

# JOHNSON & JOHNSON

## COMMENTS ON THE PRELIMINARY REPORT OF THE PHARMACEUTICAL SECTOR INQUIRY BY DG COMPETITION.

### 1. Introduction

As one of the important investors in pharmaceutical innovation in the European Union, with research entities in Belgium, the United Kingdom, Spain, France (and Switzerland), and with pharmaceutical manufacturing plants in Italy, Belgium, France, Ireland, the Netherlands (and Switzerland), and with offices in almost every member state, Johnson & Johnson's focus has always been on delivering high therapeutic value to patients, while creating substantial economic and social value within the European Union at the same time.

Our company has constructively engaged in the different initiatives by the Commission to better understand and address the challenges of Pharmaceutical Research and Development within the European Union.

Similarly, our company has been participating in DG Competition's Sector Inquiry in a constructive manner.

However, and although we respect DG Competition's authority to identify and investigate possible violations of competition rules, we are at the same time concerned that the methodology used for this review (leading to the conclusions as they are presented in the report) contains some important flaws. Consequently, future pharmaceutical research and innovation and the critical importance of intellectual property in protecting such innovation may come under pressure, while the conclusions of the preliminary report at the same time risk to create an unjustified negative impact on the reputation of the research-based pharmaceutical industry.

Our company also fully supports the comments and suggestions submitted by EFPIA. In addition to those, Johnson & Johnson also wanted to provide a wider perspective on the current nature of pharmaceutical innovation, as applied in our company.

### 2. Methodological comments

The Sector Inquiry set out to identify the decline in innovation and the obstacles/delays for generic entry. One would therefore expect that the Inquiry would look into the broader structural challenges of the sector as well as the behaviour of all market players. However, DG Competition clearly states that it can only investigate and draw conclusions that fall within its authority, i.e. the potential anti-competitive behaviour of companies.

#### Presentation of the statistic data

In order to be able to relate the conclusions to those aspects that fall within DG Competition's authority, we suggest the presented statistics be corrected for all "obstacles and delays" that have other causes than company behaviour.

Like the rest of the research-based pharmaceutical industry we know out of experience that the delays presented in the Preliminary Report are predominantly due to the time required by the European and national authorities for market approval and pricing & reimbursement approvals. The data presented in the Preliminary Report in relation to the generic approvals show clear analogies with the approval timelines (and related delays) for innovative medicines.

In addition we suggest DG Competition to correct the data in the final report for those delays resulting from the commercial strategy of generic companies in terms of launching sequence of their products or selected galenic formulations or dose strengths of the original products. Indeed, it is of interest to notice that the least-selling medicines and/or formulations of medicines, in the smallest countries, and the markets with the lowest prices, witness the longest delays for generic market entry, whereas the

biggest-selling molecules and/or formulations of medicines in the largest countries experience almost immediate generic entry upon loss of relevant IP protection.

Failure to correct the data and findings as aforementioned, or alternatively, to objectively assess the impact of the structural challenges of the pharmaceutical market and the commercial strategies of the generic companies, would inevitably lead to incorrect conclusions, solely based on the behaviour of the market actors ( or better, of only one part of market players, see below).

#### Presented data are asymmetrical

The data presented in the Preliminary Report are asymmetrical; they have been selected with the assumption that the cause of the delays has to be found within the originator industry and the behaviour of the different originator companies. It would be in the interest of objectivity and fair balance that the same data are presented on the generics industry as those that are presented on the originator industry. The investigation starts with the assumption that the research based industry uses a “toolbox” to hinder or delay market entry for generics ( thereby ignoring that these are legitimate means to protect the commercial and IP interest in its products), but fails to investigate the means or behaviour of the generic industry when launching generic version of originator products..

In that respect we suggest that DG Competition investigates:

- The patenting strategies by generic companies: often, generic companies will file patents on (sometimes minor) changes to the original molecule or technology and defend their IP in a similar way as the research based pharmaceutical industry. By and on itself this is a legitimate strategy, but it should be reviewed in a similar way as was done for the originator companies;
- The regulatory strategies of generic companies: they will often submit several files for the same generic product per country with the sole intent of increasing the chances of getting market access first, yet increasing the administrative burden substantially, thereby contributing to the undue delay, both for other generic companies as well as research based industry;
- The commercial strategies of generic companies; as indicated above and as extensively illustrated in the EFPIA submissions, generic companies often delay the launch of a generic product in certain markets for good (internal) commercial reasons.
- The intra-generic competition dynamics: an aspect, not covered in the report, which should be reviewed to fully understand the pricing dynamics in a generic market.

