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PART 2

COMMISSION STAFF WORKING DOCUMENT

IMPACT ASSESSMENT

Accompanying the document

Proposal for a
DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

relating to the transparency of measures regulating the prices of medicinal products for human use and their inclusion in the scope of the national health insurance systems

{COM(2012) 84 final}
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ANNEX 1

SUMMARY OF RESPONSES TO THE PUBLIC CONSULTATION

The European Commission (DG Enterprise and Industry) conducted a public consultation on the possible revision of Directive 89/105/EEC. An electronic questionnaire was published on the Europa website and interested parties were invited to submit their contributions from 28 March 2011 to 30 May 2011. The consultation was open to all interested parties, with distinctive modules for competent authorities, originator companies, generic companies, medical devices companies and other stakeholders.

The consultation received 102 contributions. Respondents included:

- Competent national authorities
- Public health insurers, including sickness funds and payers
- Pharmaceutical companies and representative organisations (originator and generic sectors)
- Medical devices/in-vitro diagnostics companies and representative organisations
- Consultancies and law firms
- Professional organisations representing healthcare professionals, in particular pharmacists
- Supply chain companies, including full-line wholesalers and importers
- Patient groups
- Individual respondents

Contributions to the public consultation by type of respondent

Main categories of respondents		**Number of contributions**
National, regional or local administration		**19**
Public health insurer (e.g. sickness fund, third party payer)		**6**
Pharmaceutical company/industry association – originator products:		**30**
Including	*- individual companies* *- representative organisations (EU and national)*	*15* *15*
Pharmaceutical company/industry association – generic products		**17**
Including	*- individual companies* *- representative organisations (EU and national)*	*13* *4*
Medical devices/in-vitro diagnostics company/industry association		**10**
Pharmaceutical company/industry association – generic products		
Including	*- individual companies* *- representative organisations (EU and national)*	*5* *5*
Others		20
Total		**102**

The public consultation questionnaire addressed five main issue areas. The comments received on these issues are summarised below.

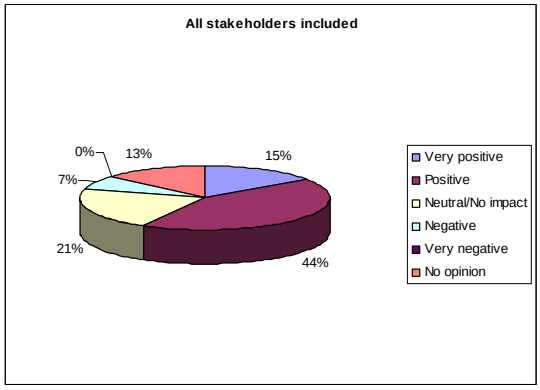
1. IMPACT OF THE EXISTING DIRECTIVE

The public consultation clearly shows that Directive 89/105/EEC is perceived by all stakeholders as a useful instrument to ensure the respect of the principles of the common

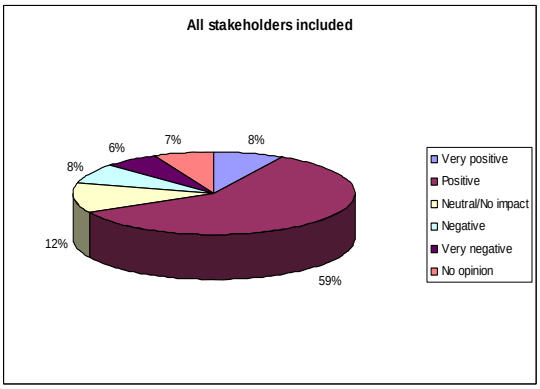
market in the field of pharmaceuticals. The impact of the directive is largely considered positive, even if not all of its aims are fully achieved and there is still room for improvement in several respects.

With regard to the most important goals of the directive as a common market instrument, namely the transparency of procedures and equal treatment between domestic and imported products, the picture to be drawn from the public consultation is unanimously positive. None of the respondents across all stakeholder groups sees a negative impact on equal treatment and very few consider that the directive does not achieve its transparency objectives at all. Moreover, the industry – both from the originator and generic sectors – almost unanimously considers the impact in this respect as positive or even very positive. This perception is shared by a strong majority of respondents from both the public sector and from civil society.

Impact on equal treatment between domestic and imported products

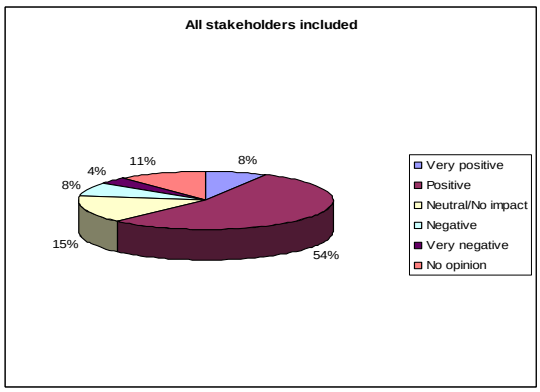


Impact on the transparency of pricing and reimbursement procedures

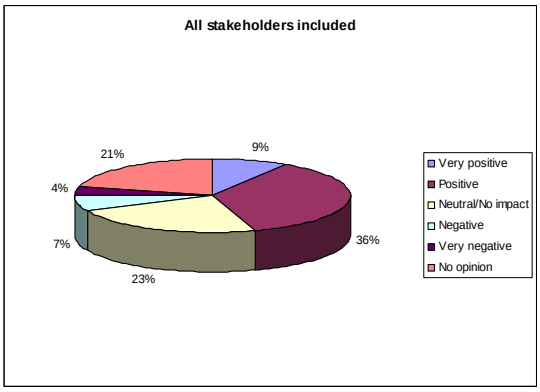


Concerning the transparency and speed of pricing and reimbursement decisions, as well as the availability of legal remedies, the number of contributors that see a negative impact is negligible (3 replies in this sense altogether).

Impact on the speed of pricing and reimbursement decisions



Impact on the availability of legal remedies



With respect to all these issues, the overwhelming majority of respondents among all groups of stakeholders see a positive or even very positive impact. The only exception concerns the availability of legal remedies: almost half of the national authorities do not see any impact of the directive as the principle of judicial appeal is anyway enshrined in their legislation.

The consultation enquired about other policy aspects not directly addressed by the directive but where a certain influence is however possible, such as access to medicines for patients and competitiveness of the pharmaceutical industry. In these areas, the positive perception of the impact of the directive still prevails but is, unsurprisingly, less pronounced. Concerning

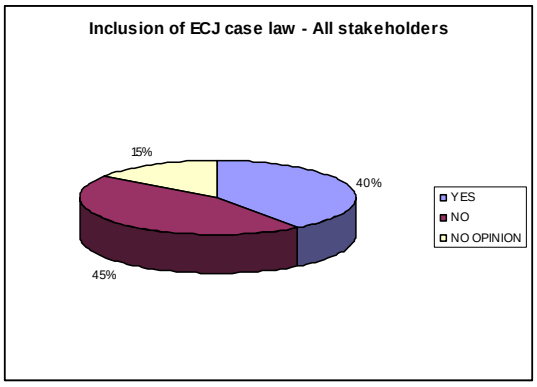
patient access to medicines, roughly half of the respondents report a positive impact and the other half either sees no impact at all or has no opinion on the matter. The positive answers here overwhelmingly came from the originator industry, while the generic industry mainly sees no impact and public authorities are split between positive impact and no impact. A similar picture can be drawn with regard to the effect on the competitiveness of the pharmaceutical industry. Interestingly, pharmaceutical companies (originators and generics alike) consider that the directive has had positive or very positive effects on the competitiveness of the industry.

Many respondents mentioned that there is room for improvement with respect to the enforcement of the rules laid down by the directive. A significant number of contributions referred to cases of incorrect application of the directive. They also stressed the difficulty of applying the rules of the directive to the ever more complex and rapidly changing scientific and economic realities of the pharmaceutical sector and to the specific legal frameworks of the Member States. More guidance, though not necessarily in the form of legislative changes, is therefore advocated by many stakeholders.

2. GENERAL VIEWPOINTS ON A REVISION

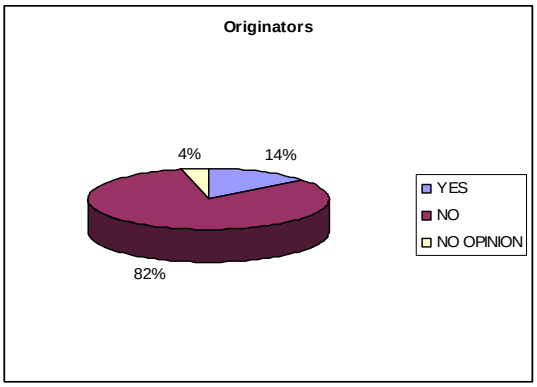
The above-mentioned problem of a rapidly evolving regulatory framework in the Member States – which is in fact partly due to the dynamic changes in the pharmaceutical sector as well as to pressure on public health budgets – has until this day been taken into account only through the interpretation of the text of the directive (especially through the case-law of the Court of Justice). The text of the directive itself has never been adapted to these new developments. The question of a possible integration of these new realities, and notably the existing case-law of the Court, was therefore raised in the public consultation. Positions on these questions in the public consultation are differentiated.

Revision of the directive to include ECJ case-law



In general terms, the originator industry does not advocate any regulatory amendments to incorporate the case-law into the directive or to adapt outdated provisions. Originator companies instead favour a soft law approach based on the adoption of an interpretative Communication on the implementation of the directive and Commission guidelines. On the other hand, more than 75% of responding originator companies declare themselves at least favourable to an explicit inclusion of demand-side measures into the scope of the directive.

Revision of the directive to include ECJ case-law: originator industry



The generic industry is almost unanimously in favour of the incorporation of the ECJ case-law, as well as an inclusion of demand side measures and the repeal of outdated provisions.

Opinions on these questions differ within the public sector. A small majority of national authorities advocates the inclusion of case-law, while 25% is not favourable to this option and the rest has no opinion. Public health insurers are equally divided. Half of the national authorities are in favour of the repeal of outdated provisions, one fourth is against and one fourth has no opinion. Here the public health insurers join the favourable answers. As for the explicit inclusion of demand side-measures, half of the national authorities and nearly all public health insurers are not favourable to such a change and expect a considerable additional administrative burden and cost from it. However, 25% of respondents from national authorities do not expect such a burden.

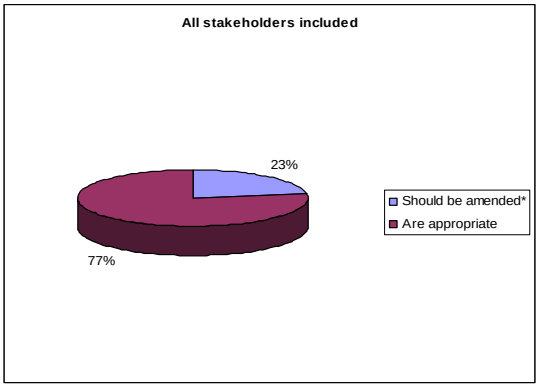
3. TIME-LIMITS FOR PRICING AND REIMBURSEMENT DECISIONS

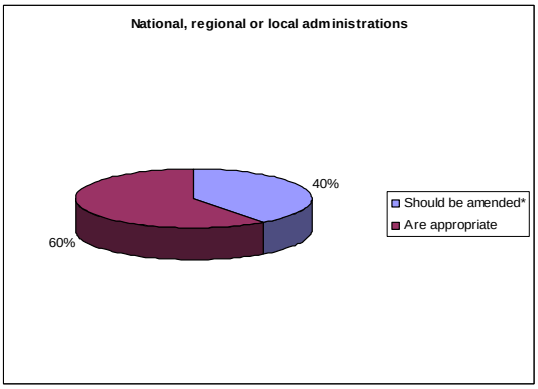
Part of the public consultation focused on the appreciation by stakeholders of the time-limits set out in the directive for pricing and reimbursement decisions. It gave the opportunity to share experiences concerning their application in the different Member States. It also asked for the views of public authorities and the generic industry regarding the possibility of introducing shorter time-limit for generic medicines.

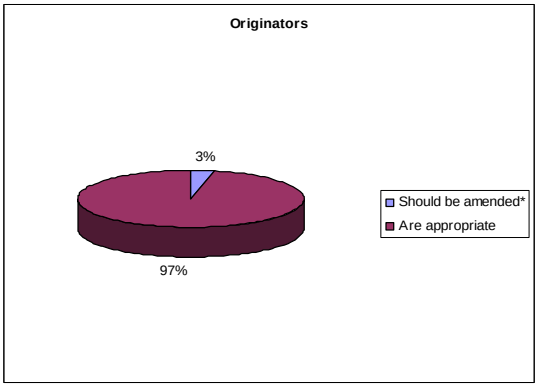
3.1. Time-limits for originator medicines

More than 75% of respondents consider the current time-limits (90/180 days) to be appropriate for originator products. A large majority of national authorities and nearly all contributors from the originator industry share this view.

Are time-limits for originator products, as defined in the directive, appropriate ?







However, many replies from industry confirm that the time-limits are not always respected. Many respondents declare having experienced or knowing about cases in which the time-limits were not respected without any legitimate reason (e.g. publication delays). There seems to be at least equal concern among industry and their representatives about delays caused by stop-the-clock periods used by Member States to request additional information.

The question of whether and how any failure to comply with the time-limits should in the future be addressed by the directive received a differentiated reaction with the public consultation. While some replies from the industry sector indicate that sanctions in the event of non-compliance with the time-limits should be defined in the directive, it is noteworthy that a large majority of more than two thirds of the responses from industry favour a case-by-case decision by the competent national/regional courts. Unsurprisingly, most national authorities take the view that sanctions should be defined by national authorities and the remaining third opts for case-by-case decisions by national courts. None of them envisages a definition of sanctions in the directive.

3.2. Time-limits for generics medicines

On the question of a possible reduction the 90/180 time-limit for generics, the public consultation shows a clear demand from the relevant industry sector for considerably shortened delays. Roughly 80% of the answers from the generic industry call for immediate pricing and reimbursement (0 day) while the others consider a 30-days time-limit to be

adequate. National authorities and public health insurers provide in their answers a much more mitigated picture. While about half of the national authorities wish to keep the current time-limits for generics, others would support a reduction but on different scales: 4 answers favour a 30-days time-limit, 2 express a preference for 45 days, one for 60 days and one would not object to a 0-day time-limit. The main reasons given by the national authorities for their reluctance to accept shorter time limits are the necessity for price negotiations and the additional administrative burden that they anticipate with an accelerated procedure. However, national authorities did not seem able to give an estimate of the increase in administrative costs that they fear.

Time-limits considered appropriate for the swift pricing and reimbursement of generics

	Generic industry *(16 contributions)*	**Public authorities & public health insurers** *(17 contributions)*	**Patient organisations** *(3 contributions)*
0 days	81,3%	-	-
30 days	18,7%	23,5%	-
45 days	-	5,8%	-
60 days	-	11,8%	-
No change to current time-limits	-	58,9%	1
Reduction of time-limits (no timeframe specified)	-	-	2

4. MARKET AND POLICY DEVELOPMENTS

4.1. Managed entry agreements

A total of 9 replies from national authorities declare that managed entry agreements are used in their counties. In most cases, the declared market share covered by managed entry agreements is small (less than 5%), although two countries report market shares above 20%. Most of the responses from national authorities do not see any role for the Transparency Directive with respect to managed entry agreements: only three respondents were in favour of explicitly extending the scope of the directive to such agreements (their main argument being that the role of managed entry agreements as a derogatory procedure needs to be clarified).

Nearly all contributions from the originator industry see a possible role for the directive in the field of managed entry agreements. However, an equally large majority of them considers that these agreements do not pose any problems in terms of interface with regular pricing and reimbursement procedures. Among these contributions, a widespread point of view is that the directive does in effect already apply to managed entry agreements.

4.2. Tendering

National authorities from only 6 Member States declare using tendering or public procurement procedures for pricing and reimbursement purposes (i.e. besides hospital tendering. These schemes are often used exclusively for generics and only cover a small share of the market (at most 8 %). In two cases, these procedures are used for vaccines only. Opinions are divided as to whether the directive should play a role in ensuring a higher level of transparency than provided by the general rules on public procurement in this field. Interestingly, this also true for those respondents who declare using tendering procedures themselves. Half of them advocate a role for the directive, while the other half considers that existing rules are sufficient.

Contributions from the originator industry almost unanimously consider that the existing transparency guarantees through public procurement regulations are sufficient and that the Transparency Directive should not apply in this field. However, many of them call for guidelines clarifying the demarcation between the scope of the directive and the body of law regulating public procurement. The very few contributions calling for a role of the directive (3 in total) are concerned about tendering procedures not in the field of generics, where they are most frequently used, but in the field of innovative medicines: they fear that tendering as a cost-containment strategy will discourage innovation and even create trade barriers.

In contrast to the originator industry, most replies from the generic sector favour a role of the directive with respect to tendering. At the same time, nearly all contributors from the generic industry are satisfied with the existing transparency guarantees in the public procurement framework. This discrepancy can be explained by the fact that most of these responses take a very critical point of view on the use of tendering procedures as a cost containment measure in general and not so much with regard to any specific transparency issues. They mention in particular the risk that companies might drop out of the market completely if they do not win enough tenders or if the procedure leads to unsustainable price levels, thereby diminishing competition and access to medicines for patients.

4.3. Personalised medicines

The linkage between a medicinal compound and a specific diagnostic element in personalised medicine raised the question of a possible role for the transparency directive in order to provide some form of coordination between these two elements. The public consultation shows, however, that the majority of stakeholders seem reluctant to engage in this direction. A large majority of national authorities speak against any explicit regulation of the matter in the directive, while the originator industry is divided. Interestingly, two thirds of the respondents from the medical devices industry declare having no opinion on the matter. Several contributions from industry express their conviction that personalised medicines are covered by the directive anyway in the light of the jurisprudence of the Court of Justice. Some of them suggest a clarification of the issue by way of Commission guidelines.

