IN 1 TERRITORY

Product A
Vacancy Primary Care: Sep 05 to May 06

Gap 25%

Product B
Vacancy Primary Care: Sep 05 to May 06

Gap 37%

Red line: Estimate if the vacancy would have not been covered

Source: Carried out by authors based on Novartis data.

EXHIBIT 10
DIOVAN LIFECYCLE MANAGEMENT

Source: Carried out by authors based on Novartis data.
**EXHIBIT 11**

**MECHANISM OF ACTION OF ANTIHYPERTENSIVE DRUGS AND ALISKIREN / RASILEZ**

![Diagram showing the mechanism of action of anti-hypertensive drugs and Aliskiren/Rasilez](image)

- Angiotensinogen → Renin → Angiotensin I
- Aliskiren – Rasilex® Increases plasma renin activity
- Angiotensin I → Angiotensin II
- ARA2 – Diovan®
- AT1 Receptor in the muscular cells of the vessels
- Aldosterone
- Vasodilators
- Retention Na+/H2O
- ARAs II – Antagonists of Angiotensin receptors

**EXHIBIT 12**

**NOVARTIS MASS MARKET / GENERAL MEDICINES BUSINESS ORGANIZATION 2007**

![Diagram showing the Novartis mass market/ general medicines business organization](image)

- Assistant
- Head of General Medicines
- Head of Sales
- Sales Strategy Manager
- Assistant
- CNS
- CVM
- ORC
- Mature
- New Products
- New Channels
- Field Force
- FF Effectiveness
- Training

**MARKETING**

**FIELD FORCE**
EXHIBIT 13

GENERAL MEDICINES SALES FORCE ORGANIZATION IN 2007 BEFORE LAUNCHING EXFORGE
EXHIBIT 14

NOVARTIS CASE - REFERENCE LIBRARY.

ANTI-DIABETIC: An anti-diabetic is a drug used for treating Diabetes Mellitus, which works by lowering the glucose levels in the blood. The selection of the most appropriate drug for each patient depends on the nature of the diabetes, age and health of the person.

BLOCKBUSTER: In the pharmaceutical sector, it is a medicine that is successful on the market. It is typically those that generate sales of over $1,000 million per year.

BRICKS: The minimum unit in which a certain geographical area is divided up before defining different sales areas. In general terms, a certain geographical area is divided up into many bricks, which refer to different criteria (nº of health centres, nº of inhabitants…), subsequently gathered to make up territories which have similar sales’ potential. Bricks are also the minimum unit of measure used when analysing information about sales.

CALL FREQUENCY: Index that represents the results of certain sales, as a function of the number of medical details. It is normally represented as a graph so that it is easy to identify the optimum level of productive frequency. If that optimum level is exceeded, leading to a plateau situation, no higher sales are obtained.

CONCENTRATION CURVE: Graph that represents the % of sales in a market, in function of the % of physicians responsible for prescribing the product within that market. The curves are specially developed for each market, and can differ a lot from one market to another. As an example, in the graph below, we can see that 30% of the physicians are responsible for 80% of the sales.

CYCLE: Each one of the periods of time in which companies review their promotional material and carry out changes in their promotional grids.

DETAIL: It is often common to use the term detail (which means “to give information”, instead of the word visit. The visits to physicians carried out by a medical representative are the key factor in terms of direct promotion.
DIABETES MELLITUS: This is defined as a higher than normal level of glucose in the blood. This is because the body either does not produce enough, or does not properly respond to insulin, a hormone produced in the pancreas. Insulin is the hormone in charge of regulating the blood-sugar level. During digestion, food is decomposed in order to generate glucose, which is the most important energy source for the body. This glucose travels to the blood, where insulin helps it to be absorbed by the cells. In patients with diabetes, one of the components of this system fails:

- Diabetes Mellitus type 1: the pancreas does not produce or only produces a very low level of insulin. Insulin – either inhaled or injected – is therefore supplied to the patient.

- Diabetes Mellitus type 2: body cells do not respond properly to the insulin produced. So, in order to treat the disease it is common to resort to agents that increase the amount of insulin secreted by the pancreas or to those that enhance the cellular sensibility to insulin, or to other agents that decrease the speed at which glucose is absorbed by the digestive tract.