### **3. The importance of innovation**

The Preliminary Report rightly points out the importance of pharmaceutical innovation as being essential for patients and for public health. Without the research and the funding of the development of new medicines by the top-20 pharmaceutical companies, not many medicines would see the light of day. According to the European Commission’s Innovation Scoreboard 2007, the top-20 pharmaceutical companies invested over 54 billion euro in R&D, which is close to the totality of the investments made globally by the whole industry. The gigantic research investments made by the innovative industry is paid for by today’s medicines sales, not by public funding as is often wrongly assumed. We suggest the Final Report clarifies this insight more since it is an important dynamic of the research based pharmaceutical industry. A reduction in sales and related income for a research based company will have an immediate effect on R&D investments, as well as on related employment. If the European Union wants to reclaim its leadership position as the innovation leader in the world, the first prerequisite would be to offer the correct financial reward for innovation risks, reflected in the price of new medicines. In this respect we refer to our comments and the need to create headroom for this innovation reward, amongst others via the stimulation of price competition in a generic market

#### ***3.a. The decline in innovation output.***

The perceived decline is not a decline in innovativeness, but in innovative market introduction. The number of investigational new drugs (IND) submitted for approval in first-in-human studies, reached the record level of more than 700 in 2006, which is twice the amount that it was in 1996. Meanwhile, we notice that within the same ten-year time-span, the number of drugs that were approved for market

introduction was halved. Both figures taken together demonstrate that the investment risks for a research-based company have quadrupled over the same period.

It is clear, also from our company perspective, that many factors come into play:

- the increased complexity of the diseases investigated,
- the increased cost of research & development forces companies to be more selective in the products they bring to the market,
- the increased requirements by the public health authorities, that make innovation even more risky : requirements change in the course of the product development, the required number of clinical trial studies has increased, the required number of patients per trial has increased, the required number of procedures per patient has increased, the cost per patient has increased (doctor fees and insurance fees)
- next to that, the national pricing and reimbursement authorities as well as the different health technology assessment centres have increased the number of data required to demonstrate the health-economic value of the medicine.

If we take all those additional complexities into account, the actual overall research cost per launched new molecular entity (NME) has drastically increased in the past decade. Companies work with annual research budgets, based on the expected sales of that year. In 2006, the pharmaceutical industry spent 60 billion € worldwide on R&D, for 22 NMEs that were reimbursed that same year, or an R&D investment of 2.7 billion € per launched NME. Even when calculated over the life-span of the development of one drug, and taking into account the capital cost for making that investment, the total cost is well over 1 billion €<sup>1</sup>. The calculation in the Preliminary Report that states that the total cost of developing a new drug is a little over 400 million euro is not in line with our investment reality.

Despite these extremely challenging conditions, we are proud that our company discovered and launched several very innovative new products in the last years, such as: new treatments for HIV/AIDS, the most promising new compound against tuberculosis in forty years, new innovative treatments for schizophrenia and cancer, and this month a breakthrough medicine against psoriasis, to name but a few..

### ***3.b. The importance of incremental innovation***

New opportunities created by advances in science and technology offer unprecedented promise and hope to create new and better possibilities to bring patient and societal value, but unavoidably also increase dimensionally the inherent investments by the R&D driven companies.

Incremental innovation is essential for therapeutic added value.

Very often, the continued improvements to existing drugs, which are subject to full scope development cycles averaging close to 8 to 10 years development, lead to optimal therapeutic value over time. First-in-class is not necessarily Best-in-class!

Incremental innovation leads to :

- better efficacy
- patient compliance
- better patient adherence
- better patient comfort
- fewer incidents or relapse
- broadening the physician's array of therapies
- speedier delivery
- increase of quality of life
- ...

In many instances, this leads to reduced costs for the healthcare system.

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<sup>1</sup> DiMasi et alii (2003)

### ***3.c. A few examples of incremental innovation from Johnson & Johnson :***

#### *The evolution of our antimycotics franchise.*

Over a period of more than 30 years, our company has achieved and maintained its global leadership position in the treatment of fungal infections. The first antimycotics discovered by our company, were for topical use (miconazole), we then discovered a new molecule (ketoconazole) for oral use, which had a broader therapeutic spectrum than the first one. Our knowledge of fungal infections ultimately led to the discovery of itraconazole, a drug with a very broad spectrum, with oral and intravenous delivery systems. Over the years the therapeutic value increased with the discovery of new compounds belonging to the same class of drugs.

#### *Manufacturing technology*

Our company developed a spray-drying technology, that increases the bio-availability of drugs in the blood, thus drastically decreasing the pill-load necessary to deliver the same dosage. For some of our HIV drugs, we were thus able to reduce the pill burden for AIDS patients with factor four, from 16 pills per day to 4, with the same therapeutic effect.