Role for the directive to increase transparency in the area of personalised medicines

	No	Yes	No opinion
National, regional or local administration	9	3	2
Public health insurers	4	1	0
Pharmaceutical originator industry	11	12	4
Medical devices industry	1	2	6
TOTAL	*25*	*18*	*12*

5. POSSIBLE EXTENSION OF THE DIRECTIVE TO MEDICAL DEVICES

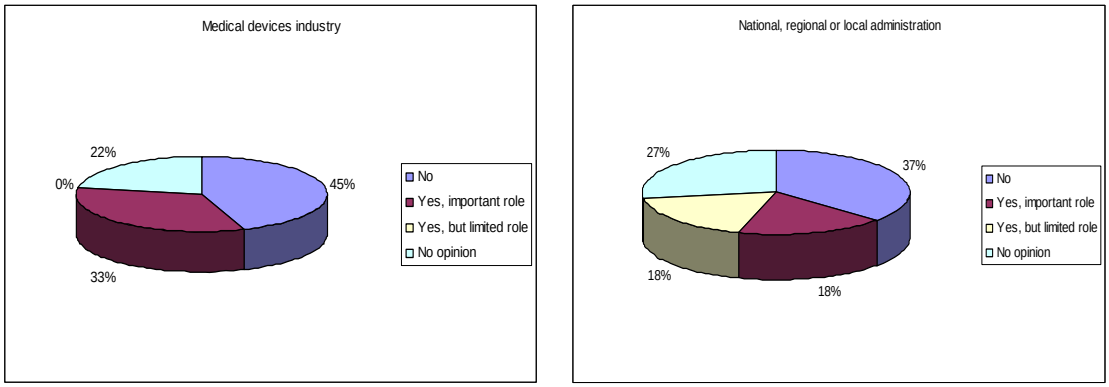
An important aim of the public consultation was to find out if stakeholders felt any need at all for Directive 89/105/EEC to address not only medicines but also medical devices and, if so, what kind of role the directive could possibly play in this field. In order to get as much informed input as possible, the public consultation asked for the stakeholders' opinion on the three different ways a public authority can cover the cost of and put a specific price to a medical device: a listing and reimbursement process, financing as part of a global health

intervention and via public procurement procedures. Only the first of theses categories undergoes a similar process as the medicines currently addressed by the directive.

The number of contributions from both the medical device industry and national authorities/public health insurers that see a role for the directive with respect to medical devices financed within a global health intervention or purchased through a public procurement process is negligible (1 or 2 answers in each case). The majority of respondents see no role for it at all, the others having no opinion on the matter and very few envisaging a limited role. Even though some contributions from the medical device industry mention problems in some countries in these areas, there seems to be a large agreement that these issues can not usefully be addressed by the transparency directive, but are either to be solved at member state level or fall into the scope of the public procurement directive.

Concerning medical devices which undergo a listing and pricing process, only one third of industry respondents and 20% of the national authorities would like to confer an important role to the directive in this matter. These contributions often give as a reason that to extend the scope of the directive that they wish for more detailed rules on European level than provided today by the medical devices directives concerning the quality of the products and not so much rules on the listing process itself. The majority of contributions which do not see any role for the directive in the medical devices sector, even for medical devices which undergo a listing process, consider the market for medical devices to be too fragmented and the market share of listed products too small for the Transparency Directive to make a meaningful contribution (market share estimated at 15% and decreasing). Several national authorities also mention the significant additional administrative burden that an extension of the directive to medical devices would entail.

Possible role of the directive to increase the transparency of procedures for medical devices subject to price regulation and reimbursement listing



6. CONSULTATION OF SMALL AND MEDIUM SIZE ENTERPRISES (SMES)

A specific public consultation was conducted for SMEs in the framework of the Enterprise Europe Network in order to find out about the specific experiences and expectations of SMEs.

While the general public consultation yielded an overwhelmingly positive reaction on the impact of the current directive, the responses from SMEs are less unanimous. Roughly a third of all respondents see a positive impact on equal treatment of domestic and imported products, the speed and transparency of pricing and reimbursement decisions and the availability of legal remedies. A fourth to a third of the answers even identify a negative impact in these fields. The others consider the effect to be neutral or do not have any opinion on this matter. This is in striking contrast to the general consultation, where the number of

answers with a negative perception was negligible in all groups of stakeholders. On the other hand, when asked about the burden of pricing and reimbursement procedures for SMEs, one half of the respondents take the view that this burden would be higher or even substantially higher in the absence of minimum harmonisation as provided by the directive and the other half consider it to be similar.

The SME consultation does not yield any conclusive result as regards the possible adaptation of the directive to the rapidly evolving framework of pricing and reimbursement procedures in the Member States. Nearly half of the respondents do not have any opinion on that matter and the rest is almost evenly divided between a positive and a negative answer. While half of the respondents have no opinion on whether the directive should address pricing and reimbursement procedures for personalised medicine, the other half is clearly in favour of such an explicit extension of the scope of the directive.

As far as the possible inclusion of medical devices is concerned, the consultation shows an evident dissatisfaction (roughly two thirds of the replies) with the transparency of existing procedures concerning listing processes as well as public procurement and financing as part of global health interventions. Consequently, there is a corresponding call for a role of the directive in the medical devices sector, even though the contributions show that in most cases the respondents do not make any distinction between the three kinds of price stetting procedures and are unable to outline concretely the role that the directive should play in their opinion.

ANNEX 2

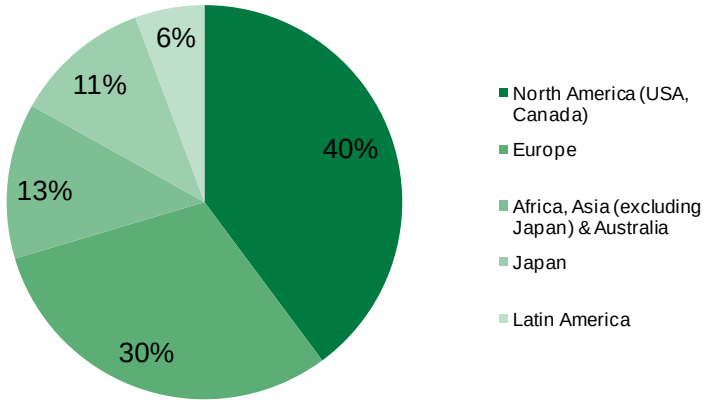
EVOLUTION OF THE PHARMACEUTICAL MARKET AND OF PUBLIC EXPENDITURE ON MEDICINES[1]

1. EVOLUTION OF THE EU PHARMACEUTICAL MARKET

1.1. Size of the market

The total European pharmaceutical market was worth an estimated €177,330 million at ex-factory prices in 2009. This is approximately 30.6% of the total world pharmaceutical market (€579,510). The growth of the European market was estimated at 5.5%. In contrast the Asian region demonstrated an estimated growth of 16%[2].

Figure 1 - Breakdown of the world pharmaceutical market – sales 2009



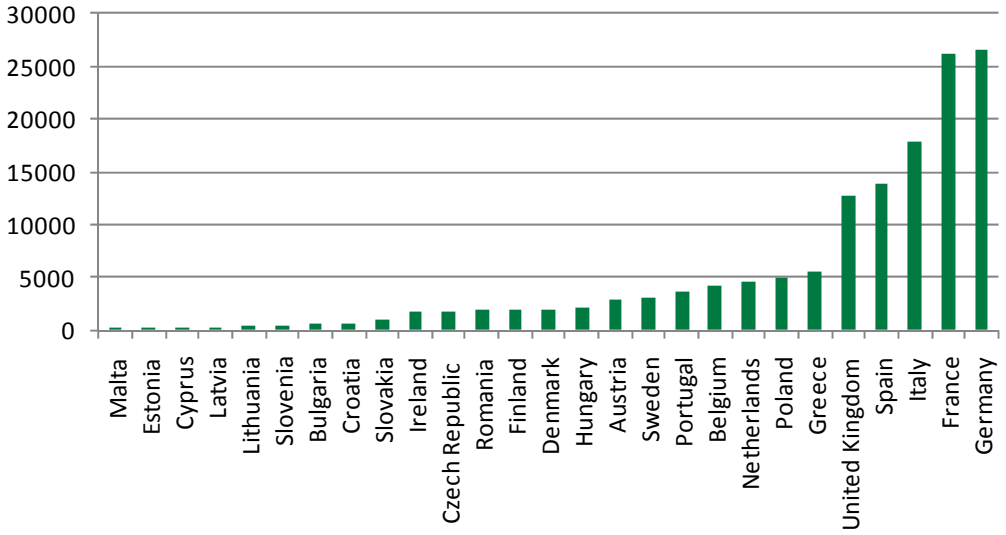
Source: IMS Health Market Prognosis, March 2010 (data relate to the total 2009 unaudited and audited market at ex-factory prices), as cited in EFPIA (2010) The Pharmaceutical Industry in Figures.

In terms of Member States, Germany and France have by far the largest pharmaceutical markets at €26.6 million and €26.2 million respectively. Italy, Spain and the United Kingdom also have relatively large markets, whilst the remainder of Member States all have a market size of less than €6 million. The breakdown of the total pharmaceutical market value by Member State (at ex-factory prices) is shown in Figure 2.

1 Working document based on research by Matrix Insight Ltd for DG Enterprise and Industry. This document does not represent an official position of the European Commission.

2 EFPIA (2010). The Pharmaceutical Industry in Figures.

Figure 2 - Total pharmaceutical market value (ex-factory prices, €m, 2008)



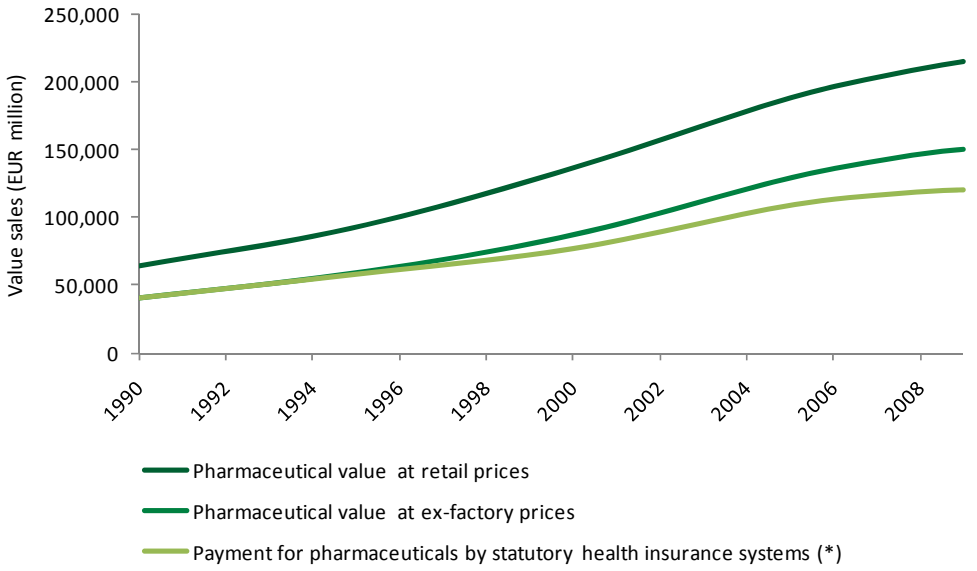
Source: EFPIA member associations (official figures) – Bulgaria, Estonia, Lithuania, Malta, Romania: IMS Health as cited in EFPIA (2010) The Pharmaceutical Industry in Figures.

1.2. Pharmaceutical sales

1.2.1. Major trends

There is a clear upwards trend in both pharmaceutical sales and production in the EU. In the period between 1990 and 2008 total pharmaceutical sales in the 27 EU Member States (plus Croatia, Iceland, Norway & Switzerland) rose from just over EUR 40bn (at retail prices) to almost EUR 215bn in 2009. The figure below shows the evolution of pharmaceutical sales across the EU.

Figure 3 - Pharmaceutical sales 1990-2009 (EUR million)

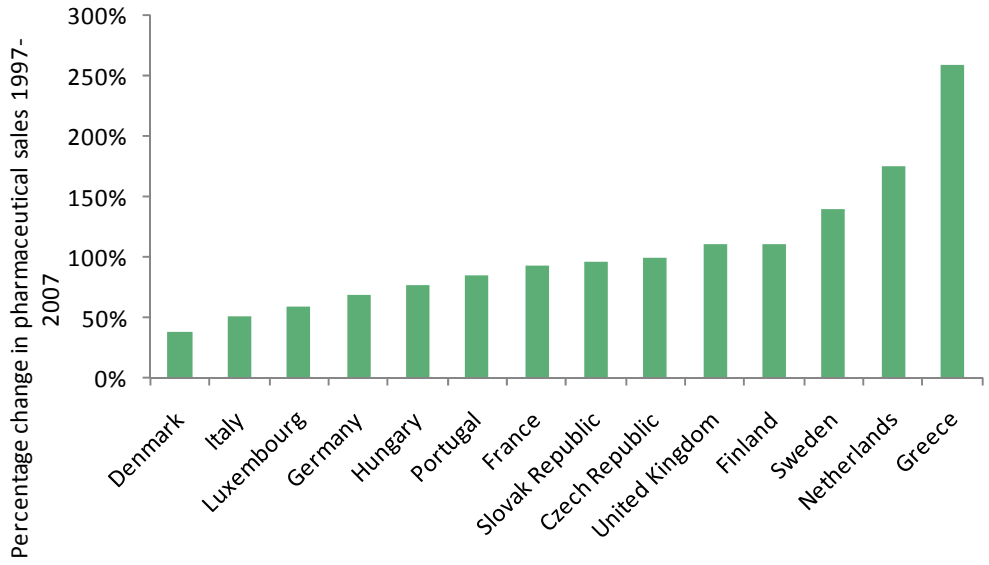


Notes: Data relate to EU-27, Croatia, Iceland, Norway and Switzerland since 2005 (EU-15, Norway and Switzerland before 2005); (*) Since 1998 data relate to ambulatory care only; Source: EFPIA, The Pharmaceutical Industry in Figures, 2010.

This upward trend in pharmaceutical sales across the EU is mirrored at Member State level (Figure 4). Comparing 1997 with 2007, all 14 Member States for which figures were available recorded a significant increase in pharmaceutical sales. The increase was most marked in Greece (more than 250%) and least significant in Denmark (less than 50% increase in sales).

A combination of drivers explains differences in growth of pharmaceutical sales across Member States. Rather than price increases, in most countries the increase in sales value is driven by volume increases.[3] For example in Greece, parallel exports accounted for 22% of the total prescription pharmaceutical market[4], thus adding to sales growth. In Denmark, cost containment measures imposed by government may have contributed to comparatively lower growth than in other European countries.

Figure 4 - Percentage change in pharmaceutical sales 1997-2007



Source: OECD Health Dataset; original figures in USD million (PPP), Exchange rate 1.2836

Table 1 below shows 2008 pharmaceutical sales for a selection of EU Member States and forecasts the growth of the market until 2013. There are marked differences in the sales forecasts per country. Within the EU, the Baltic countries (Latvia, Lithuania and Estonia) show the lowest growth, up to 1%. Romania, Greece, Poland and Spain expect the highest growth in pharmaceutical sales (7.1 to 14.2%). Of the four largest Member States, France, Italy and the UK expect only a modest growth (1.1%, 1.8% and 1.5% respectively), while Germany keeps up with average growth on the world market (4.4%).

3 IMS Health (2005), *Intelligence 360: Une vision panoramique du marché pharmaceutique mondial*, Presentation of data from IMS Health (in French).

4 Kanavos, P. and J. Costa-Font (2005), "Pharmaceutical Parallel Trade in Europe: Stakeholder and Competition Effects", Economic Policy, pp. 751-798.

Table 1 - Prognosis for pharmaceutical sales in EU countries, 2008-2013

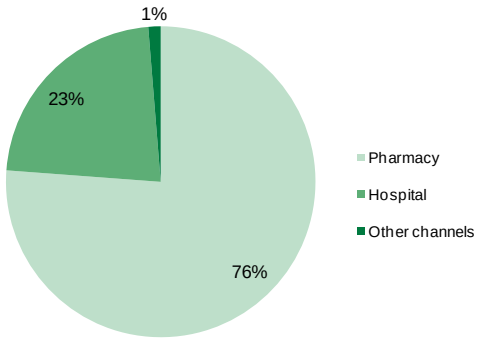
Country	Market Sales 2008, Euro '000	Compound Annual Growth rate 2003-2008	Compound Annual Growth Rate 2008-2013	Estimated size of the market in 2013
EU-27	**249,060,461**	**-**	**4.00%**	**303,375,683**
EU-15	**224,777,147**	**-**	**3.70%**	**268,950,920**
Austria	4,950,811	6%	4.40%	6,140,042
Belgium	7,360,218	5%	5.60%	9,642,982
Bulgaria	1,078,387	9%	6.00%	1,442,484
Cyprus	471,412	-	4.00%	573,459
Czech Republic	3,267,290	7%	6.30%	4,431,850
Denmark	3,122,408	8%	5.70%	4,111,774
Estonia	262,803	11%	1.00%	276,414
Finland	3,180,119	5%	2.40%	3,583,746
France	48,658,527	5%	1.10%	51,427,140
Germany	47,609,313	4%	4.40%	59,186,823
Greece	8,669,458	15%	9.10%	13,430,321
Hungary	3,378,479	7%	6.20%	4,569,085
Ireland	2,953,315	16%	6.80%	4,103,194
Italy	30,658,935	4%	1.80%	33,440,663
Latvia	450,348	24%	0.40%	459,282
Lithuania	739,588	13%	0.70%	766,023
Luxembourg	282,147	5%	3.70%	337,654
Malta	206,690	-	4.00%	251,315
Netherlands	7,913,185	2%	6.00%	10,612,991
Poland	8,262,559	6%	7.50%	11,885,865
Portugal	6,159,709	5%	3.20%	7,206,903
Romania	3,295,561	35%	14.20%	6,399,802
Slovak Republic	2,012,004	11%	3.20%	2,352,912
Slovenia	858,189	6%	3.40%	1,016,272
Spain	24,179,199	8%	7.10%	34,080,118
Sweden	4,695,229	5%	2.80%	5,402,063
United Kingdom	24,384,579	4%	1.50%	26,244,506

Source: ECORYS Competitiveness of EU Market and Industry for Pharmaceuticals - Volume 2, pg.56; Note: converted from US$ using exchange rate of 1.2836

1.2.2. Breakdown by main distribution channels

Pharmaceutical sales are largely distributed through pharmacy and hospitals. Pharmacy accounts for the largest distribution channel, with over three quarters (76%) of pharmaceutical sales. The remaining 23% are distributed through hospitals, with approximately 1% through other channels such as dispensing doctors, supermarkets and other retail outlets.

Figure 5 - Pharmaceutical sales by distribution channel (2008)



Source: EFPIA (2010) The Pharmaceutical Industry in Figures.

There is considerable variation across Member States in terms of the size of the two main distribution channels. Pharmacy is the largest distribution channel in all countries except for Cyprus. However the proportion of sales through pharmacies ranges from 91% (Slovakia) to 48% (Cyprus) across Member States. Conversely, the proportion of sales coming through hospitals ranges from 9% (Slovakia) to 52% (Cyprus).

Table 2 - Breakdown of the total pharmaceutical market value (at ex-factory prices) by main distribution channels, 2008

Member State	Pharmacy	Hospital	Other channels
Slovakia	91%	9%	0%
Romania	89%	11%	0%
Belgium	88%	12%	0%
Poland	87%	13%	0%
Lithuania	86%	14%	0%
Bulgaria	86%	14%	0%
Germany	85%	14%	1%
Ireland	82%	16%	1%
Latvia	82%	18%	0%
Sweden	82%	17%	0%
Hungary	82%	18%	0%
Slovenia	81%	19%	1%
France	80%	20%	0%
Croatia	79%	21%	0%
Netherlands	76%	20%	4%
Czech Republic	75%	25%	0%
Spain	75%	25%	0%
Finland	74%	25%	1%
Greece	74%	26%	0%
Portugal	70%	29%	0%
Austria	69%	31%	0%
Italy	66%	34%	0%
United Kingdom	63%	32%	4%
Denmark	59%	40%	1%
Cyprus	48%	52%	0%
Total	**76%**	**23%**	**1%**

Note: Denmark, Finland, Iceland, Latvia, Norway, Slovenia, Sweden: pharmaceutical market value at pharmacy purchasing prices; Belgium (2008 provisional), France, Germany, Ireland, Italy, Norway, Spain: estimate; Greece: including parallel exports; Source: EFPIA (2010) The Pharmaceutical Industry in Figures.

