Pharmaceuticals Sector Fiche (16.12.2011)

Executive Summary

1. Pharmaceuticals sector in the EU

The following document aims to give an overview of the EU's pharmaceuticals sector, both innovative and generic, in relation to external EU trade, the EU industry's position within the global pharmaceuticals market, and the trade barriers faced when importing medicines to third country partners. Key points within the document include:

- The pharmaceutical industry's intrinsic link to public health, and the complex regulatory burdens arising from this relationship that can potentially have an impact on trade.
- A strong EU industry presence, providing over 640,000 jobs directly, 113,000 of which are highly skilled.
- The high level of research and development spending on new drugs outlaid by the EU's innovative pharmaceutical sector (16% of business expenditure: the highest percentage of any industrial sector), and the extended length of time (8-12 years), it can take for a new drug to enter the market.
- Increasing importance of biological products (biopharmaceuticals and biosimilars).

2. Main trade issues

The EU as a World leader in the trade of pharmaceutical products, enjoying a trade surplus of €47.8bn in 2010, a steady growth in exports witnessed since 2001 and an ability to adapt to and enter new and growing markets. It does, however, face strong competition from traditional producers such as the US and Japan, along with growing competition from fast developing economies such as China and India.

EU industry continues to encounter some tariff barriers in certain countries, such as India. However, it is the wide range of non-tariff barriers (NTBs) that are the key focus of the industry. The different sub-sectors and type of pharmaceutical products face the same type of NTBs. Such barriers can arise due to a divergence in international regulatory regimes, which can be the result of a country's public health history and culture. Such barriers can also be used as protectionist measures to help foster local industry.

The key NTBs include:

- Regulatory barriers such as the registration and certification of new and generic drugs,
- Other barriers related to market authorisation such as unnecessary repetition of clinical trials in third countries and burdensome good manufacturing practice requirements;
- A lack of transparency in the amendment and implementation of pricing and reimbursement regimes in third countries.

Intellectual property rights and the counterfeiting of medicines are also concerns for EU industry, as a leader in R&D and in new fields within the sector such as biologicals and biosimilar pharmaceuticals. A lack of patent protection or data protection in certain third country markets could lead to abuses of EU industry patent right, while the counterfeiting and

falsification of medicines is a clear danger to the health of patients. The potentially flawed practice of patent linkage is also a specific concern for the EU's generic industry.

In addition to the above, there appears to be a growing trend towards local preference policies in third country markets. This can sometimes take the form of direct subsidies, however, numerous indirect policies are also being practiced, such as discrimination in public procurement and pricing polices and local production incentives.

3. Conclusions

Industry and EU Member States have advocated a number of trade policy recommendations, including more direct assistance from EU institutions when dealing with third countries, particularly on the ground level of EU delegations. They also call for IPRs to be properly balanced within multilateral and bilateral agreements, and where appropriate for the negotiating of harmonisation and reciprocity of regulatory regimes in such agreements.

The EU has set out a number of tools available to tackle relevant trade barriers, including the WTO's Technical Barriers to Trade Committee and possible resort to the Dispute Resolution settlement mechanism.

Such barriers can also be considered within the framework of the EU's existing and future Free Trade Agreement negotiations, and through the dialogues and resolution mechanisms provided for in existing FTAs. Finally, the Market Access Strategy provides a useful tool to identify and deal with specific key trade barriers for a number of sectors, including pharmaceuticals.

In conclusion, the EU's pharmaceutical industry is a trade success story, and retains a strong position with the global market, despite facing numerous barriers to trade and increasing competition. The Commission will look to work with industry to identify key barriers and concerns that impede its trade in third countries.

Follow-up point: *the list of NTBs compiled by the industry will be analyzed to determine priorities and the best course of action, including under the Market Access Strategy. Action should also be pursued to ensure that sectoral concerns, especially regarding tariff and non-tariff barriers, continue to be properly addressed in multilateral and bilateral negotiations.*

1. Pharmaceuticals sector in the EU

1.1 Definition sector and sub-sector:

Though there are many different types of pharmaceutical medicines, broadly, as a sector, pharmaceutical products can be placed in either of two camps: innovative and generic. Innovative pharmaceuticals are essentially 'new' medicines brought to market, that remain under patent protection ('on patent'). Once patent and data protection have expired (also referred to as loss of exclusivity), other pharmaceutical companies are able to market their own, identical and cheaper versions, labelled 'generics', of the previously patented, innovative medicine. A number of the large innovative pharmaceutical companies will produce both types of products while there are many generic-only companies. Both innovative and generic pharmaceutical firms share many trade barrier problems in terms of non-tariff barriers (NTBs) and general market access issues, while tending to hold divergent positions on some issues i.e. length and nature of Intellectual Property Right (IPR) protection.

An important distinction can be made between 'chemical' and 'biological' products. The latter is a pharmaceutical product that contains biological material such as proteins, DNA or bacteria, as opposed to a 'non—biological' chemical compound. Both industry and Member State responses have highlighted the increasing importance of this type of product that can be subdivided into biopharmaceuticals and biosimilars (the term for a biological medicinal product claimed to be similar to an already approved reference product), for the sector. These two types of pharmaceutical products can be produced by both innovative and generic companies. In terms of trade barriers these two categories of products face many of the same barriers and challenges. Indeed, as far as newer fields such as biosimilars are concerned, the EU has taken a notable lead in providing a sound regulatory framework, which has not yet been reciprocated in many of the World's leading producers and economies.[1]

Due to its obvious relationship with public health, the pharmaceuticals sector is heavily regulated compared to other industrial sectors, and subject to government interventions, both within the EU and in third countries. Such interventions range from the regulatory standards and frameworks that a pharmaceutical product must go through before it can be placed on the market (e.g. clinical trial testing, formal registration and certification), to controlling the price and/or reimbursement for drugs where there is a public health system in place, either to control budgets or to ensure the public an adequate access to medicines. Access to medicines is also an important issue for the industry on a broader level. Third countries and other interested bodies often promote or justify the imposition of certain trade barriers and price regulation as a means to ensure access for the poor, and it is clear that the sector has to balance its activities as a private, profit making industry with its role as the provider of essential medicines.

[1] See Directive 2001/83/EC, as amended: http://ec.europa.eu/health/files/eudralex/vol-1/dir_2001_83_cons/dir2001_83_cons_20081230_en.pdf; and the EMA website: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000408.jsp&murl=menus/regulations/regulations.jsp&mid=WC0b01ac058002958c

1.2 Employment and size of industry in the EU

The European pharmaceutical industry is one of the largest industrial sectors within the EU, and is a significant source of employment. According to industry sources, it directly employs 640,000 people and generates three to four times more high-tech industry jobs indirectly – upstream and downstream – than it does directly. Of the direct employment, 113,000 jobs are in specialised R&D areas.