DIOVAN: Oral medication commercialized by Novartis which is used for the treatment of high blood pressure and heart failure. Its main active molecule is Valsartan. It belongs to a group of drugs called angiotensin II receptor antagonists.

DIOVAN FAMILY: Group of different presentations of the same molecule: Valsartan, whose brand name is Diovan. They include Diovan 320, Diovan 160, Co-Diovan Forte and Co-Diovan 160. The differences between them are in the concentration of the active principles they contain, and if the main principle is combined or not with another active principle. Co-Diovan, as an example, is a combination of the Valsartan molecule with a very commonly used diuretic (Hydrochlorothiazide), to treat hypertension, eliminating the need to take 2 different pills and the subsequent oversights that this may entail.

EMEA: European Medicines Agency. This is a decentralized body of the European Union whose main responsibility is the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinarian use.

EQUIVALENT REPRESENTATIVES: This is a coefficient that represents the number of sales representatives that the promotion of a certain product would require if the promotion of the product was made during 100% of the sales representative’s time. As an example, supposing a commercial team with 200 representatives, with the following promotional grid and time distribution, the number of equivalent representatives would be:

<table>
<thead>
<tr>
<th>Drug</th>
<th>% of promotion*</th>
<th>Equiv. Rep.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug A</td>
<td>P1:60%</td>
<td>200*0,6= 120</td>
</tr>
<tr>
<td>Drug B</td>
<td>P2: 30%</td>
<td>200*0,3= 60</td>
</tr>
<tr>
<td>Drug C</td>
<td>P3: 5%</td>
<td>200*0,05= 10</td>
</tr>
<tr>
<td>Drug D</td>
<td>P4: 5%</td>
<td>200*0,05= 10</td>
</tr>
</tbody>
</table>

* % of the time of the visit devoted to the promotion of each product.

ETMS (Electronic Territory Management System): Electronic system used to manage commercial areas. These systems work like simulators. They help to define the optimum territories in which a certain geographical area should be divided up so that all the territories have similar sales potential. The ETMS works grouping different bricks, optimizing the size and the distance between
them. It is also used as a management tool because it allows for the control and monitoring of the commercial activity.

**EUCREAS:** Oral anti-diabetic used for the treatment of Diabetes Mellitus type II. It is commercialized by Novartis. It is a combination of two active principles, metformin hydrochloride and vildagliptin. Eucreas is specified for patients that either cannot achieve a good glycemia control with the maximum tolerated dose of metformin in monotherapy or who are already under treatment with the combination vildagliptin/metformin but in two different pills.

**EXFORGE:** Oral medicine specifically used in the treatment of high blood pressure. It contains two active principles, amiodipine and valsartan. It is suitable for patients whose hypertension is difficult to control with either amiodipine or valsartan in monotherapy.

**FDA:** Food and Drug Administration. This is the agency within the Department of Health and Human Services in the United States that is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, the nation’s food supply, cosmetics, and products that emit radiation. It is also responsible for advancing the public health by helping to speed up innovations that make medicines and foods more effective, safer, and more affordable; and helping the public to get accurate, scientifically-based information that they need to use medicines and foods to improve their health.

**GALVUS:** Oral medicine used for the treatment of Diabetes Mellitus type II. It contains vildagliptin as the only active principle.

**GENERIC DRUG:** According to the WHO (World Health Organization), it is a medicine that is sold under the name of the active principle it contains. It can be recognized because on the medicine’s packaging, instead of finding a commercial brand, there is the name of the molecule that it is made up of (called active principle), followed by the name of the laboratory that produces it. A generic drug can be produced once the patent of a branded medicine has expired, and only if it satisfies all the conditions of quality and bio-equivalence. It must offer the same safety as any other medicine.

**HYPERTENSION:** Medical condition characterized by an increase in blood pressure values to higher than 135/85 mmHg. It is one of the main problems of Public Health in developed countries, and it affects around one thousand million people in the world. It is usually an asymptomatic disease that is easy to detect. However, it causes serious and lethal cardiovascular damage (heart attack, brain hemorrhage…) if it is not treated in time. In the 90% of the cases, the origin is unknown; that is why it has been named “essential arterial hypertension”. It has a high hereditary component.