1.3. Pharmaceutical consumption

Data on pharmaceutical consumption is difficult to compare across Member States. Member States use varying units of measuring consumption – i.e. packs, defined daily dose (DDD), units of administration and others use weight in mg.

The PHIS report (2010) provides data on annual in-patient pharmaceutical consumption in Austria, Slovakia, and Portugal each of which measure consumption in different units. In Austria consumption is measured in packs, Slovakia uses DDD, and Portugal uses units of administration. In Austria there was a total increase in annual consumption from 20 million packs to 24 million packs between 2000 and 2005. In Slovakia, there was an increase in annual consumption from 200 million DDD to 300 million DDD between 2001 and 2008. In Portugal, there was no increase in annual consumption between 2007 and 2008; consumption remained flat at 78 million units of administration.

While pharmaceutical consumption provides part of the picture of the overall market there is no straightforward relationship between consumption and expenditure and the leading drug across the EU in terms of volume is not the leading drug in terms of expenditure. Based on survey data from 25 Member States (all but Greece and Luxemburg) the leading substance for consumption is *paracetamol* whereas *trastuzumab* leads in terms of expenditure. A list of the top 10 substances can be found in Table 5.

Table 3 - Top 10 active ingredients by consumption and expenditure

Position	Top 10 active ingredients used in hospitals, ranked with regard to consumption	Top 10 active ingredients used in hospitals, ranked with regard to expenditure
1	Paracetamol	Trastuzumab
2	Electrolyte	Rituximab
3	Furosemide	Docetaxel
4	Acetylsalicylic Acid	Interferon beta-1a
5	Epoetin beta	Etanercept
6	Albumin	Epoetin alpha
7	Omeprazol	Imatinib
8	Ranitidine	Oxaliplatin
9	Prednisolone	Adalimumab
10	Coagulation factors IX, VII, and X	Bevacizumab

Source: PHIS, pp. 65-67

2. PUBLIC EXPENDITURE ON PHARMACEUTICALS

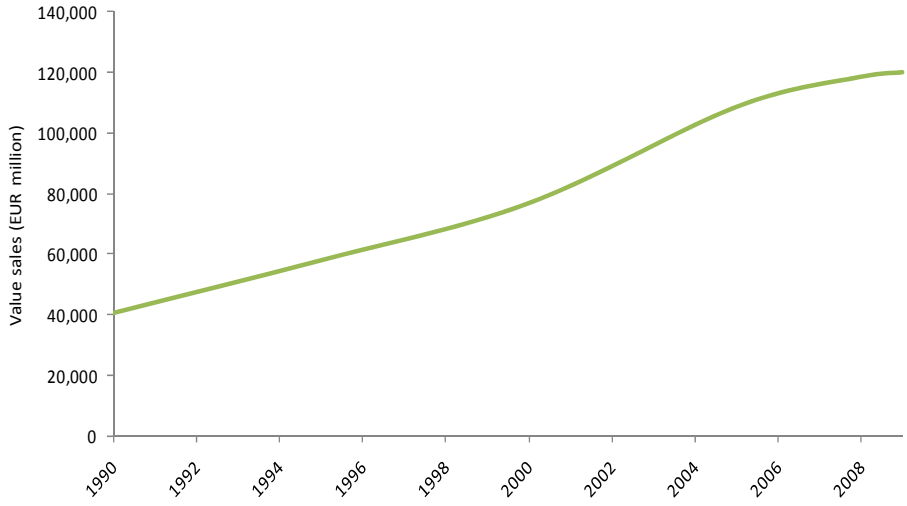
This section focuses on the share of the market which is reimbursed and is covered by public expenditure. This part of the market is of greatest relevance for the Transparency Directive's provisions on pricing and reimbursement.

2.1. Overall public expenditure on pharmaceuticals

Public expenditure on health has followed a similar rising trend to pharmaceutical sales. The pharmaceutical sector accounts for an average 17% share of total health expenditure in most OECD countries.[5] Since 1980 pharmaceutical expenditure in the EU countries has been increasing more than total health expenditure (net of pharmaceutical expenditure). In the period 1980-2005 the mean annual growth of pharmaceutical expenditure was 5.0% in comparison to 4.1% of health expenditure.[6]

Figure 6 shows the total public expenditure on pharmaceuticals for the period 1990-2009 in all 27 Member States plus Croatia, Iceland, Norway and Switzerland. Over that period, total public expenditure on pharmaceuticals in these countries increased from EUR 40bn to over EUR 120bn.

Figure 6 - Public pharmaceutical expenditure in the EU 1992-2009 (EUR million)



Notes: Data relate to EU-27, Croatia, Iceland, Norway and Switzerland since 2005 (EU-15, Norway and Switzerland before 2005); Since 1998 data relate to ambulatory care only; Source: EFPIA, The Pharmaceutical Industry in Figures, 2010.

Table 5 below presents expenditure per capita on pharmaceuticals in 17 Member States over 6 years (2000-2006). In Europe, on average, expenditure has been increasing every year due to aging population and other factors. At Member State level, there is a significant positive relationship between per capita income and per capita pharmaceutical expenditure (including prescribed and non-prescribed drugs). Whereas Belgium and France lead the table, Poland and Denmark spend the least. In Poland it is important to note that this is mostly attributable to an average low pharmaceutical price level since per capita consumption by volume is second in Europe, with an average unit consumption of 33 packs (France 49 packs, Italy 27 packs).[7]

5 OECD Health Policy Studies (2008) Pharmaceutical Pricing Policies in a Global Market. pg 28.

6 ECORYS Research Consulting (2009) Competitiveness of the EU Market and Industry for Pharmaceuticals: Volume 2: Markets, Innovation, and Regulation. Rotterdam, Netherlands. pg. 52

7 ECORYS Research Consulting (2009) Competitiveness of the EU Market and Industry for Pharmaceuticals: Volume 2: Markets, Innovation, and Regulation. Rotterdam, Netherlands. pg 51.

Table 4 - Total expenditure per capita on pharmaceuticals, other medical non durables, (Euro PPP)

	Year						
Country	**2000**	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**
Average	**392**	**422**	**444**	**479**	**505**	**541**	**564**
Austria	435	431	479	520	530	540	576
Belgium	-	-	-	-	-	741	750
Czech Republic	294	334	366	416	443	467	448
Denmark	268	298	339	330	341	349	367
Finland	350	379	417	443	490	512	499
France	538	592	630	641	673	710	724
Germany	466	512	543	574	565	632	642
Greece	326	349	386	442	504	543	562
Hungary	-	356	395	453	483	565	598
Italy	580	641	641	635	655	650	673
Luxembourg	359	404	408	444	467	448	-
Netherlands	350	383	417	-	-	-	-
Poland	-	-	267	291	307	303	318
Portugal	433	463	495	501	537	564	579
Slovak Republic	263	290	349	391	426	462	499
Spain	420	444	489	602	621	648	684
Sweden	406	449	486	499	526	529	547

Note: converted from US$ using exchange rate of 1.2836; Source: ECORYS Competitiveness of the EU Market and Industry for Pharmaceuticals V 2. P.51.

Public expenditure on pharmaceuticals as a proportion of total pharmaceutical expenditure has also been increasing from just over 60% in 1997 to close to 68% in 2007. These figures suggest that the value of the reimbursed market as a proportion of the total market has increased considerably between 1997 and 2007 in the countries covered by the data. The figure below charts the evolution of public expenditure on pharmaceuticals as a proportion of total pharmaceutical expenditure over time.

Figure 7 - Public expenditure on pharmaceuticals as a proportion of total pharmaceutical expenditure 1997-2007

Includes medical non-durables; Member States included: Austria, Czech Republic, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Spain, and Sweden; Source: OECD Health Dataset; original figures in USD million (PPP), Exchange rate 1.2836.

ANNEX 3

OVERVIEW OF THE PROVISIONS OF DIRECTIVE 89/105/EEC[1]

Article 1	**SUBJECT MATTER**	Any national measure to control the price of medicinal products or to restrict the range of products covered by the national health insurance system must comply with the requirements of the Directive.

Article 2	**INITIAL PRICE DECISION**	Provisions which apply when marketing is only permitted after the price of the product has been approved by national authorities:
Article 2.1	Time-limit for decision	- The price decision must be adopted and communicated to the applicant within 90 days. - If the decision is not made within this period, the applicant is entitled to market its product at the price proposed.
Article 2.2	Motivated decision communicated to the applicant	If the price proposed is not accepted by the national authorities: - the decision must be motivated (statement of reasons) based on objective and verifiable criteria. - the applicant must be informed of the remedies available and of the time limits for applying for such remedies.
Article 2.3	Publication and communication of prices	At least once a year, list of prices fixed must be: - published in an appropriate publication. - communicated to the Commission.

Article 3	**PRICE INCREASE**	Provisions which apply when price increase is only permitted after approval by national authorities:
Article 3.1	Time-limit for decision	- The decision must be adopted and communicated to the applicant within 90 days (+ 60 days if exceptional number of applications) - If the decision is not made within this period, applicant is entitled to apply the price increase requested.
Article 3.2	Motivated decision communicated to the applicant	If the proposed price increase is not accepted by national authorities: - the decision must be motivated (statement of reasons) based on objective and verifiable criteria - the applicant must be informed of the remedies available and of the time limits for applying for such remedies.
Article 3.3	Publication and communication of price increases	At least once a year, a list of price increases must be: - published in an appropriate publication - communicated to the Commission

Article 4	**PRICE FREEZE**	
Article 4.1	Annual assessment of macro-economic conditions	- At least once a year, Member States must carry out a review to determine if the macro-economic conditions justify maintaining the price freeze. - Possible price increase/decrease must be announced within 90 days after the start of the review.
Article 4.2	Possibility to request derogation from	- In exceptional cases, the marketing authorisation holder may apply for a

[1] Working document prepared for information purposes by the services of DG Enterprise and Industry. This document does not represent an official position of the European Commission.

	price freeze	derogation from price freeze. The Application must be motivated. - A reasoned decision on the application must be adopted and communicated to the applicant within 90 days (+ 60 days if exceptional number of applications).

Article 5	**PROFIT CONTROL**	If a Member State adopts a system of direct or indirect controls on profitability, the following information must be published and communicated to the Commission:
	Provisions applicable to profit control systems *(only example to date is in the United Kingdom)*	- method used to define profitability - range of target profit permitted - criteria according to which target rates of profit are defined and criteria according to which profit can be retained above the companies' targets - maximum percentage of profit which can be retained by companies above their target. Information must be updated once a year or when significant changes are made.

Article 6	**DECISION ON REIMBURSEMENT (POSITIVE LIST)**	Provisions which apply if a medicinal product can be reimbursed only after the competent authorities have decided to include it in a positive list of products covered by the national health insurance system:
Article 6.1	Time-limit for decision	- The decision to include a product on the positive list must be adopted and communicated to the applicant within 90 days (+ 90 days if pricing decision is made during the same procedure or after decision on reimbursement). - If national rules impose that the reimbursement decision must be made after pricing decision, both procedures must be completed within 180 days.
Article 6.2	Motivated decision communicated to the applicant	A decision not to include a product on the positive list: - must be motivated (statement of reasons including, if appropriate, expert opinions or recommendations) based on objective and verifiable criteria. - the applicant must be informed of the remedies available and of the time limits for applying for such remedies.

Article 6.3	Publication and communication of criteria	The criteria used to decide upon inclusion of products on positive list must be published and communicated to the Commission before 31/12/1989.
Article 6.4	List of reimbursed products	A complete list of reimbursed products and their prices must be published and communicated to the Commission before 31/12/1989. The list must be updated at least once a year.
Article 6.5	Decision to exclude a product from the positive list	A decision to exclude a product from the positive list: - must be motivated (statement of reasons including, if appropriate, expert opinions or recommendations based on objective and verifiable criteria. - the applicant must be informed of the remedies available and of the time limits for applying for such remedies.
Article 6.6	Decision to exclude a category of products from the positive list	A decision to exclude a category of products from the positive list: - must be motivated (statement of reasons) based on objective and verifiable criteria. - must be published in an appropriate publication.

Article 7	**DECISION ON EXCLUSION FROM REIMBURSEMENT SYSTEM (NEGATIVE LIST)**	Provisions which apply if national authorities can adopt decisions to exclude individual products or categories of products from national health insurance system:
Article 7.1	Decision to exclude a category of products	A decision to exclude a category of products from reimbursement system (inclusion in negative list): - must be motivated (statement of reasons) based on objective and

		verifiable criteria. - must be published in an appropriate publication.
Article 7.2	Publication and communication of criteria	The criteria used to decide upon exclusion of products must be published and communicated to the Commission before 31/12/1989.
Article 7.3	Decision to exclude an individual product	Decision to exclude a specific product from reimbursement system: - must be motivated (statement of reasons including, if appropriate, expert opinions or recommendations on which the decision is based) - must be based on objective and verifiable criteria. - applicant must be informed of the remedies available and time limits for applying for such remedies.
Article 7.4	List of products excluded: publication and communication to the Commission	- Complete list of excluded products must be published and communicated to the Commission before 31 Dec 1990. The list must be updated at least every six months.

Article 8	**CRITERIA FOR THERAPEUTIC CLASSIFICATION AND TRANSPARENCY OF TRANSFER PRICES**	
Article 8.1	Criteria for therapeutic classification	The criteria concerning the therapeutic classification of medicinal products must be communicated to the Commission before 31/12/1989.
Article 8.2	Transparency of transfer prices	The criteria to verify the fairness and transparency of prices charged for the transfer of active substances or intermediate products within a group of companies must be communicated to the Commission before 31/12/1989.

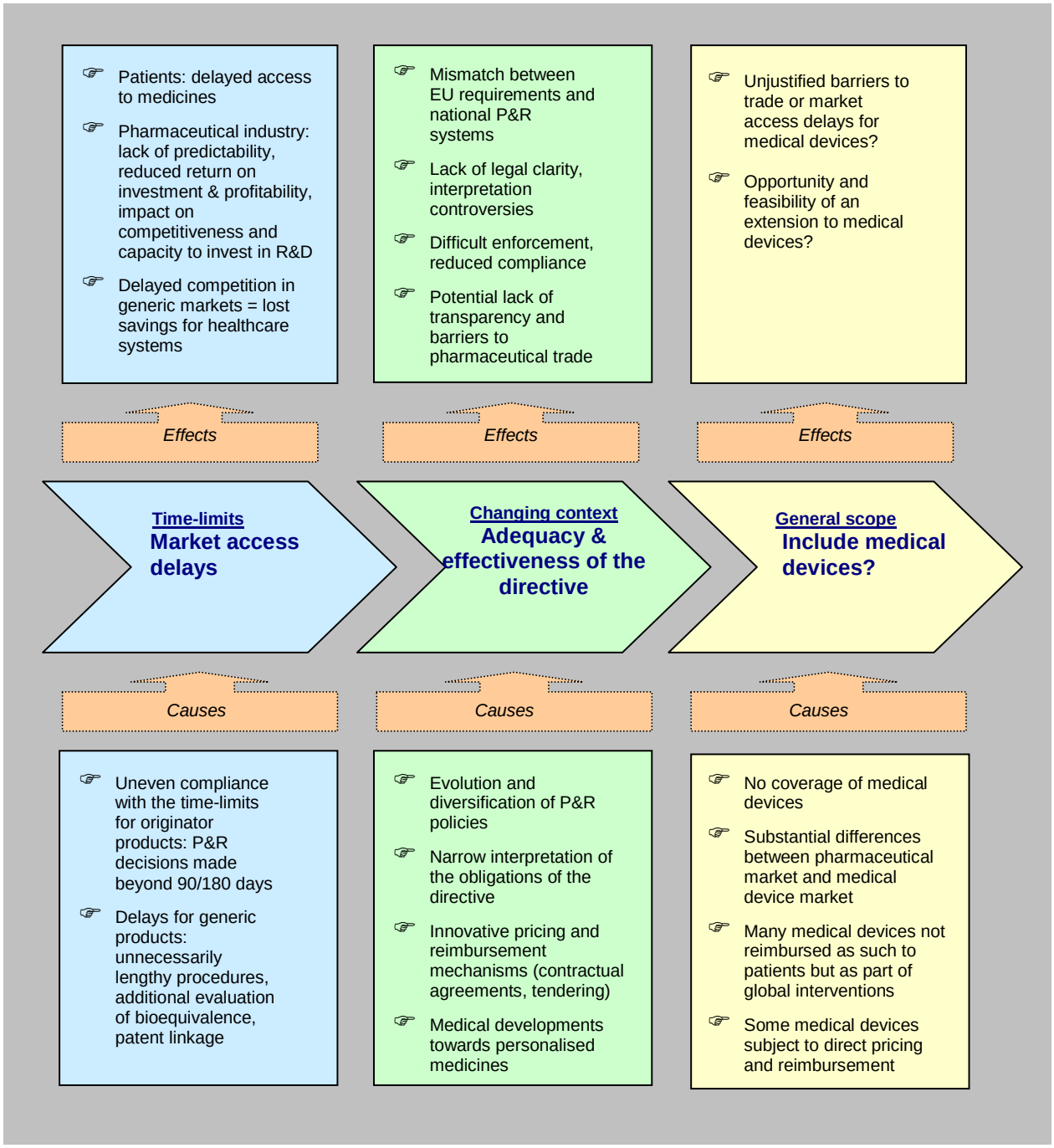
Article 9	**REVIEW OF DIRECTIVE**	
Article 9.1	Commission proposal within 2 years	The Commission must submit a proposal within two years with appropriate measures for the abolition of any remaining barriers to the free movement of medicines.
Article 9.2	Adoption by Council within one year	The Council must decide on the Commission's proposal within one year after its submission.

Article 10	**TRANSPARENCY COMMITTEE**	
Article 10.1	Creation of a 'Consultative Committee'	Consultative Committee for the implementation of Directive 89/105/EEC attached to the Commission.
Article 10.2	Tasks	Examine questions relating to the application of the Directive
Article 10.3	Membership	One representative and one deputy for each Member State.
Article 10.4	Chairmanship	Committee chaired by a representative of the Commission.
Article 10.5	Rules of procedure	The Committee shall adopt its own rules of procedure.

Article 11	**FINAL PROVISIONS**	
Article 11.1	Deadline for transposition	31/12/1989.
Article 11.2	Communication of existing legislation and practices	- Before 31/12/1989, Member States must communicate to the Commission their laws, regulations or administrative provisions relating to the pricing of medicinal products, the profitability of manufacturers and the coverage of products by the national health insurance system. - Amendments and modifications to these laws, regulations or administrative provisions must be communicated to the Commission.