It is difficult to put a figure on the total number of independent companies, both originator and generic. As the Commission's July 2009 sector enquiry into the sector reported, probably due to the declining number of new originator products entering the market, and large originator companies seeking to take advantage of a growing generics market, "an intensified consolidation in the sector has been observed in recent years. Originator companies have undertaken various acquisitions of both originator companies and generic companies."[2] That report focused on 43 originator companies and 27 generic companies, which represented over 80% of the total turnover generated with prescription medicines in the pharmaceutical sector of the EU in 2007. However, Member State and industry association contributions to this sector fiche indicate that there are numerous smaller scale companies operating within the EU 27, some focusing on research and development including biotechnology, some concentrating on generic medicines for both domestic and export markets.[3]

***Table 1**: Number of companies and employees, based on Member State replies to this date, and subject to amendments and clarifications from Member States*

Member State	No. Companies	Employment
BE	134	31,000+
BG	40	6,700
CY	5	1,300
CZ	122	9,291
DK	132	20,000
EE	6 SMEs	300
FI	3	5,300
HU	14 (4 large, 10 SME)	13,000+
DE	550	100,000+
IE	80	25,000
IT	334	66,700
LV	27 (2 large, 25 SMEs)	2,000
MT	16 (2 large, 14 SME	1,000
PL	105	22,948
PT	130	9,500
RO	51 (7 large)	N/A
SE	181	13,700
UK	365	77,795
ES	85 national, 101 international	46,500

[2] Commission Communication – Pharmaceuticals Sector Inquiry, July 2009

[3] European Generics Association listed 617 companies as reported by its member associations, EFPIA, EVM (European Vaccines Manufacturers) and EBE (European Biopharmaceutical Enterprises) memberships encompass over 2000 companies and 31 national associations

As Table 1 demonstrates, there is a wide diversity in this sector amongst EU Member States. From the responses received, 10 Member States have indicated that their production value from pharmaceuticals is worth over €1bn. Germany has the highest reported production figure (€26.9bn), closely followed by Italy (€25bn), France (€25bn), and the UK (€18.2bn). Member States including Portugal and Hungary have sectors worth producing more than €2bn. The Czech Republic has a sector producing approximately €1,14bn, while available figures indicate 7 Member States have pharmaceutical sectors are worth less than €500m (Bulgaria, Cyprus, Estonia, Latvia, Lithuania, Malta and Romania).

1.3 Characteristics of the industry

1.3.1 Public health and Regulation

Since pharmaceuticals are inextricably linked with issues of public health and the governments' overarching policies on health, the industry is, understandably, subject to heavy regulatory burdens both at national, regional and international level. In the EU, the European Medicines Agency (EMA), is tasked with co-ordinating and seeking to harmonise the regulatory regimes of Member States. The EMA does not replace the work of existing national medicine regulatory bodies, but does provide for a centralised marketing authorization procedure for some medicinal products that is valid in all EU and EEA-EFTA states (including Iceland, Liechtenstein and Norway). The EMA also offers advice on best practice on a number of areas, such as Good Manufacturing Practice (GMP), along with scientific advice. It does not seek to harmonize rules on the pricing and reimbursement of pharmaceutical products, which is controlled by individual Member States (see section 3.2.4 below).

Internationally, the World Health Organization has an oversight role within the UN to monitor health trends and to advise on the health policies and practices of individual nation states and more generally. Guidelines for regulatory procedures and practices are issued by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). This organisation is made-up of the regulatory authorities and industries of the EU, Japan and the US, and its aim is to, *"make recommendations towards achieving greater harmonisation in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration, thereby reducing or obviating duplication of testing carried out during the research and development of new human medicines."*[4] It should be noted that the ICH is an advisory body only, and that individual countries often implement regulatory practices that do not conform to these guidelines. For this reason, the EU and its industry have been supportive of the inclusion of emerging markets within the ICH work platforms (e.g., China, Brazil, Russia, South Korea, India, Taiwan and Singapore).

1.3.2 R&D Intensity

EU industry data indicates that the pharmaceutical industry is the sector with the highest ratio of R&D investment to net sales. It amounts to approximately 3.5% of total EU manufacturing value added and 18.9% of the total worldwide business R&D expenditure. This in part explains why the pharmaceutical industry places great emphasis on the importance of IPR

[4] ICH Website: http://www.ich.org/about/vision.html

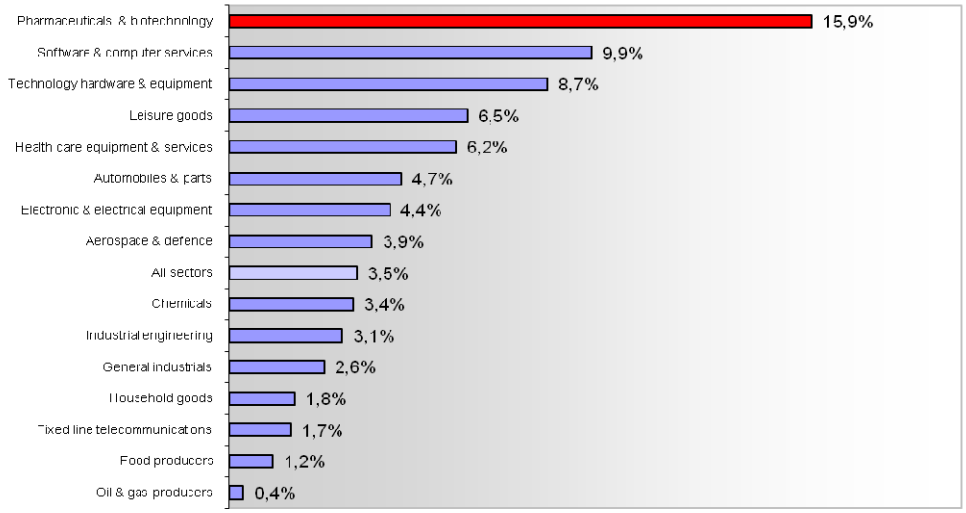
protection in order to ensure that the effort going into producing a new product is properly rewarded. In addition to patent protection (20 years starting from the date of the grant of the patent and, possibly, 5 more years of Supplementary Protection Certificate up to a maximum of 15-year protection period starting from the date of the first Marketing Authorisation, the EU has a data exclusivity regime of u 10 to 11 years.

New medicines introduced into the market are the result of lengthy, and potentially cost intensive R&D conducted by pharmaceutical companies:

- On average, 8-12 years will have elapsed between the first synthesis of the new active substance and a new product entering the market;
- Although there are various estimates, one study assessed the cost of researching and developing a new chemical or biological entity in 2005 to be €1,059 million ($1,318 million in year 2005 dollars)[5];
- On average, only one or two of every 10,000 substances synthesized in laboratories, will successfully pass all stages to become marketable medicines.

Pharmaceuticals is one of the most research intensive sector of EU industry when it comes to the innovative part of the sector. Figures for 2009 suggest R&D represented 16% (source EFPIA), of the total expenditure of innovative companies, with generics companies also spending a significant percentage of their revenue (7% in 2007[6]). This figure is backed by some Member State responses. For example: Italy responded that their pharmaceuticals industry ranks 2nd in terms of absolute value of R&D investment (after aeronautics and transport vehicles) in the country, but first for R&D /sales ratio. In Belgium the sector represents almost 30% of total private sector expenditure in R&D. In Denmark, it represents 23% of all private research.

Ranking of Industrial Sectors by Overall Sector R&D Intensity (R&D as Percentage of Net Sales – 2009 – source EFPIA):



[5] Di Masi J., Tufts University, Centre for the Study of Drug Development, 2007.
[6] IMS report :"Generic Medicines: Essential contributors to the long-term health of society – Sector Sustainability Challenges in Europe" 2010