**IMPACT:** Numbers of mentions made about a certain medicine.

**IMS:** Leading company in the world in providing market information to the pharmaceutical and human healthcare industries. IMS buys information about the different transactions carried out between wholesalers and drugstores (Primary Care) or directly from hospital chemists. Then, they analyze it and offer their customers sales information by country, by brick, by hospital…, and a wide variety of additional services about the monitoring of pharmaceutical products’ uses, as well as personalized information.

**KEY OPINION LEADERS:** Physicians with high relevance and a recognized career in a specific knowledge area.

**LESCOL:** Medicine commercialized by Novartis. It has Fluvastatin as its active ingredient, which acts by reducing cholesterol in the blood.

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6 Bio-equivalence: the galenic formulation of the generic gives the active principle the same future treatment in the body (kinetics, circulating amount) so that its clinical effect is similar to the branded medication.
**LINES OF REPRESENTATIVES:** Group of medical representatives that promote the same products (sales force teams). The grid, or the position of the products in the grid can be the same or different.

**MAPS:** Computer program that works like a simulator and helps to define the areas in which it would be convenient to divide up a certain geographical area according to similar sales potential criteria. With that previous objective, it puts different bricks into groups, optimizing the size and the distance between them.

**MASS MARKETING:** This is a kind of strategy used for market coverage which is directed towards an indifferent customer so that the global market is dealt with through a single offer. The idea is to spread a message that will reach the maximum possible number of customers.

**MEDICAL REPRESENTATIVE:** Medical consultation professional who has received extensive scientific training about the Pharmaceutical Laboratory’s medicines as well as training in other subjects specifically related to Pharmacology: drug surveillance and adverse effects reports, promotion rules handed down by the European Medicines Agency. Also, as other commercial representatives, they receive training about territory management, communication and negotiation skills.

**MIRROR LINES:** Sales lines that promote the same products portfolio to the same physicians. The objective of designing mirror lines is to improve the impact of the products.

**OTC:** Over The Counter. Drugs that do not require medical prescription; free to sell in American drugstores and by chemists in Spain. This market is also called self-medication market.

**P1 EQUIVALENT:** This is a coefficient which is calculated for each promoted product, and it represents the impact that a medicament promoted in the X position of the grid would have had if it had been promoted to the first position. As an example, let’s suppose that a medical representative makes an average of 16 visits per day, with the following promotional grid, and time distribution. In that case, the nº of details and the P1 equivalent for each product would be:

<table>
<thead>
<tr>
<th>Drug</th>
<th>% of promotion*</th>
<th>Nº visits/day</th>
<th>P1 Equiv.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug A:</td>
<td>P1: 60%</td>
<td>16</td>
<td>16*1=16</td>
</tr>
<tr>
<td>Drug B</td>
<td>P2: 30%</td>
<td>16</td>
<td>16*(30/60) =8</td>
</tr>
<tr>
<td>Drug C</td>
<td>P3: 5%</td>
<td>16</td>
<td>16*(5/60) =1,3</td>
</tr>
<tr>
<td>Drug D</td>
<td>P4: 5%</td>
<td>16</td>
<td>16*(5/60) =1,3</td>
</tr>
</tbody>
</table>

* % of time of the visit devoted to the promotion of each medicament.

**PATENTED MEDICAMENT:** Those drugs that are under the commercial protection of an International Patents Agency. The patent is not only limited to the molecule, but also to the formulation, the synthesis mechanism, or association with some other molecules. Once the patent is approved, a brand generic is not allowed.