ANNEX 4

PROBLEM TREE



ANNEX 5

DELAYS OBSERVED IN PRICING AND REIMBURSEMENT PROCEDURES[2]

The Transparency Directive specifies a maximum amount of time permitted for competent authorities in Member States to take decisions on pricing and reimbursement. Article 2 of the Directive stipulates that decisions on prices must be communicated to the applicant and adopted within 90 days of receipt of the application. Similarly, a decision on whether to include the product in the list of those covered by the national health insurance for reimbursement purpose must also be made within 90 days. For both of these processes, the timescales can be extended by a further 90 days if the competent national authority deems there to have been insufficient supporting information provided with the application, and request additional information. Any further delays for reasons other than this are considered to be a breach of the Directive.

This annex provides details of the actual pricing and reimbursement delays for innovator and generic medicines based on the available data.

1. PRICING AND REIMBURSEMENT DELAYS FOR INNOVATOR MEDICINES

1.1. Delays observed – originators

Data collected as part of the Commission's inquiry into competition in the pharmaceutical market[3] suggest that originator companies object to the extent of delays and uncertainties created by national pricing and reimbursement procedures. They argue that these delays have reduced the period of exclusivity that they hold over patented medical products and thus reduces their expected revenue. Although the Transparency Directive clearly stipulates that decisions on pricing and reimbursement should be taken within 180 days, the report suggests that in several Member States it takes considerably longer for such decisions to be taken. Indeed, it is suggested that originator companies face delays ranging from a few months to several years with respect to the pricing and reimbursement decision.[4] This may be in part due to request for further information, which enables a further 90 day delay to be taken.

As part of an OECD study, the holders of marketing authorisations for 78 pharmaceutical products granted marketing approval between 1997 and 2001 were surveyed to ascertain the average delays that occur from P&R application to the decision to approve. Figure 1 outlines the extent of and variation across several Member States in terms of delays. The total delay comprises of the following three types (where relevant) of delay:

(1) **Pricing delay** – the elapsed time from the date the pricing application was made to the date price approval was granted

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2 Working document based on research by Matrix Insight Ltd for DG Enterprise and Industry. This document does not represent an official position of the European Commission.

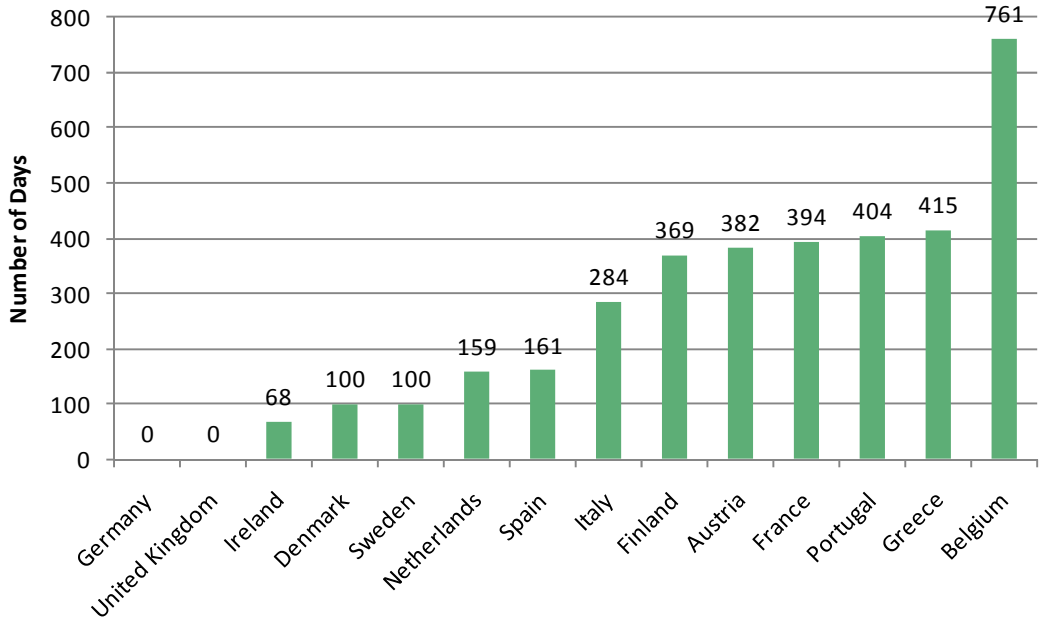
3 European Commission (2008) *Pharmaceutical Sector Inquiry Preliminary Report.* Brussels, DG Competition, pp. 390-400.

4 European Commission (2008) *Pharmaceutical Sector Inquiry Preliminary Report.* Brussels, DG Competition, pp.390-400.

(2) **Reimbursement delay** – the elapsed time from the date the reimbursement application was made to the date the company "was first informed about the reimbursement decision";

(3) **Publication delay** – elapsed time from the date the company was notified of the reimbursement decision to the date the authorities published the decision (only in countries for which publication of a decision in an official journal is a prerequisite for reimbursement)[5]

Figure 1 - Average number of days from pricing and reimbursement application to decision, 1997-2001



Source: OECD (2008) Health Policy Studies Pharmaceutical Pricing Policies in a Global Market, pg. 133

As the figure highlights, the average delay in Belgium is particularly long, and almost twice as long as in the country with the second longest delays, Greece. A further six Member States have delays that exceed the 180 day period stipulated by the Transparency Directive for pricing and reimbursement decisions, although it is unclear whether this is as a result of 'stop the clock' procedures used to request additional data, or due to the publication delay. For instance, the Portuguese competent authority suggested that the stop the clock provision is almost always used for new medicines and sometimes more than once within the same application process. The average stop the clock lasts for about 10 days though this has stretched to 6 months in extreme cases. The objective of stopping the clock is to gather additional information for the "value added" analysis. Nevertheless, the Portuguese competent authority suggested that the deadline for pricing and reimbursement are usually met except for a small number of complex products where the deadline is significantly exceeded. Portuguese legislation stipulates a maximum delay of 75 days for reimbursement which is usually met though this can be extended to 120 days for complex products. The average delay for a pricing decision (by the Ministry of the Economy) is about 60 days. The Italian competent authority confirms that P&R delays are very product specific. A study from Hungary suggested that a number of new pharmaceutical products have taken two to three years from submission of an application to decisions being made. It is thought that this was in part due to

[5] Cambridge Pharma Consultancy (2004), *Pricing and Reimbursement: Review 2003*, Cambridge PharmaConsultancy, Cambridge, England.

changes in personnel at ministerial and administrative levels, as well as other factors. Interviews with stakeholders in the pharmaceutical sector as part of the study found the general consensus to be that decisions for innovative drugs are rarely made within the timescales permitted by the Directive[6].

At the other end of the scale, reimbursement and pricing delays do not exist in Germany and the United Kingdom as drugs are reimbursed as soon as they are approved, unless or until added to the negative list. While more recent data suggests that delays have increased in most countries[7], there have also been improvements; most notably in Belgium, Denmark, France, Austria and Finland. For example, a 2008 report from the Pharmaceutical Industry Association, Pharma.be in Belgium, analysed reimbursement decisions for 46 new and innovative drugs in 2008. It found that pricing and reimbursement decisions were made by the competent authority for all 46 new drugs within the 180 days permitted by the Directive, and the average delay was 73 days. However, despite these improvements the industry association has still expressed concern that the delays are too long[8]. In 2008 the French Pricing Committee (CEPS) published a report that stated the average time to process pricing applications (for first applications) was 102 days, with the average time for new drugs being 201 days[9]. In 2009, CEPS annual report published the following processing times.

Table 1 – France: Processing times for drug listing applications in by type (in number of days)

Type of product	Accepted	Abandoned, withdrawn or rejected	All
Generics	65	124	66
Non-generics	213	579	256
All	89	468	106

Source: CEPS, Annual Report 2009.

In Denmark, the maximum time for reimbursement applications concerning medicinal products with an entirely new constituent or new medicinal product forms is 90 days, calculated from the time when the marketing authorisation is available. Usually, reimbursement decisions are made within 1-2 months. Applications for reimbursement for a new medicinal product form with the same method of administration (e.g. ointments/creams/liniments or tablets/capsules) are usually granted within 2 weeks and generic products are automatically reimbursed if the originator product is reimbursed. If the Danish Reimbursement Committee recommends a negative outcome, the applicant is granted a 14 day stop-clock to make a statement before the committee formally makes its decision.

The figure below shows average pricing and reimbursement delays at two different points in time. The graph shows that Austria, Finland, Denmark and Belgium have improved delays. At the same time, delays in other countries have increased.

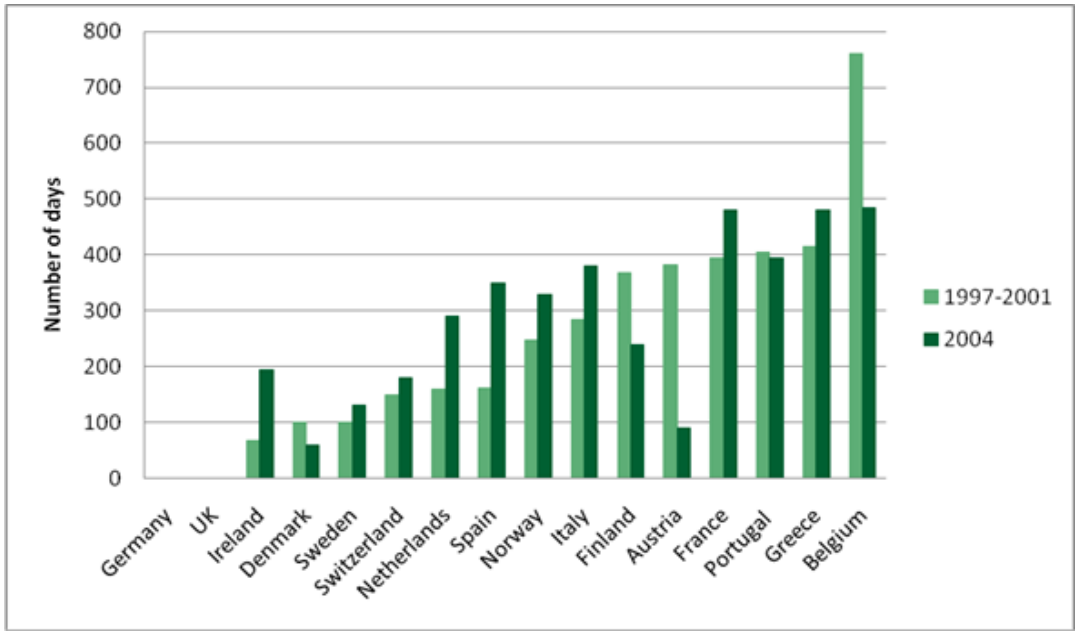
6 Hungary: Industry Seeks Greater Policy Bite. (2008) *IMS Pharma Pricing and Reimbursement*, 13(11). Pg 326-329.

7 OECD Health Policy Studies (2008) *Pharmaceutical Pricing Policies in a Global Market*.pg. 133

8 Belgium: Industry Reports on Access to Innovative Drugs in 2008. (2009) *IMS Pharma Pricing and Reimbursement*, 14(9). Pg 263

9 France: CEPS Publishes Annual Report for 2008. (2009) *IMS Pharma Pricing and Reimbursement*, 14(10). Pg 304-305.

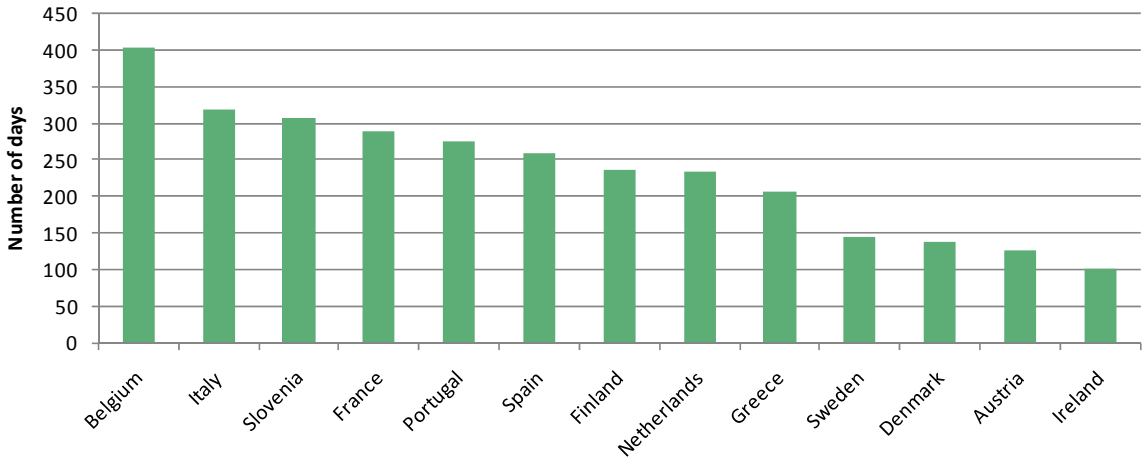
Figure 2 - Average number of days for pricing and reimbursement decision - 1997-2001 compared to 2004



Source: 1997-2001 data from OECD (2008) Health Policy Studies Pharmaceutical Pricing Policies in a Global Market, pg. 133. 2004 data from Pharmaceutical Industry Competitiveness Task Force Competitiveness and Performance Indicators (2005), pg. 42.

Another way of estimating pricing and reimbursement delays is by disaggregating the EFPIA WAIT indicator. The W.A.I.T indicator (2009) shows that the average time delay between market authorisation and "accessibility" ranges from 101 to 403 days in the 14 Member States covered. Belgium has the longest delay, followed by Italy at 318 days, whilst the shortest delays are evident in Ireland, Austria and Denmark. In order to bring delays down further, the Italian Medicines agency (*AIFA*) and the State-Regions Conference (*Conferenza Stato Regioni*) have signed an agreement for automatic inclusion in regional hospital formularies of innovative drugs.[10] In addition to bringing down overall accessibility delays after a reimbursement decision has been taken at national level, this move should help reduce regional disparity in access to drugs.

Figure 3 - Average time delay between marketing authorisation and "accessibility"



Source: EFPIA

[10] IMS, *Pharma Pricing and Reimbursement*, January 2011.

The W.A.I.T. indicator does not reveal the share of the delay in time to market that can be explained by pricing and reimbursement procedures. However, combining WAIT data with information from the pharmaceutical sector inquiry on which countries are approached first by originator companies for pricing and reimbursement can provide an initial insight into the share of time to market that can be explained by delays in pricing and reimbursement. The upper left cells in the table below (France & Italy) indicate countries that are among the first to be approached for pricing and reimbursement and which, at the same time, exhibit long times to market. This suggests that in these Member States pricing and reimbursement delays could explain a larger proportion of the WAIT indicator. Countries in the lower left cell (Denmark) combine a short WAIT indicator with a relatively late approach for pricing and reimbursement which suggests that P&R procedures in these countries are comparatively quick.

Table 2 - WAIT indicator and relative timing of pricing and reimbursement applications

	Among first to be approached for P&R	**Approached after the first wave**
Long WAIT	Italy France	Belgium
Medium WAIT	Netherlands Spain	Greece Finland Portugal
Short WAIT	Sweden Ireland	Denmark

Note: only countries in both WAIT and studies. Source: EFPIA for WAIT indicator, sector inquiry for timing of pricing and reimbursement applications.

Finally, it should be noted that data on time delays do not in themselves inform about the quality of the pricing and reimbursement procedure. Interviews with sector representatives as part of a study on the "Competitiveness of the EU Market and Industry for Pharmaceuticals" for DG Enterprise also specified that such delays occur across the EU. In particular, it was stated that some countries' administrations bring out an automatic negative advice after 180 days, forcing the pharmaceutical applicant company to resubmit its pricing and reimbursement application. This way, the countries comply with the Transparency Directive, but stall the procedure by giving a negative evaluation to the application.

1.2. Main reasons for delays – originators

A number of reasons have been put forward to explain why delays occur in the pricing and reimbursement decision making process for new products. Information collected from the pharmaceutical sector suggests that they see the following as being the main reasons for the delays:

- Fragmentation of national decision making processes, including more decision making at regional, local or even hospital levels. Such fragmented decision making requires negotiations with many different parties, delaying the process and increasing administrative costs[11];

[11] European Commission (2008) *Pharmaceutical Sector Inquiry Preliminary Report.* Brussels, DG Competition.pg. 391-392.

- Price conversions within the EU, driven by cross-border price referencing, i.e. the practice of some Member States referring to other countries' pricing and reimbursement decisions before taking their own decision. As a result of such practices, originator companies will often apply for pricing and reimbursement in Member States where they expect high prices, and then (if at all) apply in other countries[12];

- Practices to control expenditure such as therapeutic reference pricing (and the inclusion of patented products), which places medicines to treat the same medical condition into groups or 'clusters' with a single common reimbursed price;

- The increasing use of health technology assessments; and

- Publication delays.

Delays may also occur as a result of pharmaceutical companies strategically holding off submitting applications in countries where strict price control referencing exists, or where the markets are smaller. In addition, because lower prices in some Member States may influence prices in others, through parallel trade and price referencing, manufacturers may prefer longer delays or non-launches to the acceptance of a relatively low price. This suggests that pricing regulations can exacerbate delays in time to market in some countries[13], and countries with low prices for pharmaceuticals generally have fewer launches and longer launch delays.

2. PRICING AND REIMBURSEMENT DELAYS FOR GENERIC MEDICINES

2.1. Observed delays - generics

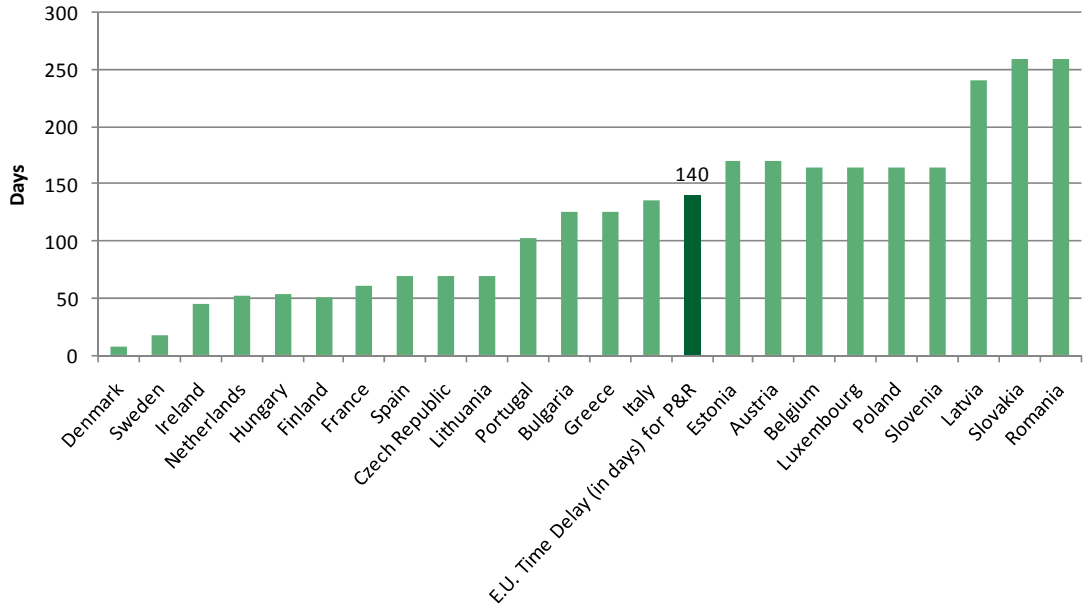
Patent protections for specific pharmaceuticals are valid for a fixed period of time during which they have exclusive rights to manufacture and market the product. When patent protection expires, originator companies lose these exclusivity rights and generic manufacturers can enter the market with equivalent medicines. These generics are usually sold at significantly reduced prices, which can reduce the strain on public health budgets, as well as creating incentives for continued innovation.