2. Competitive position in the world

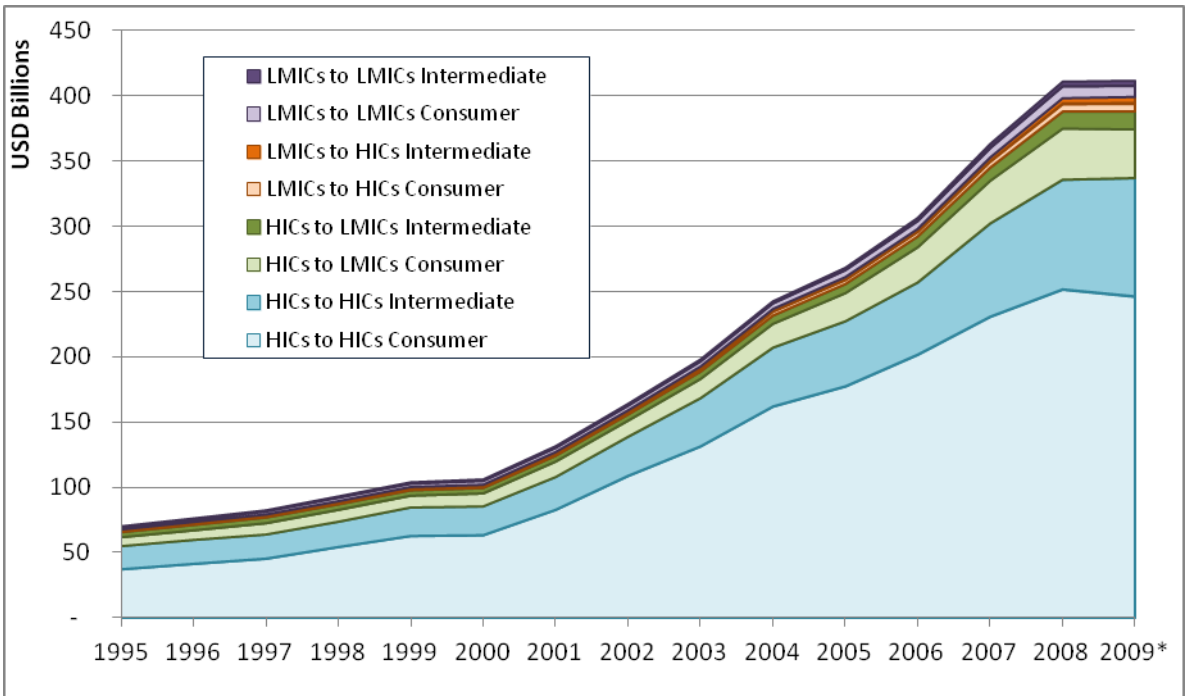
2.1 Trade statistics and trends for sector and subsectors

The exports statistics for both world trade and EU trade appear to indicate that the industry has performed well since the 2001 (The EU trade surplus in 2001 stood at €19.3bn, rising to €47.8bn in 2010), and weathered the 2008-2009 crisis period better than other large industrial sectors. Furthermore, the EU sector has largely mimicked the global trend (see figures below). This may be for a number of reasons: rapidly increasing exports to new, emerging markets such as the BRICS; governments with extensive public health systems being reluctant to cut expenditure on an essential service to the public. Concerning the latter, it should be noted that there is evidence that many countries are cutting health expenditure and reimbursement prices as a way to cut costs during the global downturn, and this may alter export value in pharmaceutical exports in future years, but which may not be immediately evident in the statistics.

World Trade 1995-2009 (source OECD):

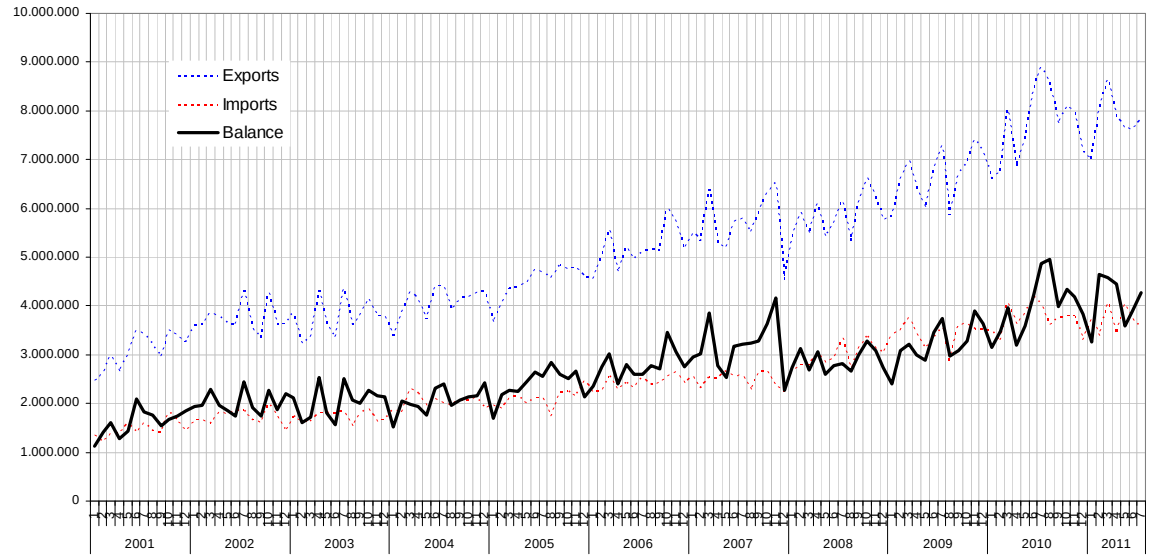
Global Exports in pharmaceuticals^

(a) export value



*** HICs: High Income Countries. LMICs: Low to Medium Income Countries**

EU27 Monthly Balance - January 2001- July 2011, 1000 euros (source Eurostat):



2.2 Main competitors

Traditionally, companies in the US, Switzerland and Japan have been the EU's main competitors in the global export market for pharmaceuticals, as well as the largest trading partners for the EU in this sector. Of these major partners, only Switzerland has a trade surplus with the EU, standing at approximately €6.1bn for the period January to December 2010. The EU is the second global manufacturing location for pharmaceuticals behind the US and ahead of Japan, and holds a dominant position in a number of areas, including the production of vaccines where 90% of major manufacturer's global output is produced in Europe. The EU's exports accounted for an estimated 15.5% of the global pharmaceuticals market in 2010. Europe is now facing increasing competition from emerging economies, which are fast-growing but also fast-changing markets. In the generics sub-sector China, and notably India have made rapid progress due to low cost and less regulated production conditions compared to the EU. For example, until 2005 there existed process patents in India, but not products patents, and the medicines themselves were not protected making foreign medicines were easier to copy.

In addition, there is rapid growth in the research environment in emerging countries such as Brazil, China and India, resulting in further migration of economic and research activities outside of Europe to these fast-growing markets. China increased the yearly value of its exports to the EU by 720% between 2001 and 2010, and India's development has seen it create a trade surplus with the EU in this sector (€-428m January-December 2010), which has increased significantly over the last decade, and particularly from 2005 onwards, as India has steadily grown into one of the world's leading producers and exporters of generic medicines.

2.3 Key markets

The main export destinations for the EU in 2010 were the US (32.3%), Switzerland (10.2%) Russia (7.1%) Japan (5.8%), and Canada (4%). Detailed monthly balance charts with these countries can be found at Annex I.

Along with the above, traditional markets, industry points to an increasing focus on emerging economies (China, Brazil, Russia, India, Turkey, Mexico, ASEAN), with markets in Asia and Latin America recording double digit growth rates (source: OECD Pharmaceuticals Trade and Innovation paper 2010). It should be noted that the EU is currently negotiating trade agreements with some of these countries, including Canada, India, MERCOSUR and the ASEAN countries. The Chinese market, in particular, has rapidly increased in importance over the last decade. From a relatively small export market destination, it is now the 7th largest destination for EU pharmaceutical exports according to Eurostat data (€2.8bn with a trade surplus of €1.3bn in 2010, compared to just €400 - €238.6m surplus - worth of exports in 2001). This trend is likely to continue. China is keen to rapidly develop its public health system, and in 2010 committed $123bn over the 3 years, much of which will be focused on drug provision and treatment.

Growing populations with increasing purchasing power in the CIS, Middle East and Africa also represent a key export opportunity for the European industry. There is strong sectoral interest in other regions, particularly by the generics sector. In North Africa, countries such as Morocco and Egypt have seen large spending increases in pharmaceuticals over the past decade, with EU exports to the latter increasing by over 90% between the years 2001-2010 (€287m to €550m). Similarly, in the Middle East EU exports to economies including Saudi Arabia have risen sharply in value over the same period (€657m to €1.56bn). However, unlike the BRIC economies, these regions do not appear to be increasing their exports to the EU.