#### *The use of nanotechnology in value enhancing drug delivery technologies*

In this dynamic landscape, the scope of innovation is changing continuously and goes beyond the discovery only of a new molecule. Many of the most valuable types of innovation and innovative products come not from advancing in one particular area of technology, but by combining existing and new technologies in novel and creative ways, such as, for instance, combining chemistry and biology with engineering and the physics of nanotechnology.

The new dynamism in of innovation is the product of converging scientific and technological advances, evolving patient needs, and not least of all, multi-disciplinary collaboration as a means of creating novel health care solutions. These recent examples of convergence - the innovative combination of drugs, or devices to create an improved health product -- enhance care and compliance, reduce long-term costs and improve patient health.

One example in our company be found in the domain of schizophrenia, where we developed a long acting product following a clinical research and development process of close to 10 years. The product is the combination of risperidone, a highly effective molecule resulting from our R&D legacy in the area of mental health, with an innovative drug-delivery technology developed by a specialized biotech company. The result - an injectable anti-psychotic that patients receive every two weeks - provides significant compliance advantages over the oral formulation. As patient compliance is the single biggest problem with schizophrenia, this product offers a constant delivery of the drug to the patient for two weeks through just one injection that allows a significant reduction of the risk to relapse.

We are currently developing a once-monthly injection. The therapeutic added value resulting from the shift from the daily pills to the injection is considerable, and the step from a two-weekly to a monthly, and eventually a four-monthly injection means a total change in the treatment of the disease.

#### *Pain management*

In the late 60s, our labs developed one of the most potent anaesthetics, fentanyl, several hundred times more potent than morphine, and allowing anaesthesiologists the possibility for precise dosing, allowing for long procedures such as open-heart surgery, but also for more short term interventions. In the 90s, we developed the administration of fentanyl through a patch system, thus creating a totally new application, and a new therapeutic instrument to treat chronic pain patients, because it replaced the use of the morphine pump. The advantages for patients are huge : three-day constant pain relief, easy to administer and use outside of a hospital environment, drastically increasing patient's quality of life.

#### *New indications*

From a commercial and patient benefit perspective, it would be ideal to launch all indications for multiple patient groups at the beginning of a product's lifecycle. However, this almost never occurs:

- Many products fail during the costly full development phase; thus we try to manage the risk and prioritise our global R&D investments by focusing initial development to the key medical needs
- For ethical reasons, it is customary to establish efficacy and safety in the adult population before further developing a product for "special populations" such as children and the elderly, which may require different dosages or dosage forms. These populations also typically require additional clinical and non-clinical studies to be completed prior to undertaking larger clinical trials in these groups.
- Clinical study timelines vary according to the required endpoints, patient populations, disease, etc.
- Potential new uses for a product may be recognized only during the post-launch phase, after it has been used in a "real life" setting and based on experiences and input from the medical community as well as patients. Oncology products are an often-cited example of this: One of our cancer compounds, VELCADE, is a very effective treatment for multiple myeloma. It was approved by the European Medicines Agency for second line treatment of multiple myeloma in 2004. In 2008, after additional studies, it was approved for first-line treatment of multiple myeloma, broadening its application base significantly. In the meantime, clinical trials are ongoing to determine its potential value in other areas of oncology: Non-Hodgkin Lymphoma, lung cancer, prostate cancer, ovarian cancer, breast cancer and colorectal cancer.

Several of the above considerations (e.g. risk-management and prioritisation of considerable R&D investments, a staged approval process whereby broader use of the product will only be allowed following additional clinical data or after considerable patient years of experience) do not apply to generic submissions. Normally when a generic submission is approved, it will immediately obtain all the indications for which the originator obtained approval during the lifecycle of the product.

### *Conclusions*

From a stakeholder's perspective, incremental innovation brings substantial value.

From a company's perspective, it means considerable research and development investments comparable to the development of a new molecular entity (see for instance above the development of our company's long acting anti-psychotic).

Considering the investments required to develop these incremental improvements as well as the need to protect valuable proprietary know-how that may be involved, it is normal and legitimate that research based companies will try to protect inventive improvements via proper IP protection.

One should also realise that patenting these improvements has no relationship with the final therapeutic or societal value of these incremental improvements. If the stakeholders are not convinced of the added value of the incremental improvement, the product will not prevail; doctors will not prescribe it, patients may not use it or payors will refuse to reimburse it.

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In summary, Johnson & Johnson fully supports the comments submitted by EFPIA and hopes that DG Competition will consider the recommendations made in order to come to a more balanced view on the status and tremendous importance of the pharmaceutical industry in Europe for the patient and society, such that the report effectively contributes to the broader ongoing initiatives recently launched by the Commission in this respect.