As with new pharmaceutical products, the Transparency Directive specifies a 90-day limit for adopting decisions on pricing and a further 90 days for reimbursement. However, studies have shown that in practice these time limits are often exceeded. Moreover, there is considerable variation across Member States.

Figure 4 - Time delay (in days) for P&R approval for a generic medicine after granting of market authorisation (2005)

[12] ECORYS Research and Consulting (2009) *Competitiveness of the EU Market and Industry for Pharmaceuticals: Volume 1: Welfare Implications of Regulations.* Rotterdam, Netherlands. pp. 62-67

[13] ECORYS Research and Consulting (2009) *Competitiveness of the EU Market and Industry for Pharmaceuticals: Volume 1: Welfare Implications of Regulations.* Rotterdam, Netherlands. pp. 62-67



Source: EGA

The figure above shows the results of a survey carried out by EGA (2005) of pricing and reimbursement delays for generics across 23 Member States. Whilst some Member States are well within the 90/180 days permitted, others exceed these timescales considerably. For example, a generic product approved through the same EU registration procedures is typically launched one year earlier in the Netherlands than in Belgium due to delays in pricing and reimbursement approvals. Latvia, Slovakia and Romania have the longest delays, whist Denmark, Sweden and Ireland have the quickest pricing and reimbursement procedures for generics.

Although it has been suggested that the delays for generics have improved as a result of the Transparency Directive, time delays are a challenge to the competitive generic medicines industry and can make it difficult for generic manufacturers to assess how long it will take for them to launch a product onto a particular market[14].

2.2. Main reasons for delays – generics

Findings from the sector inquiry for pharmaceuticals suggest that the main obstacles for generic companies are discrepancies in assessment criteria, patent linkage (i.e. some regulatory bodies consider whether the generic product may infringe the originator company's patents). Generic companies have also argued that these delays result not only from the decision making procedures, but often also from the additional requirements for obtaining pricing and reimbursement status for generic medicines, e.g. information on the patent status or concerning complete equivalence between the originator and generic product. These additional requirements seem to give opportunities for originator companies to intervene and hence prolong the de-facto exclusivity period of their product.

Alleged claims of patent infringements are another potential reason for delays in pricing and reimbursement decision making. Specifically, it has been suggested by some generic companies that alleged claims of potential patent infringements can delay the process because

[14] Perry, G (2006). The European generic pharmaceutical market in review: 2006 and beyond. Journal of Generic Medicines, 4, 4 – 14.

some Member States' pricing and reimbursement authorities prefer to wait until the situation is clarified before coming to a decision[15]. For example, in Portugal, the pricing decision is often suspended due to interim injunctions that have been filed against the marketing authorisations. The pricing decision remains suspended until the court has ruled on the marketing authorisation.

Another potential obstacle for generic entry lies in the need for absolute equivalence between generic versions and the originator, requested by pricing and reimbursement authorities in some Member States in order to allow substitution. These requirements go much further than the bio-equivalence requested for marketing authorisations, and can include, for example, identical pack sizes, identical doses, identical patient information leaflets and/or identical summaries of product characteristics[16].

Finally, like for originators, publication delays can have a significant impact on overall pricing and reimbursement delays.

[15] European Commission (2008) *Pharmaceutical Sector Inquiry Preliminary Report.* Brussels, DG Competition. P. 394-396.

[16] European Commission (2008) *Pharmaceutical Sector Inquiry Preliminary Report.* Brussels, DG Competition. pg.395

ANNEX 6

CASE-LAW OF THE COURT OF JUSTICE RELATING TO COUNCIL DIRECTIVE 89/105/EEC[1]

1. OVERVIEW

The European Court of Justice has examined several cases in relation to Directive 89/105/EEC. Its judgements clarified issues related to the scope of the Directive, time-limits, appeal procedures and the direct effect of several articles of the Directive.

Relevant cases:

– Case C-424/99 of 27 November 2001, Commission v. Austria

– Case C-229/00 of 12 June 2003, Commission v. Finland

– Case C-245/03 of 20 January 2005, Merck, Sharp & Dohme

– Case C-296/03 of 20 January 2005, GlaxoSmithKline

– Case C-317/05 of 26 October 2006, Pohl-Boskamp

– Case C-311/07 of 17 July 2008, Commission v. Austria

– Case C-352/07 of 2 April 2009, Menarini and joined cases C-353/07 to C-356/07, C-365/07 to C-367/07 and C-400/07

– Case C-417/07 of 14 January 2010, AGIM and joined case C-472/07

– Case C-62/09 of 22 April 2010, ABPI

At the time of adoption of the directive, in December 1988, the design of health insurance systems in the Member States was usually less complex than nowadays. Pricing and reimbursement procedures mainly involved the submission of an application followed by a decision-making process to determine the price of the medicine and/or its eligibility to reimbursement. However, since then, national pricing and reimbursement systems have evolved and more complicated mechanisms have been put in place.

In order to ensure that the objectives of the Directive are achieved, the Court adopted an extensive interpretation based on the purposes of the Directive and going beyond the mere wording of its provisions.

[1] Working document prepared for information purposes by the services of DG Enterprise and Industry. This document does not represent an official position of the European Commission.

Key Principles established by the Court

- Directive 89/105 has as its underlying principle the idea of minimum interference in the organisation by Member States of their domestic social security policies.[2] The requirements arising from Directive 89/105 affect neither the Member States' policies for determining the prices of medicinal products nor national policies on price setting or on the determination of social security schemes, except as far as it is necessary to attain transparency for the purposes of that directive.[3]

- The objective of Directive 89/105/EEC is to ensure, in accordance with its Article 1, that any national measure to control the prices of medicinal products or to restrict the range of medicinal products covered by the national health insurance systems complies with its provisions.[4]

- The fundamental principle established by the ECJ is that Directive 89/105/EEC must be interpreted in light of its objectives so as to ensure its effectiveness (*'effet utile'*).[5] An extensive interpretation of the provisions of the Directive must prevail because it is linked to the free movement of goods, which is one of the fundamental freedoms of the Community.

2. THE SCOPE OF THE DIRECTIVE

2.1. Introduction

The case-law of the Court mainly relates to national procedures on the coverage of medicines by health insurance systems (Article 6 of the Directive). The wording of Article 6 often appears too restrictive to encompass new forms of pricing and reimbursement which have been established by Member States. The article refers to "positive lists":

> The following provisions shall apply if a medicinal product is covered by the national health insurance system only after the competent authorities have decided to include the medicinal product concerned in a positive list of medicinal products covered by the national health insurance system […].

The main challenge with Article 6 lies in the fact that Member States rely "primarily on the actual wording of the introductory passage in Article 6."[6] According to advocate General Tizzano, this provision "is not particularly well worded."[7] In his opinion, the logic of this

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2 Case C-245/03 Merck, Sharp & Dohme [2005] ECR I-637, para.27; Joined Cases C-352/07 to C-356/07, C-365/07 to C-367/07 and C-400/07 *Menarini Industrie Farmaceutiche Riunite and Others*, nyr, para. 36;
Joined Cases C-352/07 to C-356/07, C-365/07 to C-367/07 and C-400/07 *Menarini Industrie Farmaceutiche Riunite and Others*, nyr, para. 35
Case C-424/99 *Commission of the European Communities v Republic of Austria* [2001] ECR 9285; Case C-229/00 *Commission of the European Communities v Republic of Finland* [2003] ECR 5727; Case C-317/05 *Pohl-Boskamp* [2006] ECR I-10611

5 Case C-229/00 *Commission of the European Communities v Republic of Finland* [2003] ECR 5727

6 Opinion of Advocate General Tizzano in Case C-424/99 *Commission of the European Communities v Republic of Austria* [2001] ECR 9285

7 Opinion of Advocate General Tizzano in Case C-424/99 *Commission of the European Communities v Republic of Austria* [2001] ECR 9285, para. 31

provision and the intention of the directive are to refer to all cases where inclusion of a medicinal product in a list entails automatic reimbursement of it. The fact that in one Member State reimbursement is also possible under certain conditions for medicines not included in the list does not detract from the relevant factor, which is that to include a product in a list normally means that it is automatically reimbursed.

This interpretation reconciles its wording with the declared intent of the Directive: "Member States shall ensure that any national measure, whether laid down by law, regulation or administrative action, to [...] restrict the range of medicinal products covered by their national health insurance systems complies with the requirements of this Directive.

Advocate General Tizzano considers that the decisive factor is the fact that this provision aims at ensuring free movement of goods. According to the settled case-law, this requires a broad interpretation of the relevant requirements and not an interpretation which is restrictive and would affect its efficacy. By interpreting this provision in a different way, it would mean that Member States would be encouraged "to evade, by means of formal and nominalistic arrangements, the obligations imposed in the directive".[8]

Several rulings of the Court also relate to Article 4, which lays down obligations on the Member States in case of price freeze. The Court ruled that Article 4(1) encompasses all national measures controlling the prices of medicinal products, in particular price reductions, even if these measures are not preceded by a price freeze.

2.2. Interpretation of Article 6: inclusion of medicinal products in the national health insurance system

2.2.1. Case C-424/99, Commission v. Austria (27 November 2001)

In *Commission v Austria*,[9] the Court had to clarify the concept of positive list in the meaning of the Directive. This judgement shed light on the scope of the Directive as well as on the interpretation of Article 6.

Facts

In Austria, medicines that appear on the register of medicinal products are reimbursed. However, there is also another possibility to have the cost of the medicinal products borne by the health insurance scheme: if the principal doctor or the supervising doctor of the competent social security institution agrees that it is necessary and appropriate for the patient, in view of his condition. In this case, prior authorization must be given by that doctor.

The Austrian government contended that Article 6 of the directive did not apply since that article referred to a positive list and that a list of medicinal products constituted a positive list only where authorization by the social security system of prescription of a medicinal product was dependant upon the inclusion in the list. The Austrian authorities argued that medicinal products which were not in the register could have been reimbursed, where patients have obtained authorization. Their position was therefore that the register is not an exhaustive catalogue of the medicinal products covered by the sickness insurance scheme but just a

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8 Opinion of Advocate General Tizzano in Case C-424/99 *Commission of the European Communities v Republic of Austria* [2001] ECR 9285, para. 33

9 Case C-424/99 *Commission of the European Communities v Republic of Austria* [2001] ECR 9285

working tool for the use of doctors, enabling them to determine which medicines were going to be covered by the social security scheme without prior authorization. The Austrian government also claimed that the Commission was interfering in the organization of the national social security systems.

Findings and main implications of the judgement

- The Court of Justice ruled that the Community did not question the method of financing or the structure of the social security system, but only sought to ensure compliance with the provisions of the Transparency Directive.

- The Court established that the sole determining factor that qualifies a positive list is the fact that inclusion of a medicinal product in this list normally means that its costs will be automatically borne by the social security system. It is irrelevant that the cost of products which are not included on the list can be covered by the scheme if there is an authorization from the doctor. Therefore, Article 6 applies where the inclusion of a medicinal product on a list leads to automatic coverage by the health insurance system.

- The Court justified this interpretation based on the purpose of the Directive, which is to ensure that any national measure to control the prices of medicinal products for human use or to restrict the range of medicinal products covered by the national health insurance systems complies with the requirements of the directive (Article 1).

2.2.2. Case C-229/00, Commission v. Finland (12 June 2003)

In *Commission v Finland*,[10] the Court had to determine whether the decisions establishing categories of products subject to higher-rate reimbursement fall within the scope of Article 6 of the Directive. The decision establishing the list of active ingredients which received higher-rate coverage was not adopted pursuant to an individual application, did not contain any statement of reasons and was not open to judicial review.

Facts

In addition to the basic scheme of insurance cover, the Finnish system provided for higher-rate reimbursement schemes with respect to medicinal products which are essential for the treatment of serious or chronic illnesses. The Council of Ministers determined by decree the serious and chronic illnesses for which patients may receive higher-rate reimbursement and drew-up a general list of the active ingredients used in medicinal products to combat these illnesses. The Institute for Social Security subsequently established a list of the medicinal products already covered by the basic health insurance scheme, which contained one of the active ingredients listed in the decree. The products present on this list were entitled to higher-rate reimbursement.

The Finish government contended that Article 6 of the Directive did not apply to the decree of the Council of Ministers since the decree did not result in the inclusion of a medicinal product on the list of medicinal products qualifying for higher-rate cover, but just drew a list of active ingredients. It also considered that the decision establishing the list of active ingredients used in medicinal products which may receive higher-rate coverage was not adopted pursuant to an individual application and therefore was not subject to Article 6 of the Directive.

[10] Case C-229/00 *Commission of the European Communities v Republic of Finland* [2003] ECR 5727

Findings and main implications of the judgement

- Article 6 applies to measures of a general nature where they amount to a bundle of individual decisions.

  The Court ruled that it is necessary to interpret the Directive in the light of its objectives and not to limit the interpretation to the wording of the articles. A measure which does not directly provide for the inclusion of the medical products on the list of medicinal products qualifying for higher-cover rate, but decides only on the active ingredients which are going to be included in that scheme, falls within the scope of the Directive. In the Finnish case, the general measure (decree of the Council of Ministers) was considered as a bundle of individual decisions because the body establishing the actual positive list had no discretion as to the choice of products to be included in the list. Therefore, any measure which affects the coverage of medicinal products by the national sickness insurance systems falls within the scope of the Directive.

- Existence of an application and protection of the parties concerned

  The Court addressed the issue of a lack of application to include a medicine on the list of medicinal products qualifying for sickness insurance cover. It ruled that the Directive should be interpreted so as to give the persons concerned the possibility to verify that the official entry of medicinal products on the list corresponds to objective criteria and that there is no discrimination between national medicinal products and those from other Member States. This issue is very important since the organisation of national systems has evolved and measures taken to determine the conditions of reimbursement of medicines are not always adopted as a result of an individual application.

- Where different categories or modalities of reimbursement exist (for instance different levels of coverage by the health insurance system), Article 6 applies to all these categories, levels or modalities

  The Court ruled that Member States cannot circumvent their obligations by creating one reimbursement category which respects the requirements of the Directive, while other reimbursement categories do not comply with these requirements.

- Principle of non-interference

  The Court confirmed that the Directive does not interfere with the organisation of the national social security schemes. The method of financing, the structure of the social security system is not called into question. Pricing and reimbursement of medicinal products clearly fall within the scope of national competence, but the Directive establishes a series of procedural requirements to provide assurance that national measures do not amount to barriers to trade. According to its sixth recital, the "requirements [imposed by the Directive] do not affect national policies on price setting and on the determination of social security schemes, except as far as it is necessary to attain transparency within the meaning of this Directive".

- It is the effect of the measure that determines whether it constitutes an individual decision

  The Finnish decree in question was found to infringe Article 6(1) and (2) of the Directive. This is important since the Finnish authorities in their defence argued that these articles are not applicable because the decree in question is regulatory in nature and therefore falls

within the scope of Article 7(3). Advocate General Tizzano[11] argued that the Council of Minister's decree was not a measure laying down general and abstract criteria to be taken into account by competent authorities in deciding whether or not to include medicinal products on the lists: the decree determined not only the active ingredients but also the individual medicinal products containing them that would be included in the higher-rate reimbursement scheme. He concluded that even if it is a piece of delegated legislation, the decree contains a series of individual decisions on the inclusion of specific medicinal products in the national health insurance scheme. Therefore, it is important to look at the effect of the measure in order to determine whether it is an individual decision.

2.2.3. Case C-317/05, Pohl Boskamp (26 October 2006)

Facts

The Court was asked to rule on a preliminary question regarding the compatibility with the Directive of a system which, after excluding non-prescription medicinal products (OTCs) from the scope of reimbursement, enables an authority to grant derogations from this exclusion to certain OTCs, without providing for the procedural requirements laid down in Article 6(1) and 6(2) of the Directive (e.g. time-limits, obligation to provide a statement of reasons, possibility to appeal). Under the system at issue, the responsible national authority – the 'Gemeinsamer Bundesausschuss' – established a list of active ingredients used in the treatment of serious illnesses which may, by way of exception, be prescribed and financed by the national health insurance system.

Findings and main implications of the judgement

- The Court confirmed the broad interpretation of the notion of positive list

  A list of active ingredients or medicinal products qualifies as a positive list as soon as the inclusion of an ingredient or product in this list entails its coverage by the national health insurance system. This conclusion applies regardless of the formal qualification of the list and regardless of the national body or institution which makes the decision.

- The Court confirmed that measures of a general nature are covered by Article 6 of the Directive if they amount to a "bundle of individual decisions"

  In the system described, the decisions made by the national authorities constitute a bundle of individual decisions affecting several interested parties. The fact that the marketing authorisation holders are affected entitles them to claim the rights accorded by Article 6 of the Directive. The Court reiterated that Member States cannot establish a dual procedure for the establishment of the list of products qualifying for reimbursement: one which complies with the Directive and one which is exempt from its obligations.

- The judgement confirmed that the Directive cannot be interpreted restrictively so as to guarantee its effectiveness:

  The reasoning of the ECJ is again based on the objectives of the Directive: ensuring the effectiveness of the Directive requires that the persons concerned can verify that the

[11] Opinion of Advocate General Tizzano in Case C-229/00 *Commission of the European Communities v Republic of Finland* [2003] ECR 5727, paras.35-40

inclusion of medicines into the list responds to objective criteria and that there is no discrimination between national products and products from other Member States.

- With regard to the claim of the German authorities that the Directive applies only to applications submitted by the holder of a marketing authorisation, the Court ruled that the marketing authorisation holders affected are entitled to claim rights.

  Failure to communicate the list of medicinal products to Pohl-Boskamp, as well as the lack of a statement of reasons and information on the legal remedies available, infringe the requirements of Article 6(2) of the Directive.

- The Court also considered that the existence of a barrier to intra-Community trade is not a pre-requisite for the application of the Directive.

2.2.4. Case C-311/07, Commission v. Austria (26 October 2006)

The Court was asked to determine whether national rules on the inclusion of products on a reimbursement list comprising several categories of reimbursement were compatible with Article 6 of the Directive.

Facts

The litigation related to national rules on the inclusion of medicinal products in a positive reimbursement list. The list in question (the Austrian reimbursement code) comprised three categories of reimbursement, designated as red box, yellow box and green box. The conditions of reimbursement of a given medicinal product were dependent on its classification in one of these categories, with the green and yellow box offering more favourable reimbursement conditions than the red box.