3. Key Trade Issues

The Pharmaceutical industry has traditionally faced a wide range of barriers to trade, including a range of TBT/NTB barriers, intellectual property rights and issues on the specific pricing and reimbursement of drugs in particular countries. On top of this, the sector can also be faced with cultural barriers to trade. For example, in 2010 Indonesia published a decree that announced its intention to ban certain products, including medical products, containing porcine material. This would have affected a large percentage of vaccines produced by the pharmaceutical industry.

3.1 Tariffs

The big, traditional pharmaceutical exporting economies (EU, US, Switzerland, Japan), have implemented the WTO Pharmaceutical agreement from 1993, eliminating duty rates for finished products[7], along with active ingredients and some chemical intermediates, and in many countries tariffs are zero or close to zero. However, the pharmaceutical industry faces duty rates for active ingredients and finished products in some third markets gaining in importance, such as China, India, Russia, Mercosur, and ASEAN countries. The EU generics industry has cited high duty rates in India, and a typical example is a 10% duty on products containing penicillin and their derivatives[8]. The industry argues that as a consequence of

[7] Signatories of the agreement are the European Union, US, Switzerland, Japan, Canada, Norway, Czech Republic, Slovak Republic and Macau.
[8] Source: EU Market Access Database

these high tariffs that are enforced by some third countries, and particularly the strong, emerging industrial economies, the EU is deprived of its competitive edge, while competitors benefit from market access opportunities in the EU. There is, therefore, continued scope for further tariff dismantling and elimination

The OECD has calculated that the major non-OECD member economies collect over 60% of tariff revenues related to pharmaceutical products and imposed an average weighted tariff weight of 7.58% in 2008.[9] However, it should be noted that this average has decreased by 2% since 2001, and during the same period new members to the WTO have decreased their average tariffs from 7.32% to 2.04%.

Table 2: *Average applied MFN tariffs and estimate of tariff revenue share by OECD and WTO Member and Non-Members*

	Simple average		Weighted average		Tariff revenue (% share)	
	2001	2008	2001	2008	2001	2008
UR Pharma participants	0.93%	0.15%	0.07%	0.01%	2.4%	0.4%
Other OECD members	4.62%	3.80%	5.38%	4.75%	16.7%	8.7%
New WTO members	4.00%	1.03%	7.32%	2.04%	15.0%	12.2%
Other non-participants	9.14%	5.81%	9.53%	7.58%	50.1%	66.8%

3.2 Non-Tariff Barriers

3.2.1 Registration and certification

Registration barriers are possibly the most common barrier to affect the sector. Despite the existence of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and efforts to harmonise regulatory requirements consistent with ICH guidelines, registration requirements vary significantly from country to country. These can be for historical and/or cultural reasons, including some countries' traditional approach to ensuring their public health standards. Several key markets of significant importance to the pharmaceutical industry have regulatory submission requirements that diverge from ICH guidelines.

In addition, some third countries have introduced potentially excessive requirements to obtain certificates or other documentation to allow importation. Such requirements may include additional and unnecessary steps in order to submit a Certificate of Pharmaceutical Product, which is a WHO recommended process to help countries assess the quality and authenticity of an imported product, prior to any domestic registration and authorisation process. The CPP is particularly important for EU companies seeking Marketing Authorisation (MA) in certain countries in the Middle East, Asia, South America and Africa. Other barriers may involve customs control measures such as examination, testing of individual products batches, and temporary storage (sometimes inconsistent with appropriate supply-chain security, which may effect the stability of products). EU industry asserts that any of these measures may result in delays and unpredictability of distribution of medicines.

Example: Japan

[9] OECD: Trade and Innovation: Pharmaceuticals – working paper No. 113 March 2011

Despite progress in recent years in the specific fields of vaccines and biologicals, there is still a 'vaccine gap' between Japan and other industrialized countries. Specifications and minimum requirements of biological products (MRBP) are different from global ones. There are differences in standards and testing methods in Japan as compared to the rest of the world, meaning that overseas vaccines for routine immunization cannot be registered in Japan without adjustments to conform to MRBP and JPh.

Japan's drug penetration restrictions rule requires that for the first year that a new product is marketed, patients can only receive a 14-day prescription, resulting in an unnecessary expense to the patient and to the manufacturer as packaging of some products will need to be completely changed for Japan. This rule also does not take into account medicines that have no obvious effect for the first 14 days of consumption

Example: USA
Industry indicates the incompatibility between the USA and EU standards of APIs registration. Once EU companies have registered APIs according to EMEA standards, there is still an additional, potentially unnecessary process to register APIs in the USA, according to the USA Food and Drug Administration (FDA) standards.

Example: China
Registration of pharmaceuticals in China is hampered by requirements that are unique to the country's regulatory framework. The EU and industry are pursuing greater harmonisation by introducing a marketing authorisation system for all types of products including chemicals, biologicals and vaccines.

Example: Brazil
Industry indicates that there are significant market authorization delays in Brazil, which are now significantly higher than the standard average length of 12 months for such approvals. Conversely, there is a specific issue with regards to bio-similar molecules, with suggestions that Brazil does not always reinforce its authorization practices, leading to inadequate testing of complex substances and introduction on the market of less safe products, originating in third countries. This could result in a competitive disadvantage to EU pharmaceuticals, which undergo thorough testing procedures.

Example: India
India requires a Certificate of Pharmaceutical Product of the WHO certification scheme as a condition to start registration process in India. This means that the registration process cannot be launched in India unless the product is already registered in the reference country and a CPP is obtained, thus significantly delaying entry of the product in India compared to other countries

3.2.2 Clinical Trials

Both industry and Member States responses have highlighted that clinical trials are one of the most cost intensive factors in developing a new medicinal product. Therefore, the protection of clinical trial data is an important element in the pharmaceutical sector. Art. 39.3 of the TRIPS agreement obliges WTO Members to protect such data against unfair commercial use and disclosure.

In addition to inconsistent regulatory approval requirements, the industry also faces varying requirements for clinical trials approval in key markets around the world which are

inconsistent with ICH standards. These requirements are often out of step with scientifically proven standards. In many countries, the industry face requirements for local patients in global trials (even if not scientifically required), and in some countries, an applicant must conduct a local clinical trial prior to submission of a new drug application. There is no perceived benefit to conduct local trials in addition to global trials and this requirement delays significantly the introduction of new medicines in a market. Furthermore, most countries (notably EU, US, Japan) accept global clinical trial data in line with ICH Guidelines.

Example: Japan
The Japanese Good Clinical Practices rules are not fully in line with ICH guidelines. Foreign clinical studies, even when accompanied by adequate bridging data are not accepted.

Example: China
Local clinical trials are required prior to initiating registration of products in China, resulting in the repetition of some clinical stages for pharmaceuticals and even the full development programme for vaccines. This is not in line with international standards and can involve one to five years delay in approval and marketing of products.

Example: Russia
The new federal law on medicines circulation introduced a requirement to conduct clinical studies in Russia as a prerequisite for registration and access to the domestic market. This is contrary to the global research and development practices and to international scientific standards (e.g., ICH), impeding market access.

The registration of any generic medicine in Russia can only be done if the bioequivalence study has been performed in Russia. This leads to repetition of bioequivalence studies. In the EU there is no obligation to perform clinical studies, including bioequivalence studies, only on EU territory. Issues related to ethnicity are accepted, if performed in accordance with the International Conference on Harmonisation (ICH) standard of Good Clinical Practice (GCP).

Example: India
For the authorisation of new medicines in the Indian market i.e. for a New Chemical Entity (NCE) application, India requires clinical trial data to be conducted locally in Indian patients. Furthermore, India requires a specific Clinical Trial Report for Indian patients. The adoption by India of the ICH E5 guidelines on ethnic sensitivity would remove the need for local ‘stand-alone’ clinical data to be generated in Indian patients, thus allowing access to innovative medicines sooner (up to 1.5 years).