**PHASE IV CLINICAL TRIALS:** Clinical Studies carried out once a drug has already received permission to be sold. The main objective of these trials is to achieve a good tracking of the medicine once it has been commercialized and under conditions of normal use. Infrequent adverse effects are looked for during phase IV clinical trials and it is possible to identify unusual and rare adverse reactions. In previous phases, it is exceptional not only to find adverse reactions that occur at a frequency lower than 1/1000, but also to evaluate long term efficacy.
PRIMARY CARE: Group of professionals in charge of treating patients at the initial stage of consultation. The professionals’ profile and the welfare activities can differ from one country to another. In Spain, there are special health centres for Primary Care, where there are general practitioners as well as some specialists like pediatricians. The medical staff also includes nursing and administrative assistants. It is also very common to find other professionals and specialists such as social workers, midwives, specialists in odontology and psychology who increase the quality of the care provided and people’s access to primary care.

PRIMARY CARE VISIT LINE: Group of medical representatives that share a promotional grid and promote the same products to physicians in Primary Care.

PRODUCT BROCHURE: Scientific document that compiles all the technical and medical information regarding one product. If it is a pharmaceutical product that requires medical prescription, the competent health authorities make sure that the information supplied satisfies all the Agency of the Medicament’s requirements. The control is made subsequently since it is not necessary to have any approval for the use of promotional documentation.

PROFILING: A way to segment doctors. Considering that Exforge is a mixture of two other medicines that are well known by physicians, the best way of doing it was by using a potential criterion, where Super Target (ST) represents the top 20% of the market, T1 the next 20% and T2 and T3 the next 30% each respectively.

PROMOTIONAL GRID: This is the products’ portfolio that is assigned to each representatives’ line. For its design, it is necessary to fix the position or the order in which the different products are going to be promoted, as well as the % of time assigned for the promotion of each one. An example of promotional grid follows:

<table>
<thead>
<tr>
<th>Drug</th>
<th>% of promotion*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug A:</td>
<td>P1: 60%</td>
</tr>
<tr>
<td>Drug B</td>
<td>P2: 30%</td>
</tr>
<tr>
<td>Drug C</td>
<td>P3: 5%</td>
</tr>
<tr>
<td>Drug D</td>
<td>P4: 5%</td>
</tr>
</tbody>
</table>

SHARE OF VOICE: Indicator used as a reference of the effort that a company makes in the market, compared with that of its competitors. It is calculated by dividing the number of mentions made about a product by the total number of mentions made about the competitors’ products in that market.

SPANISH AGENCY OF MEDICINE: Organism under the auspices of the Ministry of Health in charge of guaranteeing the quality, security, effectiveness and proper information about medicines and sanitary products - medicines and Food Security Agency - in the widest sense, from the researching stage to their use, with the interest of protecting and promoting animal and human health.

SPECIALISTS’ VISIT LINE: Group of medical representatives that share a promotional grid, and promote the same products to specialist physicians in Primary Care and/or hospitals.

TERMALGIN: Medicament commercialized by Novartis, which has as its active ingredient paracetamol. It is commonly used for the treatment of mild and moderate pain as well as fever.

TERRITORIES: Minimum geographical units that are assigned to the sales representatives. They are defined by grouping together different bricks, taking into account for that grouping, geographical and sales potential criteria. The final objective, when making up territories is that they all have similar sales potential.
RASILEZ: Oral medication commercialized by Novartis, whose active ingredient is Aliskiren (a renin inhibitor). It is suitable for the treatment of essential hypertension. It can be used in monotherapy or in combination with other drugs used for treating hypertension.

REACH: Rate which is indicative of the promotional coverage carried out. Its main objective is to optimize the promotion according to the sales potential of the prescriptor. It is calculated by dividing the number of visited physicians by the total number of physicians.

VISIT/CALL: Meeting with a customer in which he/she is informed about the promoted products. The main indicator of representative’s productivity is the number of times that he/she visits a customer. In cases like medicines under medical prescription, health professionals are the only customers visited. In Spain, in primary care, the average number of visits is 14 visits per day.

VOLTAREN: Medication commercialized by Novartis whose main active principle is sodium diclofenac. It acts as an anti-inflammatory in disorders like extra-articular rheumatism, gout attack, and articular pain among others.

WHO: World Health Organization. Organism under the auspices of the United Nations (UN) that, since 1948 has specialized in managing policies in prevention, promotion and intervention with regards to health and on a global level.

WORKSHOPS: Seminars and hands-on conferences where physicians discuss different medical topics. Workshops are normally smaller than conferences and more local.