Upon application for inclusion in the reimbursement code, medicinal products were immediately included in the red box for a maximum period of 24 months (or 36 months under specific circumstances). During this period, the national authorities would decide if the medicinal products should be included in the yellow or green box, or excluded from reimbursement.

The Commission argued that the Austrian system did not guarantee the inclusion of medicinal products in the yellow or green box within 90 or 180 days, in contradiction with Article 6(1) of Directive 89/105/EEC. The Austrian authorities refuted this view, considering that the reimbursement code, taken as a whole, constitutes a positive list within the meaning of Article 6(1). National legislation was deemed to be in line with the time-limits of the directive, insofar as medicinal products had access to reimbursement as soon as they were included in the red box (a decision which took less than 90 days).

Findings and main implications of the judgement

- The Court dismissed the Austrian argument of interference in the organisation of its national social security scheme: the Commission only sought to ensure the observance of the requirements of the Directive but did not put into question the method of financing or the structure of the social security system. It recalled that the objective of Directive 89/105/EEC is to ensure, in accordance with its Article 1, that any national measure to control the prices of medicinal products or to restrict the range of medicinal products

covered by the national health insurance systems complies with its provisions. Decisions to include a medicinal product in the Austrian reimbursement code, and more specifically in the yellow or green box of the code, constitute such measures. They are, therefore, subject to the requirements of the directive.

- The Court concluded that the Austrian system does not comply with Article 6(1) of the directive because it does not guarantee that applications for inclusion in the yellow or green box of the reimbursement code will be addressed within 90 days (reimbursement decision only) or within 180 days (joint pricing and reimbursement decision). The fact that an application to include a medicinal product in the code leads to its temporary inclusion in the red box is irrelevant. Indeed, this temporary classification does not mean that the inclusion of the product in the yellow or green box will be decided within the time-limits prescribed by Article 6(1).

- The judgement confirmed that, if a national health insurance system comprises different categories of reimbursement, the obligations of Article 6(1) apply to the inclusion of medicinal products in any of these categories – i.e. not only to the least favourable reimbursement category, but also to the categories providing more favourable reimbursement conditions.

- This interpretation applies *mutatis mutandis* to the other provisions of Article 6. Member States cannot circumvent their obligations under the directive by creating one basic or least favourable reimbursement category which respects the requirements of the directive, while other, more favourable reimbursement categories would not comply with these requirements.

2.2.5. Case C-62/09, ABPI (22 April 2010)

Facts

Case C-62/09[12] addresses the issue of "demand-side" measures. The Court had to decide in a preliminary ruling over the financial incentives granted to doctors to prescribe specific named medicines.

Findings and main implications of the judgement

- The Court ruled that public authorities are allowed to offer financial incentives to doctors to prescribe specific named medicines belonging to the same therapeutic class: this does not constitute an advertising of medicines prohibited by Directive 2001/83/EC. However, the Court considered that these financial incentives given to doctors should comply with the provisions of Directive 89/105/EEC: measures which are addressed to doctors must be transparent, must be based on objective and non-discriminatory criteria. The reason behind this is that the incentives given to doctors affect the list of what is being reimbursed and it is important that these measures be transparent.

- This judgment is important as it tackles the “demand-side measures”. National systems increasingly use measures aimed at health professionals, such as financial incentives or prescription guidelines, to contain pharmaceutical costs. As these measures affect the

[12] Case C-62/09 *Association of the British Pharmaceutical Industry v Medicines and Healthcare Products Regulatory Agency*, nyr

medicines which are prescribed, delivered and eventually reimbursed, the Court recognized the need for the professionals in the pharmaceutical industry to verify whether these schemes are based on objective and verifiable criteria and whether there is no discrimination between national medicinal products and those from other Member States.

2.3. Interpretation of Article 4: price freezes and price reductions

2.3.1. Case C-352/07, Menarini and joined cases (2 April 2009)

The judgement relates to the interpretation of Article 4 of Directive 89/105/EEC. It highlights the procedural obligations which Member States have to follow when they introduce price freezes or price reductions (both are covered by the directive). It also clarifies the margin of discretion of the national authorities in relation to such measures.

Facts

During 2005 and 2006, the Italian authorities introduced several measures reducing the prices of medicines with a view to ensuring compliance with the ceiling of expenditure laid down by national law. These successive measures were adopted on the basis of a predicted over-expenditure, rather than on the basis of actual figures.

Several pharmaceutical companies challenged these price reduction measures before the "Regional Administrative Court of Lazio". Several questions related to the interpretation of Article 4(1) and 4(2) of the Transparency Directive have been addressed to the ECJ.

Findings and main implications of the judgement

- The Court ruled that Article 4(1) encompasses all national measures controlling the prices of medicinal products, even if these measures are not preceded by a price freeze. It considered that Article 4 should be interpreted by reference to the purpose and general scheme of the Directive. A restrictive interpretation of the Directive is not desired as this would tantamount to excluding measures reducing the prices of all, or of certain categories of medicinal products, if such measures are not preceded by a freeze on those prices. Moreover, the Court ruled that an interpretation according to which the adoption of measures reducing the prices of all, or of certain categories of medicinal products must be preceded by a freeze would affect Member States' price fixing policies and this would go beyond the purpose of the Directive.

- The Court ruled that Member States were allowed to adopt price reduction measures for all medicinal products, or for certain categories of medicinal products, more than once a year and to do so for several consecutive years. The only condition would be to carry out a review of the macro-economic conditions which justify the freeze to be continued, at least once a year. This is also a minimum requirement, meaning that Member States may carry out such a review more than once a year.
- The Court ruled that Article 4(1) of the Directive must be interpreted as meaning that it does not preclude measures controlling the prices of all, or of certain categories of, medicinal products from being adopted on the basis of predicted expenditure, provided that the requirements laid down by that provision are met and that the predictions are based on objective and verifiable data. A contrary interpretation would constitute interference in the organisation of national social security policies of the Member States. It underlined the leeway margin left to the Member States, but in the same time it is also

pointed out that this discretion is not unlimited and that the predictions used by the national authorities must be based on objective and verifiable data.

- The Court considered that it is up to the Member States to decide on the criteria on the basis of which the review of the macro-economic conditions is to be conducted. These macro-economic conditions can consist of pharmaceutical expenditure alone, in health expenditure overall or even in other type of expenditure.

- The Court ruled that Member States must, in all cases, provide for the possibility for the companies concerned by a price freeze or price reduction to apply for a derogation from the price imposed, without prejudice to the ascertainment by the national authorities that it is an exceptional case and that there are particular reasons for the company to do so. The genuine participation of the company concerned consists, first, in the submission of an adequate statement of reasons justifying the application for a derogation and, second, in the provision of detailed additional information if the information supporting the application is inadequate. The obligation for Member States to state the reasons for any refusal of such an application is also expressly imposed by Article 4(2).

2.3.2. Joined Cases C-471/07 and C-472/07, AGIM (14 January 2010)

The Court gave its interpretation with regard to Article 4(1) of the Directive 89/105/EEC. This case adds to the line of cases meant to define the scope and to clarify the provisions of Directive 89/105/EEC. In this case, the Court emphasises the margin of discretion left to the Member States in organising their national social security systems.

Facts

In Belgium, the authorities imposed a price freeze on medicinal products for the period 1 January 2003 to 31 December 2003 and from 1 July 2005 to 31 December 2005. Several pharmaceutical companies sought the annulment of the ministerial decree setting the price freeze. In both cases C-471/07 and C-472/07- the applicants claim the infringement of Article 4(1) of Directive 89/105/EEC.

Findings and main implications of the judgement

- The Court confirms the margin of discretion Member States have in determining criteria on the basis of which the review of macro-economic conditions must be carried out. It is up to the Member States to determine whether they take into account healthcare expenditure alone or other macro-economic conditions (such as those in the pharmaceutical industry sector) when reviewing the macro-economic conditions which justify a price freeze. It is also up to the Member States to determine whether the review of macro-economic conditions would be based on general trends, such as the financial balance of national health systems. However, those criteria must be in compliance with the objective of transparency pursued by Directive 89/105; thus, the criteria must be based on objective and verifiable factors.

- The judgement clarifies the situation where a price freeze is imposed after an interruption of 18 months from the previous price freeze, which lasted for 8 years. The Court rules that in such cases the new measures freezing prices can be taken without carrying out a review of the macro-economic conditions. The whole reason of having such an annual review is to make sure that the macro-economic conditions justify the price freeze to be continued.

3. TIME LIMITS

3.1. Case C-245/03 Merck, Sharp & Dohme (20 January 2005)

Questions related to the nature of time-limits and the consequences of exceeding the time-limit within which the competent authority is to respond have been addressed in *Merck*.[13]

Facts

In 2003, the Belgian Council of State requested interpretations from the Court of Justice with respect to the time-limit for reimbursement decisions laid down in Article 6(1) of the Directive (90/180 days). The key question was whether the absence of a decision by the national authorities within the prescribed time-limit entails the automatic inclusion of the product into the national health insurance system.

Findings and main implications of the judgements

The Court's judgements clearly establish that:

a) The time-limit for the inclusion of products into the reimbursement list is a mandatory time-limit which the national authorities are not entitled to exceed.

b) The Directive does not impose the automatic inclusion of a medicinal product on the reimbursement list if this time-limit is exceeded.

3.2. Case C-296/03, Glaxosmithkline (20 January 2005)

In this case the Court ruled that the time-limit laid down in the first subparagraph of Article 6(1) of the Directive is mandatory.

The Court also ruled on the consequences of exceeding the time-limit where a previous decision adopted in good time has been annulled. It decided that it would be for the Member State to determine whether the fact that the time-limit laid down in the first subparagraph of Article 6(1) of the Directive is exceeded precludes the competent authorities from formally adopting a new decision when the previous decision has been annulled in court proceedings, although such possibility can be exercised only within a reasonable time which may not in any event exceed the time-limit laid down in that article.[14]

This underlines the discretion left to the Member States to decide bout the consequences of exceeding the time-limit after a previous decision adopted in good time has been annulled. However, it also underlines the fact that this discretion is not limited, but the procedural rules set in the Directive must be observed.

4. APPEAL PROCEDURES

The Directive provides that the persons to whom the decisions are addressed should be informed of the remedies available and of the time limits allowed for applying such remedies.

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13 Case C-245/03 Merck, Sharp & Dohme BV vÉtat belge [2005] ECR I-637

14 Case C-296/03 *Glaxosmithkline SA v État belge* [2005] I-669, para.39

What is meant by the possibility to appeal is clarified by the Court in **Case C-424/99 Commission v. Austria (27 November 2001)**

Facts

In *Commission v Austria*,[15] there was only the possibility of complaint against the first recommendation of the small technical advisory board and a complaint to the main technical advisory board when the opinion of the board was negative. The Commission contended that these were not appeal procedures since this remedy laid not before the courts but before the administrative authorities.

Findings and main implications of the judgements

The Court ruled that appeal to independent experts could not be equated with the remedies mentioned in the Directive. Moreover, the small advisory board and the main one can issue only recommendations and have no decision-making power. The applicants must have the possibility to challenge decisions before genuine judicial bodies.

5. DIRECT EFFECT

5.1. Direct effect of Article 4 (1)

Joined Cases C-471/07 and C-472/07 Association générale de l'industrie du médicament (AGIM) and others v État belge [2010] nyr

The Court ruled that Article 4(1) of the Directive had no direct effect. It could not be considered as sufficiently precise for an individual to be able to rely on it before the national court against a Member State. Since the State was supposed to carry out a review at least once a year to ascertain whether the macro-economic conditions justify that price freeze and since the provision contained no indication as regards the matters on the basis of which measures to control the prices must be adopted, nor the criteria for such annual review, the conclusion was that there is no direct effect.

5.2. Direct effect of Article 6

Case C-317/05 G. Pohl-Boskamp GmbH & Co. KG v Gemeinsamer Bundesausschuss [2006] ECR I-10611

The Court ruled that Article 6(2) of the Directive had direct effect and should be interpreted as meaning that it confers on the manufacturers of medicinal products affected by a decision which allows the coverage by the health insurance system of certain medicinal products containing active ingredients referred to therein the right to a reasoned decision mentioning remedies, even though the rules of the Member State make no provision for any corresponding procedure or remedies.[16]

The full text of all judgements can be found on the website of the Court of Justice:

http://curia.europa.eu/

[15] Case C-424/99 *Commission of the European Communities v Republic of Austria* [2001] ECR 9285

[16] Ibid., para.44

ANNEX 7

MANAGED ENTRY OR RISK SHARING AGREEMENTS: OVERVIEW AND CASE STUDIES[1]

There is a burgeoning literature on the different types of conditional (risk sharing) agreements that have recently been introduced in different EU Member States.[2] These instruments are seen by some as potentially effective tools to contain the increase in public expenditure on pharmaceuticals, ensure that reimbursed medicines deliver on promised health outcomes and reward innovation.[3] At the same time, risk sharing is also often presented as a way of extending patient access to medicines that would otherwise not have been approved for reimbursement. For instance, risk-sharing can play a role when there is uncertainty around the effectiveness of the product.[4]

The popularity of risk sharing schemes is likely to increase over time as public health budgets come under increasing financial pressure and demand for pharmaceuticals continues to rise (as seen in the previous section). This is for instance clearly the case in the UK where the Department of Health has launched a consultation on plans to implement "value based pharmaceutical pricing". Negotiations with industry will start in April 2011 with new arrangements coming into force when the current pharmaceutical price regulation scheme (PPRS) expires in 2013.[5] This system will be designed to support the "use of risk-sharing schemes to enable early uptake of new medicines which lack cost-effectiveness data".[6]

The two main types of risk-sharing agreements that have been implemented in Europe are price volume agreements (PVA) and performance based guarantees. The box below has a list of key examples of PVAs as well as indications on the extent to which these are being used in some Member States.

Box 1 - Examples of price volume agreements and associated market share

- **Estonia** – PVA's are mandatory for all pharmaceutics on the positive list.
- **Lithuania** – Since 2008, PVAs are mandatory for all new pharmaceuticals which will increase the Statutory Health Insurance budget compared with currently available treatment.
- **France** – If sales of a particular pharmaceutical exceed projections, companies are required to pay back a certain percentage which varies by class and year. In 2004 rebates were 670 million Euros which is equivalent to 3% of the total pharmaceutical expenditure.
- **Hungary** – Similar to France, payback mechanism has been in place since 2003. In 2006 rebates amounted to 22.5 billion HUF which is equivalent to 5.96% of the budget

Source: Risk sharing arrangements for pharmaceuticals: potential considerations and recommendations for European payers, (2010) Adamski et al., volume 10(153)

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1 Working document based on research by Matrix Insight Ltd for DG Enterprise and Industry. This document does not represent an official position of the European Commission.

2 IMS, *Pharma Pricing and Reimbursement*, January 2011.

3 IMS, *Pharma Pricing and Reimbursement*, January 2011.

4 Mondher Toumi, *European Market Access Policies: Setting the Scene*, EMAUD, 8 December 2009

5 IMS, *Pharma Pricing and Reimbursement*, January 2011.

6 Conservative Party, *Improving access to new drugs: a plan to renew The National Institute for Health and Clinical Excellence (NICE)*, cited in Dr P Meir Pugatch, Paul Healy and Rachel Chu, *Sharing the burden – could risk-sharing change the way we pay for healthcare?* Stockholm Network (2010).

Table 1 provides more detail on the risk-sharing agreements outlined above and it provides a number of examples of performance guarantee agreements. The table is not a comprehensive list of such agreements but it does provide an overview of examples that are currently operating across Europe.

Table 1 - Examples of risk-sharing agreements

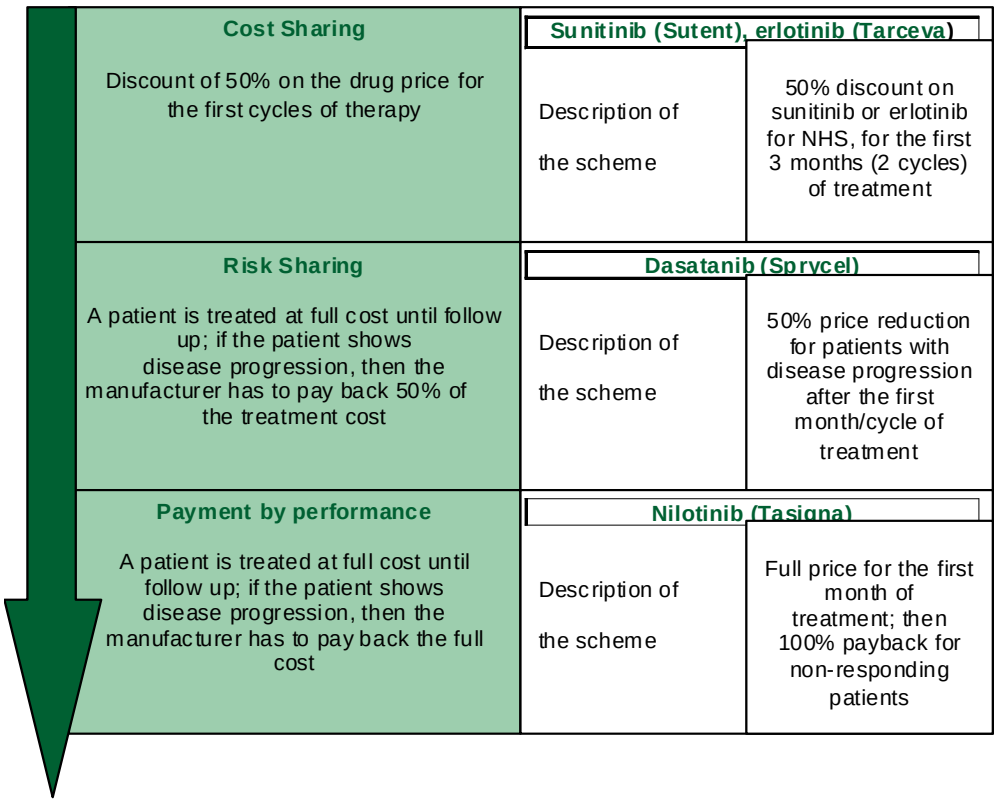
Country	Type	Disease area	Manufacturer	Agreement
Estonia	Price volume agreement	All	All	Obligatory for all pharmaceuticals on the positive list. If agreed volumes are exceeded, negotiations take place between the Ministry of Social Affairs and the pharmaceutical company to determine the rationale and course of action. Agreed actions may include lowering reimbursed prices
France	Price volume agreement	Mucopolysaccharide type VI disease Paroxysmal nocturnal haemoglobinuria	BioMarin Pharmaceutical Inc Alexion Pharmaceuticals	Two schemes exist in France. These include a payback mechanism for excessive sales by therapeutic class and are based on pharmaceutical company's agreed turnover with annual financial adjustments. They also include regular price reviews based on the average daily costs, the average dose or the total number of units established at the time of reimbursement. Payback mechanisms per class are not the same each year. In 2004, total rebates amounted to €670 mn - some 3% of total pharmaceutical expenditure. There were two schemes in 2008; the first involved Naglazyme - for the treatment for mucopolysaccharide type VI disease - and the second involved Soliris - for the treatment of paroxysmal nocturnal haemoglobinuria - rebates were €260 mn.
France	Coverage with evidence development	Schizophrenia	Johnson & Johnson	France's health care authority agreed to cover Risperdal Consta at the asking price if J&J performed studies to show that the product helps patients stay on medication. Otherwise, J&J will reimburse a proportion of the money spent on the drug.
Germany	Performance guarantee	Kidney transplant	Novartis	Novartis and DAK (a German insurance company) have an agreement to fund money for Sandimmun Optoral (cyclosporin), Myfortic (mycophenol) acid) or Certican (everolimus) if a patient loses his/her donor kidney.
Germany	Performance guarantee	Osteoporosis	Novartis	DAK and Barmer (a German insurance company) have a money back guarantee for Aclasta (zoledronat) if an osteoporosis-related fracture occurs.
Hungary	Price volume agreement	N/A	N/A	A general payback scheme has been in operation since 2003 based on individual products as well as total pharmaceutical expenditure. The payback in 2006 was 22.5 billion HUF (€90 mn - 5.69% of the budget).
Lithuania	Price volume agreement	All	All	Since 2008 schemes are obligatory for all new pharmaceuticals that will increase the Statutory Health Insurance drug budget compared with current treatment approaches for the target patient population. Once instigated, PVA scheme are currently valid for a minimum of three years. If agreed sales volume (expenditure) exceeds the agreed target, pharmaceutical companies must refund all the difference.
UK	Performance guarantee	High cholesterol	Parke-Davis (Pfizer)	Parke-David (Pfizer) agreed to rebate the local payer if a defined patient population did not achieve a low density lipoprotein cholesterol concentration target after using statins.