3.2.3 Good Manufacturing Practice

Good Manufacturing Practice (GMP) is critical to ensuring the quality of the product is suited for purpose. EU companies manufacture products all over the world and adhere to the stringent GMP requirements of international regulatory agencies, including the EU's own European Medicines Agency (EMA) when producing medicines. The EU is also a key member of the Pharmaceutical Inspection Co-operation Scheme (PIC/S), which is an informal collaboration between members economies seeking to improve the standard of manufacturing requirements amongst its members Going further, the EU has agreed Mutual Recognition Agreements on GMP with several third countries (Australia, Canada, Japan, New Zealand and Switzerland).

Despite being a world leader in this area, EU companies have faced additional GMP site inspection and validation data requirements from various trading partners, which may constitute a *de facto* trade barrier. In some instances these requirements block access of imported products to third markets for extended periods either as a result of a third country administrations simply being unprepared for the additional burdens of inspection and approval, or as a more direct policy tool to help promote local substitution.

Example: Turkey
The Turkish Ministry of Health issued on 31 December 2009, issued a decree setting new requirements for GMP. It set out that, in order for a pharmaceutical product to be imported to Turkey the manufacturer must submit a certificate of GMP issued by the Turkish Ministry of Health or an authority of another country with which Turkey has reciprocal certification agreement. Consequently, since 1 March 2010, Turkey has not accepted the EU GMP certificates, or those of other major importers, such as the US. Instead, the manufacturers need to apply and wait to be inspected by the Turkish official inspectors for receiving this certificate for the registration of new medicines or variations of existing products. The introduction of this measure has led to significant delays and an increasing backlog in the registration of new pharmaceutical products in Turkey, stemming largely from Turkey's limited capacity to implement these requirements and deliver the GMP certificate within a reasonable period of time.

These measures are likely to be in breach of Turkey's international commitments (WTO) as well as a breach of the principle of free circulation of products between the EU and Turkey, in particular, of Articles 5 and 10.1 of the Customs Union Decision 1/95 and of Decision 2/97 since Turkey has the obligation to align its legislation on pharmaceuticals with the EU *acquis*. Furthermore, Turkey did not notify these new requirements to the European Commission prior to their entry into force, or consult the Customs Union Joint Committee. While the EU cannot force a county to accept its industry's data, it's position as a leader in the field, and the added position of Turkey as a candidate country make this particularly relevant.

Example: Japan
With regard to plasma-derived products and vaccines, national tests in Japan are still required, despite the fact that production is done according to GMP rules and PMDA periodically audits the production sites, and test results issued by countries parties to the MoU are not accepted.

3.2.4 Transparency of Government Policy on public health, including Pricing and Reimbursement Policies

Most countries around the world have implemented healthcare systems that provide some level of public duty of care, and also function as single-payer systems, meaning that importing companies must go through pricing and reimbursement processes in order to gain access to the market. The EU has to this point promoted transparency and non-discrimination for such policies and requirements, including the creation of a dedicated pharmaceutical annex to this effect in the recent Free Trade Agreement with South Korea.

However, there have been recent examples of governments putting in place policies and procedures with minimal notice to stakeholders. This has been particularly noticeable in the post-crisis period, as countries look to cut costs from their national budgets, including healthcare. It should be noted that EU Member States have also looked at taking up similar policies. EU legislation has been in place for more than twenty years to ensure the

transparency and objectivity of pricing and reimbursement decisions in the Member States (Directive 89/105/EEC). The Commission is currently assessing the opportunity to review this framework to bring it into line with the increasing complexity of national pricing and reimbursement measures.[10]

In its negotiations and dialogue with third countries, the Commission considers that there should be a defined period of time for the opportunity for stakeholders to review and comment on new government policies. This should also apply within the EU. In addition, for markets with pricing and reimbursement processes, criteria for decision making should be objective and non-discriminatory, and decisions should be communicated to stakeholders allowing an opportunity for exchange and appeal, thereby increasing predictability in the markets. Pricing and reimbursement policies should not distinguish between locally produced products and imported products, which would contravene Article III of the WTO General Agreement on Tariffs and Trade (local preference),

Recent examples include South Korea, China, Turkey, Morocco.

3.3 IPR and counterfeiting

A strong and effective protection and enforcement of intellectual property rights are key for Europe's innovation and international competitiveness. The protection of intellectual property rights by trading partners promotes equality of trading conditions and thus access to the markets of trading partners by innovative EU industry. Without such protection, it can be argued that those who do not contribute to innovation are able to free ride on the efforts of those who incur the cost and risk of innovation, depriving innovators (both European and local producers in third countries), of fair market conditions in which to compete.

An effective system for IPR protection provides an incentive and reward for successful innovation. To this end, effective patent protection (and, where appropriate, the availability of patent term restoration) is essential to promote and sustain investment in pharmaceutical R&D that may lead to the development of new and improved therapeutic alternatives and treatments.

In addition, the protection of test data submitted by innovative companies in the marketing authorisation process is gaining increasing importance in the global market as new economies emerge which are keen to develop a strong generics production base, along with a strong R&D base. Intrinsically, effective data protection is important to protect the extensive regulatory/registration data generated by innovative companies in the course of lengthy, and expensive tests and trials from disclosure to and referral by competitors.

In addition, the effective protection of trademarks is also a major concern for the pharmaceutical sector.

Increasing counterfeiting and piracy of medicines also raise serious concerns. According to the OECD[11], global trade in counterfeited and pirated tangible goods reached over €180 billion in 2007 and the pharmaceuticals industry is not immune from this problem. China

[10] See http://ec.europa.eu/enterprise/sectors/healthcare/public-consultation/index_en.htm
[11] Source OECD: The Economic Impact of Counterfeiting and Piracy 2007 - http://www.oecd.org/dataoecd/13/12/38707619.pdf

announced as recently as November 2011 that it had seized $315m of counterfeited pharmaceutical products. The EU is committed to fighting against counterfeited medicines, which represent a serious public health threat to patients, whilst not hampering the legitimate trade of medicines transiting via the EU.

An area of particular concern for the generic industry relates to the issue of patent linkage, a process which concerns the possibility for a patent-holder to invoke their patent rights before national marketing authorisation and pricing authorities in order to block approval for an allegedly infringing generic medicine. Under EU rules, in the EU currently patent linkage before marketing authorisation bodies is not foreseen. There is grey area concerning patent linkage before national pricing authorities.

As noted above, the EU's innovative pharmaceutical industries have indicated that ensuring enforceable patent rights, regulatory data protection in trade partners' markets including the BRICS countries and others is a key priority. In this respect, there are general concerns that WTO Member countries like India, Brazil and the Peoples Republic of China have not fully implemented the minimum TRIPS standards or are not effectively enforcing them, leading to an imbalance in trade to the disadvantage of imported products vs. locally produced products.

Example: India
India is a major producer and exporter of generic medicines, and it can be argued that a weak domestic intellectual property regime has helped the country achieve this position and increase competition to the EU generics sector while also making it more difficult for the innovative EU pharmaceutical companies to enter and invest in India.

Example: Canada
Despite its economic development level and significant local pharmaceutical production, Canada has yet to introduce essential pharmaceutical IPR provisions that are available in the EU and other similar markets (e.g. patent term restoration, significant regulatory data protection and equitable right of appeal in the context of patent infringements).

Example: China
Enforcement remains a critical concern in China, especially with regard to patent rights. The regulatory data protection regime needs to be strengthened as well.

3.4 Subsidies and local preference policies

Rules on procurement and subsidies from governments may diverge from internationally recognised standards (e.g. WTO public procurement agreements) resulting in discriminatory practices in allocation criteria and requirements. There are recent examples of countries that have put in place policies that favour local substitution and production over imported products. The industry has also commented that it is increasingly seeing a priority given to local companies on both private and public tenders, either directly limiting access for foreign products or allowing local companies to submit at different/more advantageous conditions

Example: Russia
The Commission Trade and Investment Barriers Report 2011 (p. 9), highlighted Russia's investment policy, "*which aims at protecting and fostering domestic industries, remains another source of significant concern. Trade related investment measures include requirements of local content, domestic sales, export performance and technology transfer. The recent "localisation initiative", which is intended to provide incentives for foreign*

companies to set up production in Russia in a number of sectors, including automobiles, electronics and pharmaceuticals, is the latest illustration of this policy".

As part of this overall policy, Russia adopted the Pharma 2020 Plan in 2009. The plan aims to increase Russia's World share of the pharmaceutical market to 3-5% within 10 years, with 90% of medicines classified as 'vital' being produced domestically. A Reported €2.8bn of targeted investment has been committed by the Russian Government for this purpose.

Example: Saudi Arabia
The current investment law in Saudi Arabia allows 100 percent ownership of pharmaceutical companies by foreign investors, provided that they establish a manufacturing site in Saudi Arabia. Otherwise, companies can only be represented by a Saudi agent and their ownership share may only be 51% during the first year, reaching a maximum of 70% ownership in the third year.

3.5 Parallel imports

Some responses to the questionnaire also raised the issue of parallel imports, or grey-market imports, which are imports of a patented or trademarked product from a country where it is already marketed. For example, a high income country might decide to import a certain drug indirectly from a low income, developing country instead of directly from the manufacturer (or its distributor), where that drug is sold at a far cheaper price in the developing country. Article 6 of the TRIPS agreement (exhaustion of intellectual property rights), explicitly states that this practice cannot be challenged under the World Trade Organization (WTO) dispute settlement system and so is effectively a matter of national discretion, and each Member can decide itself on the system of exhaustion of IP rights of its choice. The EU has implemented a system of regional exhaustion, meaning that once legally marketed in one EU Member State, the right-holder cannot, in principle, prevent the good to be resold in another Member State (subject to some exceptions and EU case law). However, a WTO member country can decide to apply international exhaustion in his territory and hence a right holder could not rely on his Intellectual Property Rights to block parallel trade of goods legally sold in other countries from this member country.

Evidence of this practice has been seen within the EU as well as the global market, and the industry has estimated that in 2009 this might have cost up to €5.2bn in lost revenue in the EU alone (Source EFPIA: The pharmaceutical industry in figures 2011). Since it is not a recognised trade barrier under the WTO rules, there appears to be limited scope to restrict this practice. However, industry argues that there are no long term benefits from such parallel importing, which deter further investment into R&D, and may lead economic operators to impose higher prices on lower income countries in order to make this practice less attractive, and consequently restricting access to vital medicines to those most in need.

4. Trade policy response

4.1 Summary of respondent recommendations

In general, many respondents to the sector fiche questionnaire, including industry, have asked for the EU to help its companies and promote the interests of EU producers. This

type of recommendation is clearly not limited to this industry. However, it could be argued that the pharmaceutical industry is almost unique in amongst industrial sectors in two key ways: Firstly, the industry is often selling its products directly to governments and their delegated public authorities. Secondly, due to the intrinsic link to public health, and the different ways governments can approach this issue (for both economic and cultural reasons), the sector often faces diverse and complicated regulatory regimes in different countries, which may differ from accepted international standards and add additional burdens on top of those standards (see under section 3 above). Specific suggestions from respondents include the establishment of local EU trade representatives in key trade partners in order to help EU pharmaceutical companies, both generic and originator, with gathering important information on regulatory requirements and overcoming trade barriers. Such a system could be complemented by setting up an information website portal with comparative information on requirements for pharmaceutical companies with regard to trade. Another suggested option would be to require a legal representative of all players to be present in the EU to even out the balance.

Seek sustainable business development and proper balance of IPR in trade agreements. Where possible, the EU can look to enforce relevant TRIPS articles regarding patents and regulatory data protection, including the protection of clinical trial data. Also, where appropriate, the EU can encourage key emerging markets to adopt international standards and avoid individual extra requirements. However, the EU should also seek to find the correct balance in bilateral and multilateral trade agreements, in order that it does not impose TRIPS+ requirements on countries where this may have an adverse affect on either public health or the ability of the EU to import its own generic medicines.

Where appropriate, trade negotiations, including FTAs could look to harmonize and reciprocate trade access, barriers, transparency (including regulations on pricing and reimbursement policies), foreign direct investment, and other areas of mutual long-term benefit to the EU and its trading partners. The majority of respondents state that fair prices and a level playing field with countries from outside the EU is key for the long term sustainability of the sector. Some of the EU's third country partners have a competitive advantage in fields such as generics and biosimilars, and can sell their products at very low prices due to environmental, economic, and taxation factors etc. Where such an advantage is has been brought about by unjustified trade barriers, the EU could seek opportunities to encourage their removal.

4.2 Policy responses

The EU trade policy agenda for the sector needs to focus on offensive demands and increasing market access to both developed and emerging country markets. As briefly summarised in Section 4.1 above, the industry is subject to diverse regulatory regimes with often direct link to government economic and public health policies. This has an effect on their ability to export.

Beyond discussing policy and regulatory issues in dialogues with third countries the EU has offered, for example, observations and training to third countries in various, related fields, from GMP inspection to the training of judges in China in recognising cases of patent infringement.

The WTO and multilateral fora

The WTO Technical Barriers to Trade Committee can highlight and attempt to tackle infringements that appear to contravene or violate international trade law. It also provides a useful forum in which to discuss such infringements. In addition, serious breaches of WTO rules can be addressed through the dispute settlement mechanism. There have been 2 previous dispute settlement cases involving pharmaceuticals and specifically the patent protection of pharmaceutical products (India and Canada which concluded in 1998 and 2000 respectively).

The WTO accession negotiations with Russia have now been completed and the upcoming WTO Ministerial Conference in December 2011 is expected to adopt a decision on the WTO accession of the country. As noted above, Russia is not only an important export market for the sector, but a country that continues to impose relatively high tariffs on pharmaceutical products and looks to increase its own market presence through domestic preference policies. Bringing Russia within the WTO framework will be a first step towards addressing these problems**,** as well as regulatory reforms such as streamlined registration and licensing requirements and stronger enforcement possibilities for IPRs. The Commission has estimated the sector in the EU will benefit from additional annual exports worth €49m and import duties foregone equal to €37m.

Finally, specific to counterfeiting and the falsification of medicines, the EU is seeking to address some of these issue within the framework of the Anti-Counterfeiting Trade Agreement (ACTA). The ACTA negotiations were finalised in November 2010, and the negotiating parties are now fulfilling their internal ratification procedures. In the case of the European Union, this means that the Agreement must be approved by the Council of Ministers and the European Parliament.

Bilateral negotiations

Bilateral trade negotiations remain one of the key fora for trade policy. Issues where this sector can benefit concern tariffs as well as non-tariff regulatory barriers, intellectual property rights and state aid policies.

Where tariffs are in place these can be addressed through current and future FTA negotiations, along with NTBs and IPR issues. FTAs currently being negotiated by the EU constitute important markets for the sector, including India, MERCOSUR, Ukraine, certain ASEAN countries (including Malaysia and Singapore), and Canada. The EU-South Korea FTA was approved by both parties in July 2011, and is now being implemented. This FTA includes a horizontal chapter on state aid and subsidies, and will eliminate Korea's import tariffs on pharmaceutical products in 3 years (average duty currently stands at 6.2%). In addition, the FTA contains a dedicated pharmaceuticals annex covering regulatory co-operation and transparency in rule making (including pricing and reimbursement proposals). A Working Group will be created to promote further co-operation and address any implementation issues. This is the first FTA to include such a comprehensive annex, and provides a template for current and future FTA negotiations.