UK	Performance guarantee	Colorectal cancer	Merck	Rebate direct to primary care trust on the cost of any vials of Erbitux (cetuximab) used for patients who do not achieve a pre-agreed clinical outcome at up to 6 weeks.
UK	Performance guarantee	Multiple myeloma	Johnson & Johnson	J&J agreed to reimburse the NHS in either cash or product for patients who do not respond after four cycles of treatment with Velcade. Responding patients receive additional four cycles.
UK	Performance guarantee/ coverage with evidence development	Multiple sclerosis	Biogen, Schering, Teva/Aventis, Serono	Patients using interferon beta or glatiramer acetate are followed for 10 years with treatment effects determined every two years. Drug price reduced to maintain cost effectiveness at £36,000/QALY.

Source: IMS 08-2009: Innovative Pricing Agreements to Enhance Access Prospects, pg. 240

There are a number of ways in which risk sharing schemes can be implemented in practice. For instance, under the Italian scheme, the National Health Service (Servizio Sanitario Nazio nale/SSN) pays only 50% of the ex-factory price during a defined period of time. After that period, if patients respond positively, the medicine is reimbursed 100%; for patients that fail to respond to treatment, no further payment is made. Alternatively, treatment is fully reimbursed for an agreed period, but continues beyond that period only for responders. If patients do not respond to the treatment, it stops and manufacturers must pay back the cost of the medicines to the SSN.[7] The figure below shows the three types of managed entry schemes available under the Italian system.

Figure 1 – Examples of three types of managed entry schemes in Italy

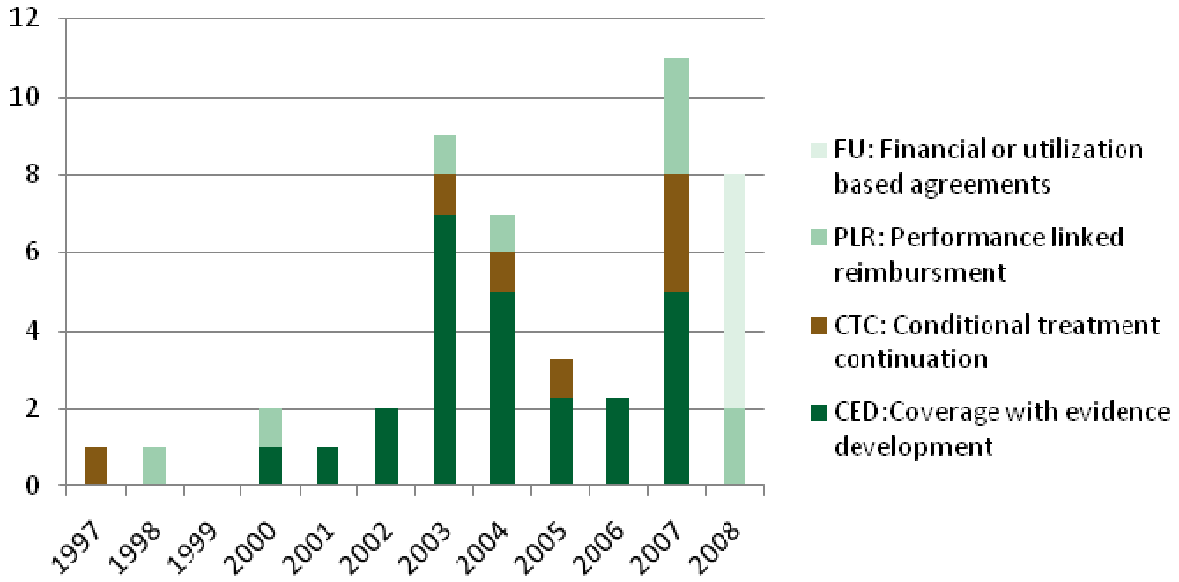


Source: Mondher Toumi, European Market Access Policies: Setting the Scene, EMAUD, 8 December 2009.

[7] Espin, Jaime, Rovira, Joan. (2009) *Risk Sharing Schemes for Pharmaceuticals: Terminology, Classification, and Experiences.* Spain, Andalusian School of Public Health. pp 13-14.

While there is a lot of literature describing different innovative approaches to pricing and reimbursement, there are no comprehensive data on the extent to which these different contractual agreements are used across Europe at present or how much of the market is currently operating under an innovative contractual arrangement. However, the figure below provides an overview of the number of performance based schemes by country in some Member States.

Figure 2 - Number of performance-based schemes in Europe, 1997-2008



Source: Mondher Toumi, European Market Access Policies: Setting the Scene, EMAUD, 8 December 2009.

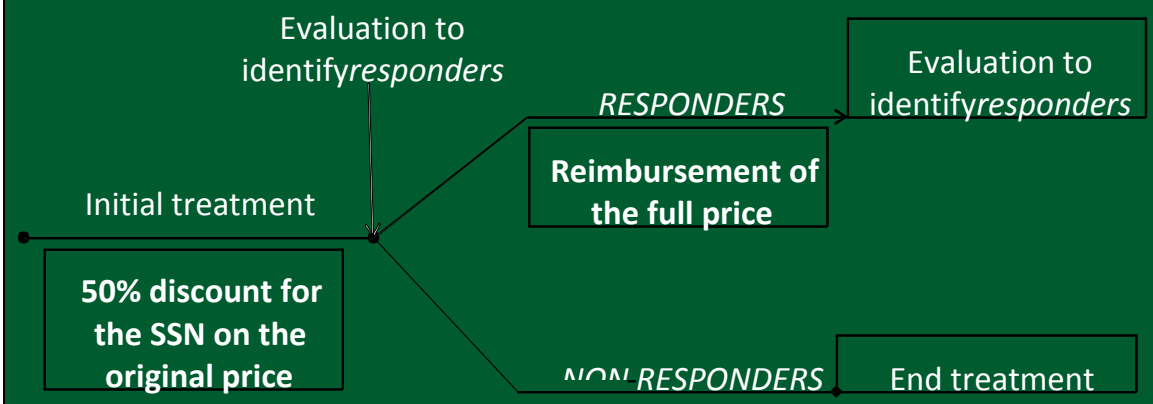
The box below presents more detailed information on risk sharing schemes in Italy

Box 2 - Overview of risk sharing schemes in Italy

The Italian Medicines Agency (AIFA) has entered into *risk sharing* agreements with pharmaceutical companies, in order to ensure the access, for all patients, to oncologic treatments. The first risk-sharing agreements, involving cancer drugs, were initiated in 2006. As of the end of 2009, schemes for at least 25 therapies existed, with around 40,000 patients enrolled in total.[8] According to AIFA, time delays for risk sharing agreements to be set up can exceed 180 days if negotiations about the details of these agreements are complex. However, once an agreement has been concluded, patient access at regional level (i.e. inclusion in the regional formulary) is much quicker than without such an agreement where regional delays can be significant.

In this framework, medicines are reimbursed according to their efficacy and, in the case in which the treatment fails, the cost will be borne by the pharmaceutical company. This *risk sharing* agreement entails a 50 percent discount for the national healthcare system (*Sistema Sanitario Nazionale, SSN)* on the original price of the medicine. The discount will be applied on each new patient for a certain number of chemotherapy treatments. At the end of this period, an evaluation will be carried out by the patients' doctors in order to identify the so-called *respondents,* who will continue the treatment. From then on-wards, the SSN will fully reimburse the cost of the medicine. The figure below present the *risk sharing* reimbursement mechanism.

Risk sharing reimbursement system in Italy



In order to ensure the effective application of this system and in order to harmonise the practices for the individuation of the respondents, AIFA has included all the pharmaceuticals reimbursed using this practice, in the so called 'registry of monitored oncologic medicines' (*Registro Farmaci Oncologici sottoposti a Monitoraggio, RFOM)*[9]. The register includes all the medicines in the following table[10].

RFOM list[11]

NAME	STARTING DATE	RISK SHARING SCHEME
Erlotinib (Tarceva)	27/07/2006	50% for the first 2 months/2 chemotherapy treatment
Sunitinib (Sutent)	09/11/2006	50% for the first 3 months/2 chemotherapy treatment
Sorafenib (Nexavar)	09/11/2006	50% for the first 3 months/3 chemotherapy treatment
Dasatinib (Sprycel)	16/05/2007	50% for the first 1 month/1 chemotherapy treatment
Bevacizumab (Avastin)	17/06/2008	50% for the first 6 weeks

The Italian government reimbursement agency now frequently insists upon agreements that link reimbursement to demonstrated efficacy. Government insistence to not pay for non-responsive patients creates objections with many pharmaceutical pricing executives who view it as unfair to first reference a drug price to other countries and then to insist on paying only for a subset of treated patients[12]. However, some experts have noted that these agreements are in reality not risk sharing agreements as such but cost-sharing agreements, the shared costs being those of identifying the value of new medicines and the patient groups where they are likely to be most effective.[13]

Experts have stressed other shortcomings of the *risk sharing system*[14]. First of all, it appears to be hard to detect the non-respondents effectively at an early phase of the treatment. Secondly, agreements are often not published and thus transparency is limited and there is limited proof that the system is homogenously applied. Moreover, there is no evidence of how the agreements (cost sharing, risk sharing or payment by results) are chosen. However, AIFA indicated that risk sharing agreements are made under public law and that most of the contract is publicly available except, in some cases, thresholds for the number of prescriptions under the contract. According to AIFA the main disadvantages of managed entry agreements relate to the burden they impose on GPs/physicians in terms of data collection and administrative burdens on AIFA itself. Also, if a pay back from industry is due (e.g. if effectiveness thresholds are missed, etc.), it can be difficult to actually activate the financial transfer foreseen by the managed entry agreement.

Most contracts have a duration of 2 years, at the end of which the competent authority (AIFA) approaches the marketing authorisation holder to request an renegotiation. According to AIFA, the requirements of the Transparency Directive would not apply in such cases because AIFA rather than the company is at the origin of the request.

In the UK, the 2009 Pharmaceutical Price Regulation Scheme introduced Patient Access Schemes (PAS) in order to enhance access to innovative treatments whose cost effectiveness was too high to meet NICE standards for NHS funding. It should be noted that the Department of Health does not consider PAS to be "managed entry agreements" because the products to which these schemes relate are already on the market and because the PAS is not in itself a contractual agreement.

A particular characteristic of UK Patient Access Schemes is that their initiation is driven by the manufacturing companies themselves rather than by the regulator as is the case for managed entry agreements in other Member States (e.g. see above for a description of the Italian schemes). The incentive for a company to propose a PAS is to avoid a negative NICE evaluation which would greatly affect the take-up of the product at GP and hospital levels. The Department of Health (and the PAS Liaison Unit in particular) advises on the possibility of a PAS for the product in question under the NHS. The main criteria for positive advice on a PAS are:

(1) Administrative burdens for the NHS
(2) Feasibility under the NHS
(3) The existence of an unmet need by the product for which a PAS has been proposed

Once a PAS has been set up, the company is then free to enter into private contractual agreements with local providers (i.e. hospital trusts). There are currently 13 national-level PAS in the NHS though there are many contractual schemes at sub-national (i.e. trust) level. The box below has a list of national level schemes:

Box 3 - List of technologies with approved Patient Access Schemes, recommended by NICE for use in the NHS

Treatment	Indication	Company
Trabectedin (Yondelis)	Advanced soft tissue sarcoma	PharmaMar
Ranibizumab (Lucentis)	Macular degeneration (Acute wet AMD)	Novartis
Lenalidomide (Revlimid)	Multiple myeloma	Celgene
Erlotinib (Tarceva)	Non small cell lung cancer	Roche
Bortezomib (Velcade)	Multiple myeloma	JC
Ustekinumab (Stelera)	Moderate to Severe Psoriasis	J&J / JC
Sunitinib (Sutent)	Gastrointestinal stromal tumour	Pfizer
Cetuximab (Erbitux)	Metastatic Colorectal Cancer (first Line)	Merck S.
Sunitinib (Sutent)	Renal cell carcinoma	Pfizer
Certolizumab pegol (Cimzia)	Rheumatoid Arthritis	UCB
Gefitinib (Iressa)	Non small cell lung cancer	AstraZeneca
Pazopanib (Votrient)	Advanced renal cell carcinoma	GSK
Azacitidine (Vidaza)	Myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia	Celgene

Source:www.nice.org.uk/aboutnice/howwework/paslu/ListOfPatientAccessSchemesApprovedAsPartOfANICEAppraisal.jsp

In the UK, these PAS take several forms[15]:

- Under free stock agreements, the company provides the first cycles of treatments for free and the NHS bears the costs of following cycles if the clinical response to first cycles is positive. For instance, UCB agreed to provide at no cost the first 12 weeks of its treatment for moderate to severe rheumatoid arthritis (certolizumab pegol) and the NHS will continue to fund the treatment if the clinical response is positive.

- Under dose capping agreements, the NHS pays for the first cycles of treatments and the company bears the costs of following treatments. For instance, the NHS pays for the first 14 doses (per eye) of treatment for acute wet-macular degeneration by ranibizumab and Novartis will cover following injections, up to three years.

- Discount agreements provide a simple minimum discount to the NHS (which can be further negotiated by local purchasers), which differs from usual confidential agreements concluded between pharmaceutical companies and public or private payers in other OECD countries in that it is public and, in some circumstances, caps the cost of the whole treatment for an individual. For instance, Roche has agreed to discount by 14.5% the price of its treatment for non-small cell lung cancer (erlotinib) in order to equalise its price to a cheaper competitor until definitive results of head-to-head clinical trials are available and a new NICE appraisal.

- A recent survey on PAS implementation in the United Kingdom concluded that refunds received by hospitals according to two of these schemes were not passed on to Primary Care Trusts, who ultimately pay for health services delivered to their patients. In addition, hospitals complained about the lack of staff to manage PAS and recuperate funds from companies.

The box below has a more detailed description of the Velcade response scheme in the UK. It should be noted that the current PAS liaison unit confirms that PAS though helpful in some instances, are not suitable for all products and that they will remain a small share of the overall pharmaceutical market.

Box 4 - Example of Velcade Response Scheme in the UK

Velcade® (bortezomib) is a drug used to treat multiple myeloma. It is given to people who have already been treated with at least one other type of chemotherapy and have already had, or are unsuitable for, a bone marrow transplant, but whose myeloma has continued to develop.

In the UK, the National Institute for Clinical Excellence (NICE) assesses the cost and clinical effectiveness of new pharmaceutical products. Based on the results of these evaluations, NICE provides recommendations to the Department of Health as to whether the products should be eligible for reimbursement on the National Health Service (NHS). In their initial evaluation, NICE found Velcade® to fall just outside their cost effectiveness threshold of £30,000 per Quality-adjusted life year, and thus recommended that it not be available for reimbursement. As a result the manufacturer, Janssen-Cilag, proposed a performance-based agreement to encourage NICE to reconsider their decision. This performance-based agreement, known as Velcade Response Scheme was evaluated and amended by NICE, who found the scheme led to a considerable improvement in cost effectiveness to the NHS, with the cost per QALY being reduced to £20,700. NICE subsequently recommended its implementation to the Department of Health.[16]

The Velcade Response Scheme is a response-rebate scheme whereby the full cost of the treatment is initially reimbursed for eligible patients. The specific details of the scheme, and the measures of its performance and effectiveness for patients are specified in a guidance document produced by NICE. Patients at first relapse who show a “complete or partial response” to Velcade can carry on with the treatment, fully funded by the National Health Service, it being seen as “an effective use of NHS resources” in this circumstance. Patients who do not show a “complete or partial response” after four cycles of treatment (measured using serum-M protein) are taken off the drug and the costs of the treatment are refunded by the manufacturer. The scheme specifies that the manufacturer will reimburse the NHS with the full cost of treatment for such patients, specified as a less than 50% reduction in serum M-protein.

The Scheme, which was subsequently agreed between the Department of Health and Janssen-Cilag, was due to be in place for 3 years, after which NICE is due to carry out another review. The specific legal nature of the agreement has not been specified in publically available documents.

In **Portugal**, "risk sharing" schemes, most of which are price-volume agreements, were first entered into in 2000 in an effort to control the cost of pharmaceutical expenditure and at the same time ensure access to treatments that could not otherwise be made available. Risk-sharing in Portugal is seen primarily as a way of targeting access to pharmaceuticals to patient groups where they are proven to be effective, where there is an unmet need and/or where there are alternative treatments for some indications but not for others. Through the PV agreement the competent authority can create incentives to target the manufacturer's marketing strategy to certain patient groups.

In the experience of the competent authority this type of agreement works relatively well in the sense that volumes are rarely exceeded. The average duration of a price volume agreement is about 2 years, contracts are made under public law and they can be accessed upon request. In addition, each contract explicitly states what will happen at the end of the agreement. Options include:

- automatic delisting within a period of 10 days unless further evidence of effectiveness is provided by the company or there is an appeal by the manufacturer;
- renegotiation of the price volume agreement for another 2-year period; or
- automatic inclusion on the positive list (no further application required)

From the perspective of the Portuguese competent authority, the main disadvantage of price volume agreements is the extent of monitoring required to ensure compliance, especially within the context of Portuguese data privacy laws which preclude the authority from accessing patient records.