High-level and regulatory dialogues

While High-level Regulatory Dialogues between EU and key trade partners are not often trade driven, they can be complementary instruments to open up market access by removing regulatory barriers and promoting harmonisation with EU and international standards. The EU conducts a number of dialogues with important economies such as China.

Market Access strategy

The Market Access Strategy allows to regularly address problems in the framework of the Market Access Partnership. The strategy offers a tool to ensure regular monitoring of outstanding issues and exchange of information between the Commission, Member States and business. It provides an efficient monitoring tool for assessment of progress on resolution of market access barriers. For instance, this was done in the case of the Working group on vaccines for Japan where significant progress was achieved in the field of vaccines recognition and approval in Japan. The pharmaceuticals sector priorities were thus widely reflected in the key barrier lists exercise.

4.3 Conclusions

The EU industry, while facing strong competition from traditional economies such as the US and Japan, and also from emerging economies such as China, India and Brazil, remains strong in the international marketplace. As the export statistics above (and below in Annex I), demonstrate, all subsectors of the EU industry appear to be able to adapt well to a changing global market place, and are able to exploit new and emerging markets throughout the World economy.

There are, however, clearly present and future challenges to the industry, both in maintaining it's strong position as a market leader, and particularly in overcoming non-tariff barriers to entry which are both numerous and diverse in nature. Indeed, the EU sector's strong presence throughout the World marketplace can be a weakness as well as a strength when attempting to tackle these trade barriers.

As a world leader in the sector, the EU industry takes a global approach to trade issues and barriers listed above There is a risk that industry is potentially focusing its efforts too widely, and this is true for both originator and generic subsectors. The sector may, therefore, face a future challenge in how it prioritises the type of barriers it wants to address and in which markets. As part of their submission, the industry has provided an extensive trade barrier list, and as a follow-up exercise the Commission will work with the industry to analyse and prioritise this list.

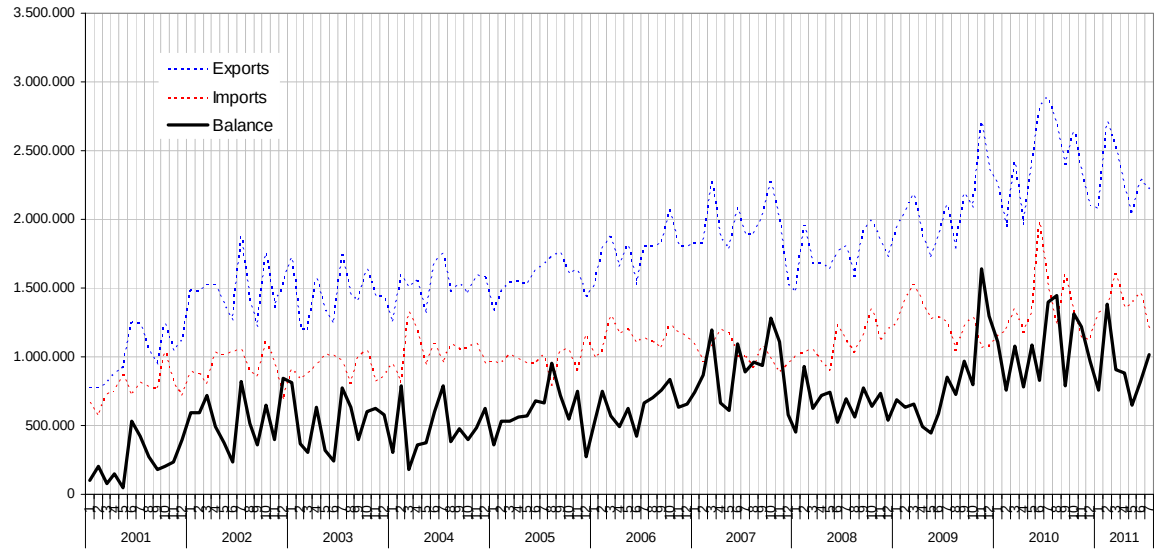
Annex I

Key Market Import-Export Trends – January 2001-July 2011

The graphics below consist of statistics from the Eurostat system (Comext, Statistical regime 4), based on Chapter 30 (pharmaceuticals), of the European Union's legislation setting out the tariff and statistical nomenclature and the common customs tariff. The statistics start from January 2001 and cover the period up until July 2011, which represents the latest information available at the time of this document's publication. The first five graphics represent the EU's five largest export destinations.

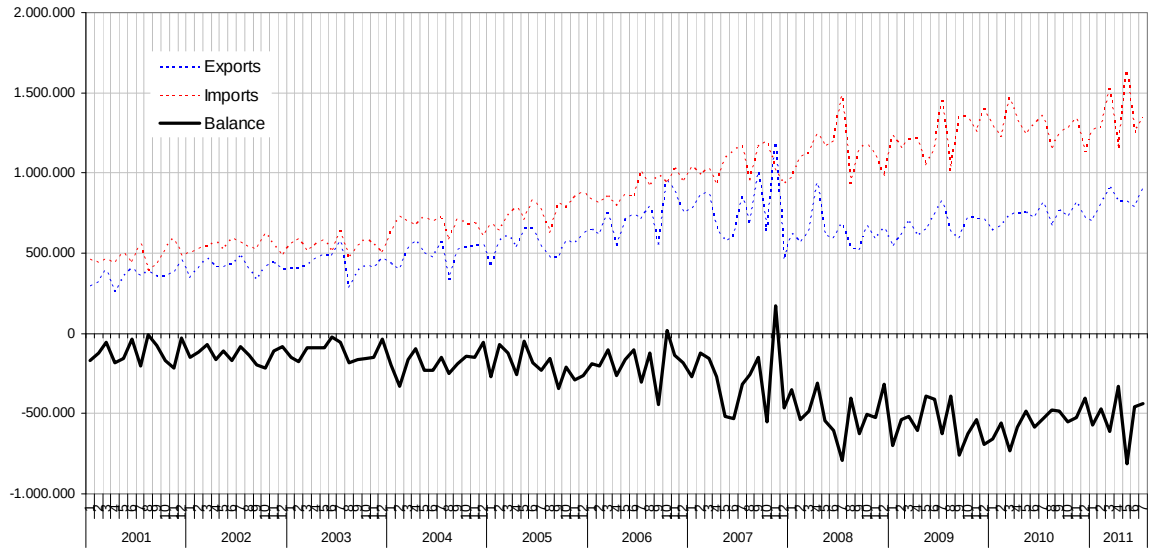
United States of America

EU27 Monthly Balance (January 2001- July 2011, 1000 euros)



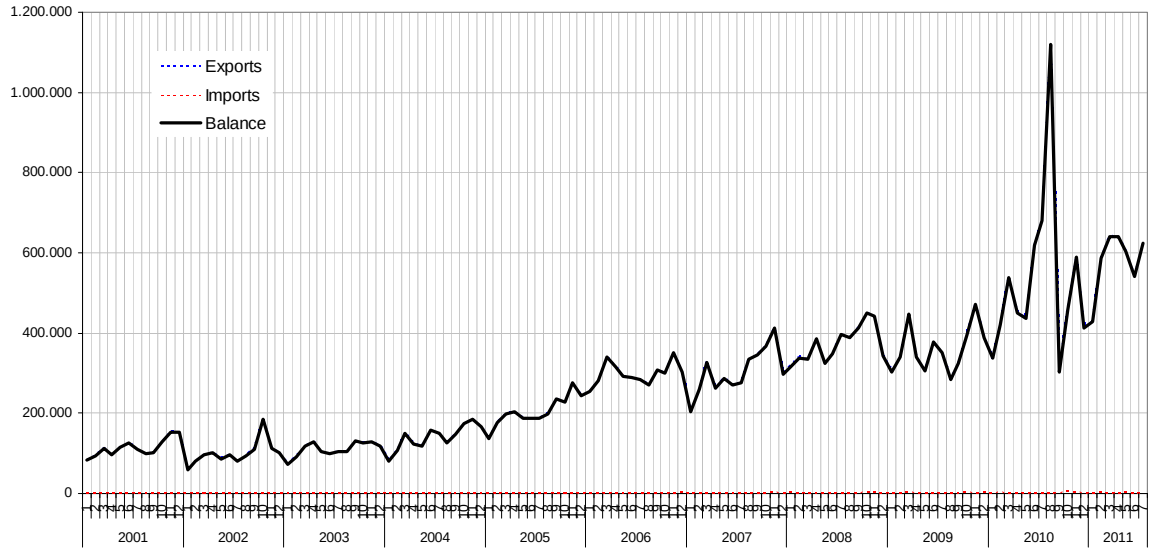
Switzerland

EU27 Monthly Balance (January 2001- July 2011, 1000 euros)



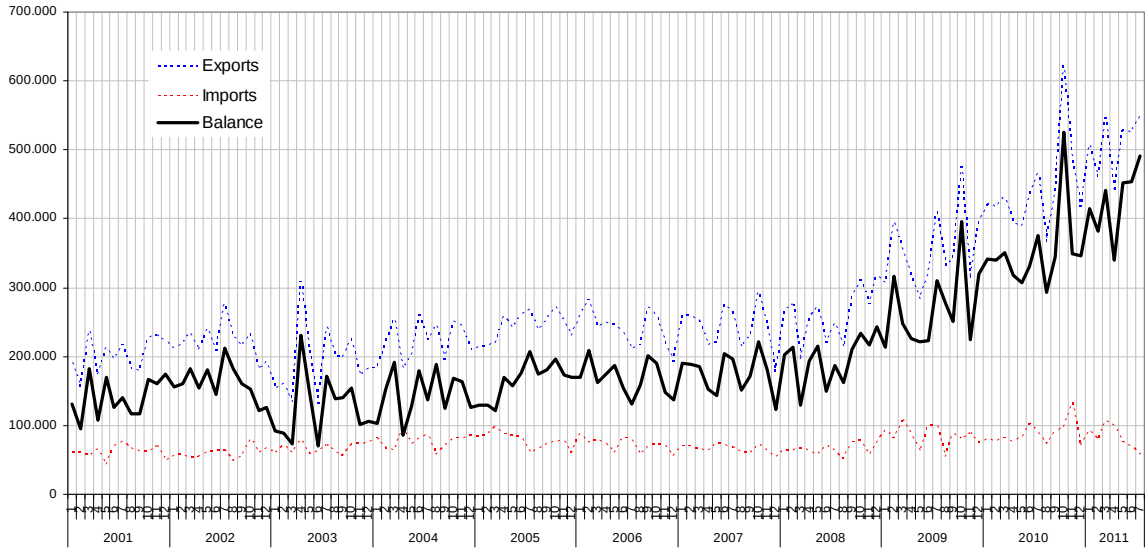
Russia

EU27 Monthly Balance (January 2001- July 2011, 1000 euros)



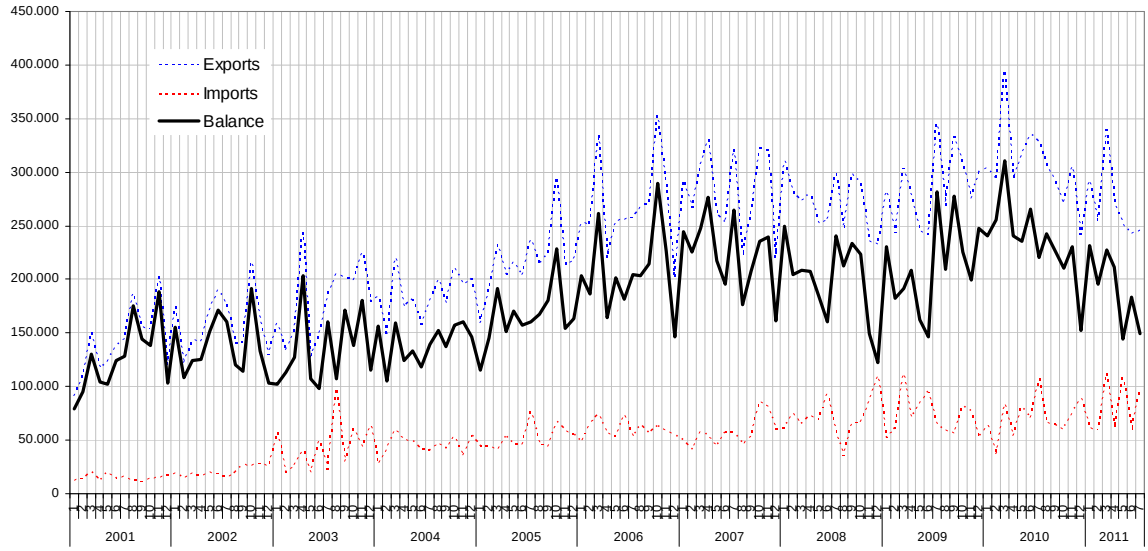
Japan

EU27 Monthly Balance (January 2001- July 2011, 1000 euros)



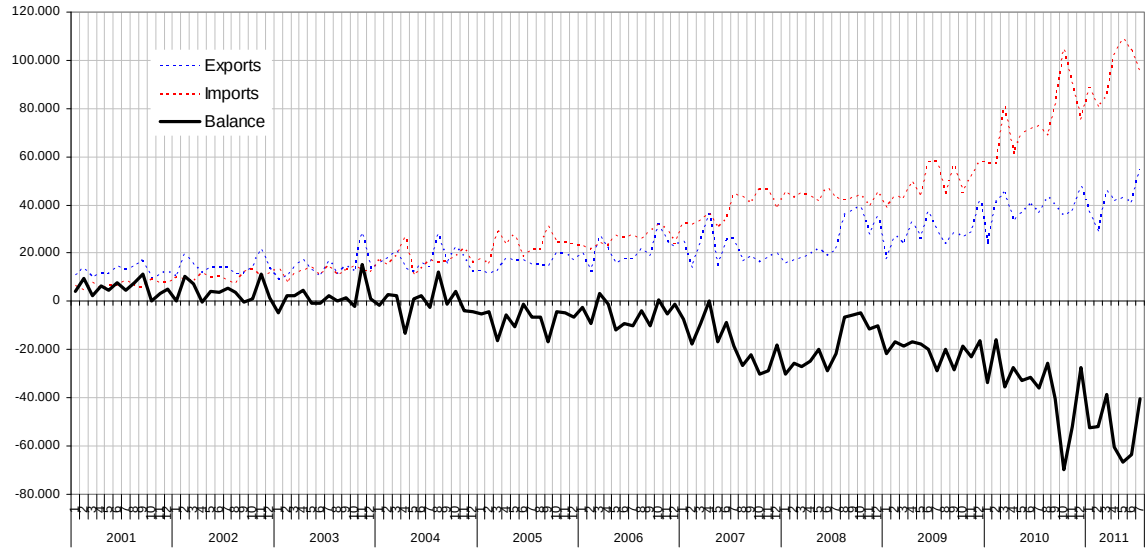
Canada

EU27 Monthly Balance (January 2001- July 2011, 1000 euros)



India

EU27 Monthly Balance (January 2001- July 2011, 1000 euros)



China

EU27 Monthly Balance (January 2001- July 2011, 1000 euros)