Finally, in **France**, price volume agreements are very prominent. However, the competent authority is wary of managed entry agreements that involve the introduction of products for which sufficient cost-effectiveness data are not available. As the competent authority points out, "in some very rare instances, CEPS has agreed to give these medicines a chance even though the evaluation per se would not warrant the price requested, but this is done under very strict conditions. In the first place, the anticipated but unproven benefit must be such that it could not reasonably have been proven during the clinical trials carried out prior to marketing authorisation and for example that the benefit can only be proven in real-life practice. In the second place, if this benefit exists, it must represent a clear advantage and must be preferable in public health terms. In the third place, a study must be devised which at the end of the fixed-term trial period will definitively prove whether or not the benefit exists and if so, whether it is significant enough. Finally, the company marketing the medicine must enter into an agreement whereby it undertakes among other things to bear the financial costs in the event of failure of the medicine".[17]

ANNEX 8

TENDERING BY SOCIAL SECURITY SYSTEMS: OVERVIEW AND CASE STUDIES[1]

To date, four countries in Europe have launched tenders for out-patient pharmaceuticals for the purpose of deciding a reimbursement price:

– the Netherlands
– Germany
– Belgium
– Denmark

In the **Netherlands** in 2005 seven health plans representing approximately 60% of the insured population, collectively decided to "tender" the purchasing of three active ingredients - simvastatin, pravastatin and omeprazole – all off-patent products under the so-called "preference policy."[2] Following an agreement between the Health Insurance Board, the generic association and the pharmacists' association for 2007-08, collective tendering was not extended to other active ingredients. However, 33 substances were listed for potential tenders, led by individual health insurers.[3] According to EGA sources, retail tendering covers 50%-90% of off-patent products.[4] Under preference policy insurers limit patients' access to certain off-patent molecules to specific preferred manufacturers which favours generic producers but also creates severe price competition in the generics market and significant savings for health insurers (e.g. average price decrease of 85% over 33 molecules). The preference policy in the Netherlands today enjoys increases in uptake with almost 25% of the market covered.[5]

In **Germany** health insurance funds can directly negotiate prices with Pharma companies with all off-patent products included. The local health insurance funds (AOKs) select active ingredients with 2-3 manufacturers per ingredient and invite manufacturers to provide rebates on their products. The first discount deal expired in 2007. It included 43 ingredients with 11 generic manufacturers and savings were estimated at 100 million Euros. In 2008 a new rebate deal was done covering 22 ingredients with 30 manufacturers and expected savings of 175 million Euros by the end of 2009. At present, 98% of all tenders up to June 2008 were for generic products and 2% for patent protected products.[6] The policy is likely to be extended more widely once a number of legal questions surrounding the use of rebate deals is resolved.[7] Indeed, one sickness fund in North-Rhine Westphalia is giving all pharmacies in that Land a €1,000 cash injection (bonus) to implement the scheme and inform patients of any changes to their drug regimen (Apotheke adhoc, 2008). Financial incentives are also planned for physicians - €0.50 per prescription and for patients in terms of zero co-payment if the price for the rebated product is 30% below the reference price.[8]

In **Belgium**, tendering has been much more limited with only one actual tender carried out (simvastatin), one aborted attempt (amlodipine) and no current plans to tender further substances. In the case of simvastatin, the winner of the tender was compensated for having the lowest price by becoming eligible for a preferential 75% reimbursement rate, while all other existing versions of the same drug are reimbursed at just 50%. The procedure encountered significant legal challenges from companies and it did not lead to expected savings as physicians switched their prescriptions to atorvastatin or rosuvastatin. In other words, tendering in itself without accompanying incentives for physicians does not encourage the prescribing of the most cost-effective treatment.[9] For the second tendering procedure

(amlodipine), the winner was a company with no capacity to procure and, as a result, the tender was abandoned.[10] At the same time, had tendering in Belgian continued, a requirement that the winning tenderer be able to supply 50% of the total market volume for the tendered molecule would have constituted a significant barrier to entry for SMEs.[11]

Finally, **Denmark** has a long standing experience with tendering driven by the Danish Medicines Agency. With a few exceptions, tendering in Denmark covers all off-patent products and tenders take place every other week. The Danish tendering system relies on generic substitution at pharmacy level and one of its drawbacks is the administrative burden that it imposes on the pharmacy sector and the logistical requirements in terms of transport of medicines to pharmacies after each tendering procedure. Another potential drawback, given the small size of the Danish market, is that some manufacturers use the tendering system to "dump" older stock of generic medicines. At the same time, the country's automatic reimbursement for generics increases Denmark's attractiveness for generics manufacturers.

In terms of future developments, the region of **Andalucía in Spain** has announced plans to introduce tenders for 10 active ingredients in the retail pharmacy sector – though the national government has questioned the legality of this move.[12]

ANNEX 9

THE EU MEDICAL DEVICES MARKET: STRUCTURE AND CHARACTERISTICS[1]

1. MARKET STRUCTURE FOR MEDICAL DEVICES

1.1. Heterogeneity of products

Within the broad sector of medical devices, an important distinction needs to be made between single-use products (e.g. artificial hips, incontinence pads, etc.) which are implanted or directly used by patients and procedural devices (e.g. x-ray, surgical instruments, etc.) which are not single-use and form part of a medical procedure. This distinction is important because these different types of devices are produced, sold and procured under very different business models and pricing and reimbursement procedures.

- For "procedural" devices, pricing is not regulated and market access is through public EU-wide competitive tendering. Reimbursement for the medical procedure as part of which the device is then used is decided by the relevant public authority in each Member State in accordance with the national health system.

- For "single-use" devices, a pricing and reimbursement procedure similar to that described for pharmaceuticals above can be applied in some Member States. Because pricing and reimbursement procedures are of greatest relevance to such single-use devices, the majority of this section focuses on this type of instruments.

One of the most interesting features of the medical devices sector, which differentiates it from pharmaceuticals, is the number and heterogeneity of products available. According to the European organisation representing the medical technology industry (Eucomed), there are more than 10,000 different product groups for medical devices on the market at the moment (the number of different products is around 500,000). The box below has a very high-level overview of the leading market segments for medical devices. This box does not aim to provide comprehensive analysis of the market but it helps conceptualise the different elements that, together, constitute the market for medical devices.

Box 1 – Main market segments in medical devices

In-Vitro Diagnostic Substance Manufacturing
Electromedical and Electrotherapeutic Apparatus Manufacturing
Surgical and Medical Instrument Manufacturing
Irradiation Apparatus Manufacturing
Laboratory Apparatus and Furniture Manufacturing
Dental Equipment and Supplies Manufacturing
Surgical Appliance and Supplies Manufacturing
Ophthalmic Goods Manufacturing

Source: Pammolli, Fabio, et al. (2005), Medical Devices Competitiveness and Impact on Public Health Expenditure, http://mpra.ub.uni-muenchen.de/16021/

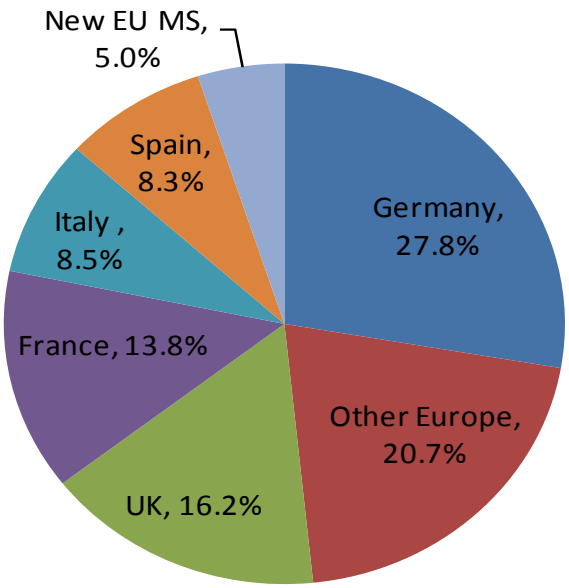
Compared with pharmaceuticals, the medical devices sector (single-use devices) is characterised by small companies (80% SMEs), extremely rapid innovation and an average product lifestyle and investment recovery period of approximately 18 months. In addition, and contrary to pharmaceuticals, the sector is based on achieving incremental improvements in efficacy and health outcomes.[2] As a result regulatory authorities find it difficult to keep up with the pace of change in the industry. For instance, Eucomed points out that "in the last years, the larger European countries (e.g. UK and Germany) each issued only about five assessment decisions regarding medical technologies each year".[3]

There are also significant differences between pharmaceuticals and medical devices in terms of performance evaluation for pricing and reimbursement purposes. Generally, pricing and reimbursment is difficult for medical devices because payers may not directly reimburse a new technology until it has demonstrated value in the marketplace, which can often take several years to prove (especially for diagnostic procedures).[4] For instance, randomized control trials (RCTs) are much more difficult to perform for medical devices than for new pharmaceuticals entering the market and the efficacy of medical devices depends to a significant extent on the skills and experience of the user (patient or physician) which can require extensive training. Similarly compared with pharmaceuticals which typically remain at the initial price point until the patent expires, the price of medical devices is likely to change over time as new products enter the market and render the initial technology obsolete.[5]

1.2. Market size

According to Eucomed figures, total expenditure on medical technology was EUR 56bn across the EU in 2008, which corresponds to 25% of world market share (EUR 219bn).[6] The EU is the second biggest market for medical devices behind the US (EUR 98bn) but before Japan (EUR 23.1bn).[7] However it should be kept in mind that medical devices remain a small share of overall health expenditure. According to Eucomed, per capita spend on medical technology in 2008 was EUR 115, out of total healthcare expenditure of EUR 2,727. The diagram below shows the share of different Member States in European medical device sales.

Figure 1 - Sales of medical technology by EU Member State, 2008



Source: Eucomed Note: Other Europe = Finland, Sweden, Denmark, Norway, Netherlands, Belgium, Luxembourg, Portugal, Austria, Greece, Ireland, Switzerland

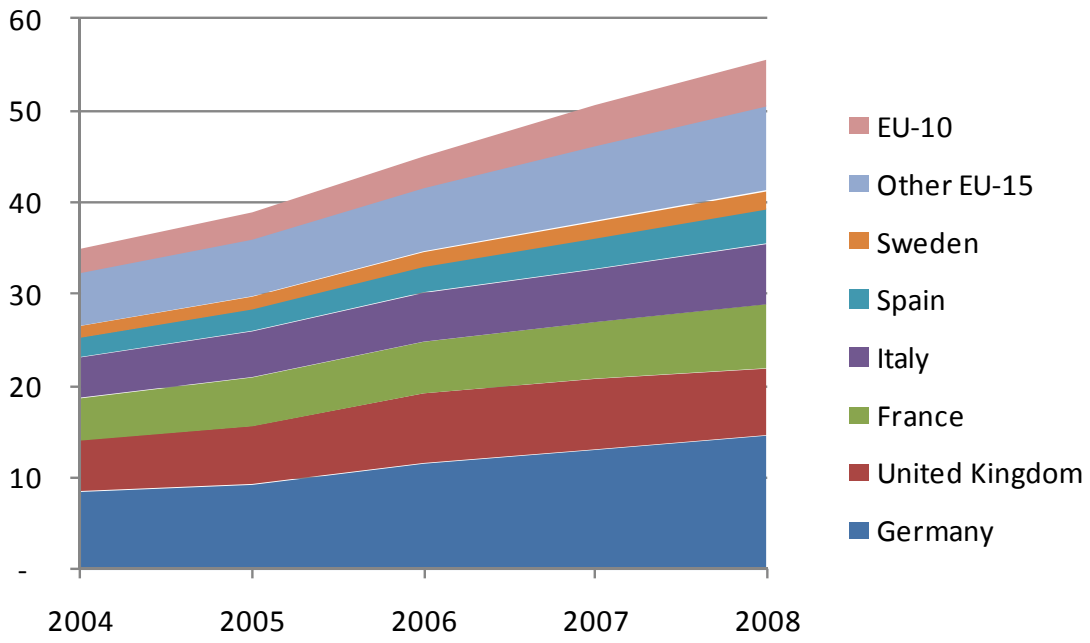
The largest share of the EU market for medical technology is in Germany with almost 28% of total EU sales. This is followed by the UK and France with 16.2% and 13.8% of the EU market respectively. The two remaining large EU Member States (Italy and Spain) command between 8% and 9% of the EU market while all 10 new EU Member States including Poland only have 5% of total EU sales.

1.3. Public expenditure on medical devices

To set these figures into context, the diagram below shows the evolution of expenditure on medical technology by Member State over the period 2004-2008. The figure shows that:

- Total expenditure on medical devices has increased significantly (by approximately EUR 20bn) between 2004 and 2008.
- Growth in expenditure on medical technology between 2004 and 2008 has exceeded 50% in all countries (groups of countries) except the UK (30%)
- The most significant expenditure growth rates are in the new Member States (92%), Germany (72%) and Spain (78%); and
- Expenditure growth has been most marked in Germany and in the new EU Member States.

Figure 2 - Expenditure on medical technology (EMT) by country (EUR bn)



Source: Eucomed

2. PRICING AND REIMBURSEMENT PRACTICES

While giving an overview of pricing and reimbursement practices for medical devices in some Member States, this section does not provide a comprehensive description of all national

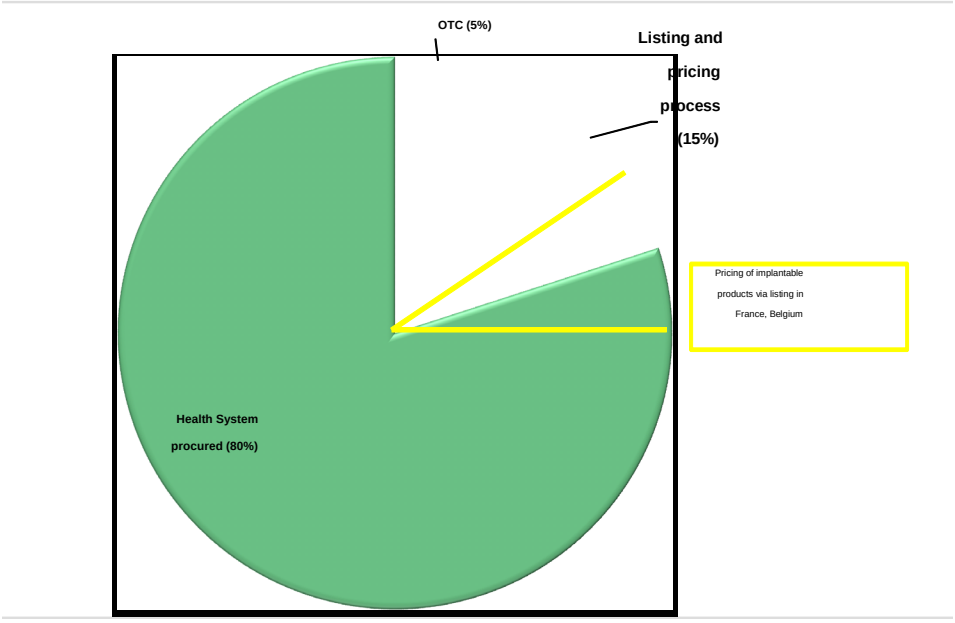
regulatory systems. Instead it provides an overview of existing practices and market shares to assess the relevance of potentially extending transparency rules to medical devices and it describes pricing and reimbursement systems in selected major Member States in more detail.

2.1. Overview of pricing and reimbursement practices for medical devices

Pricing and reimbursement systems for medical devices in Europe are highly diversified from one country to the other. Fixed and regulated product prices exist mainly in the out-patient sector. Examples of regulated markets include volume caps in Italy for incontinence pads or in France for stents and reference prices in Spain and Germany for incontinence pads.[8]

In the in-patient sector, the introduction of DRG-based payment systems[9] has led to a number of changes in the hospital environment including the creation of free market pricing (as opposed to fixed or regulated prices) for technologies, given that hospitals are paid one DRG rate by diagnosis per patient stay regardless of the length of stay or the cost of the technology. Prices are typically set through tenders by the purchaser or alternatively in negotiation with manufacturers sometimes comparing the average price of similar devices already on the market in each country. In most countries, the role of public procurement and centralized purchasing (including through purchasing consortia) is growing significantly. Figure 3 below provides a high-level overview of pricing practices in the medical device market.

Figure 3: Overview of pricing and reimbursement practices for medical devices in the EU



Source: Eucomed

As the figure indicates, the medical device market can be divided into 3 segments:

(1) The smallest share of the market covers over the counter (OTC) products (about 5% of the total) where prices are not regulated but determined freely by market forces. These products include for instance condoms, spectacles, first aid wound dressings and some commonly used diagnostics (e.g.: pregnancy tests). In this context, the Transparency Directive is not relevant because pricing is not regulated.

(2) The largest share of the market (about 80% of the total) is covered by devices that are procured through the health system. This includes almost all products used in hospitals including e.g. diagnostic devices. Pricing of these products is determined by market forced (e.g. competitive tendering) and transparency is regulated by procurement rules at national and European levels. Nevertheless prices can be influenced by procurement mechanisms (such as monopsony power in some health systems) and market access is determined by DRG processes, adherence to public procurement rules and HTA processes. Again for this segment of the market, the Transparency Directive seems to have limited relevance due to complexity of mechanisms influencing market access

(3) Clearly, European level transparency rules similar to those in the Transparency Directive would be most relevant for the part of the devices market that currently undergoes a listing and pricing process similar to pharmaceuticals (about 15% of the market with some variation across Member States e.g. France, Spain and Belgium where some implantable devices that are procured through tenders elsewhere are subject to a listing process). The size of this market differs across countries but it can include for instance diabetes products, assistive technologies, advanced wound dressing, anti-embolism devices which are supplied directly to patients via pharmacies. Pricing and access are determined by regulatory authorities based on supplier submissions, similar to the P&R process for pharmaceuticals.

On the whole, this high level overview suggests that transparency rules similar to those in the Transparency Directive might be relevant for about 15% of the medical device market.

2.2. Overview of pricing and reimbursement systems in a selected number of Member States

The remainder of this section provides examples of pricing and reimbursement practices in a number of EU Member States.

The **United Kingdom** is theoretically a free market, but in practice the NHS has "monopsony" (single buyer) purchasing power, frequently using tenders to purchase medical devices. In the primary care market, the Drug Tariff sets a maximum reimbursement price for some non-hospital devices. This list is a centrally developed list of products that may be prescribed for use in the community and reimbursed under the NHS. It contains about 10% of the medical devices used in the NHS.[10]

Italy is also a free market with several buyers, with a DRG-system for hospitals. Hospitals and local Health Authorities buy mostly through tenders. A positive list (aka. list of eligible products) nevertheless exists for ambulatory services and medical devices provided to end-users.[11]

In **Germany**, the picture is similar with the *Hilfsmittelverzeichnis* listing medical devices supplied outside the hospital sector. This list as such does not provide any provisions as to the reimbursed price, pricing being dealt with on a Länder level, not a federal level. For most product categories, pricing is accepted by SHI funds on an individual product basis.[12]

In **France**, the three most frequent reimbursement processes for medical devices are as follows:

(1) General cases: medical device used in hospitals funded through DRG tariffs

(2) Enlistment on the positive list after assessment by CNEDiMTS. This concerns ambulatory devices and expensive devices used in hospitals which are funded in addition to the DRG tariffs and as such enlisted on an “add-on list” (liste en sus)

(3) Medical device funded through a medical procedure: Assessment by CEAP