HEALTHCARE PRODUCTS PRICING COMMITTEE

ANNUAL REPORT 2009

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ILLUSTRATIONS

Under the terms of the Social Security Code (*Code de la Sécurité Sociale*), Article D. 162-2-4, the *Comité économique des produits de santé*, CEPS (the Healthcare Products Pricing Committee) must send a report on its work each year to the Ministers for Social Security, Health, the Economy and Industry respectively. Article L. 162-17-3 of the Social Security Code provides that the report should also be sent to Parliament.

This report describes the principal aspects of the committee's work during 2009.

Part one deals with medicines, looking first at the medicines market and reimbursement of medicines in 2009 (Chapter I), then at the committee's price setting work (Chapter II) and at regulation in the context of agreements between CEPS and the pharmaceutical companies (Chapter III).

Part two deals with healthcare products other than medicines. Chapter I is devoted to a description of the market and trends in spending on medical devices. Chapter II describes the Committee's work on tariffs and prices for the medical devices and services defined in Article L. 165-1 of the Social Security Code. Chapter III presents the work done on changes to tariffs and prices for medical devices.

Part three looks at the contribution made by CEPS to France's investment attraction policy.

PART ONE - MEDICINES

CHAPTER I – REIMBURSABLE MEDICINE SALES AND EXPENDITURE IN 2009

1. General market trends

The rate of growth in sales of reimbursable medicines by community pharmacies or reimbursed through the hospital system, expressed in manufacturer's price ex VAT, was the 2.8% in both 2009 and 2008. Naturally, the breakdown of the figures for these two financial years varies somewhat: slightly higher growth in community pharmacy sales in 2009 under the influence of the epidemic situation and significantly lower growth in hospital medicine sales, largely due to the lapsing of patents. However, the most important aspect is that these matching figures are a sign of continuity, indeed the growth in medicine sales has stabilised at a historical low: an average increase of just over 3% over the last five years, as opposed to almost 7% over the previous five years.

Table 1: Growth rate of sales of reimbursable medicines, 2000-2009

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Growth rate	7.7%	7.7%	5.7%	6.5%	6.9%	5.0%	1.8%	3.9%	2.8%	2.8%

Source: GERS[1] community pharmacy sales data and company declarations of sales to hospitals, processed by CEPS.

As regards the reasons for this, the discussions devoted to the subject in the CEPS 2008 Annual Report could almost be repeated word for word: the major growth classes having reached their peak, fewer fruits from research activities, progress in the effectiveness of public expenditure regulation instruments.

We are seeing the confirmation of a situation in which the most modern and effective medicines both for illnesses and for our ever-increasing prevention needs are now, or will be in the relatively short term, generics or essentially similar drugs. The situation which is taking shape is therefore radically different from the market which experienced continuous strong renewal for decades, accompanied in expenditure terms by a strong structural effect within the major drug classes.

As a result, a considerable and rapidly growing proportion of all the needs, measured in treatment days, will be fulfilled for the long term by high quality medicines whose daily cost can be expressed in tens of centimes, whilst at the opposite extreme, a few illnesses affecting very small numbers of people are associated with daily costs sometimes in excess of one hundred Euros.

This situation must be reflected in the regulatory environment. In the first instance, it dictates that the quality of generic provision must be carefully preserved, insofar as these medicines are now central to the fulfilment of healthcare needs and are no longer simply a tool for making savings.

[1] GERS: see glossary in Appendix 7.

Above all, it will inevitably mean that efforts concerning control of expenditure, over and above the progress still to be made in terms of the responsible use of medicines, must be focused on how new medicines are managed: the identifying and sorting of novel drugs, the cost-effectiveness of the funding devoted to them and balancing public health demands with those of individual patients in the context of limited resources.

2. Sales of medicines covered by the national health insurance system

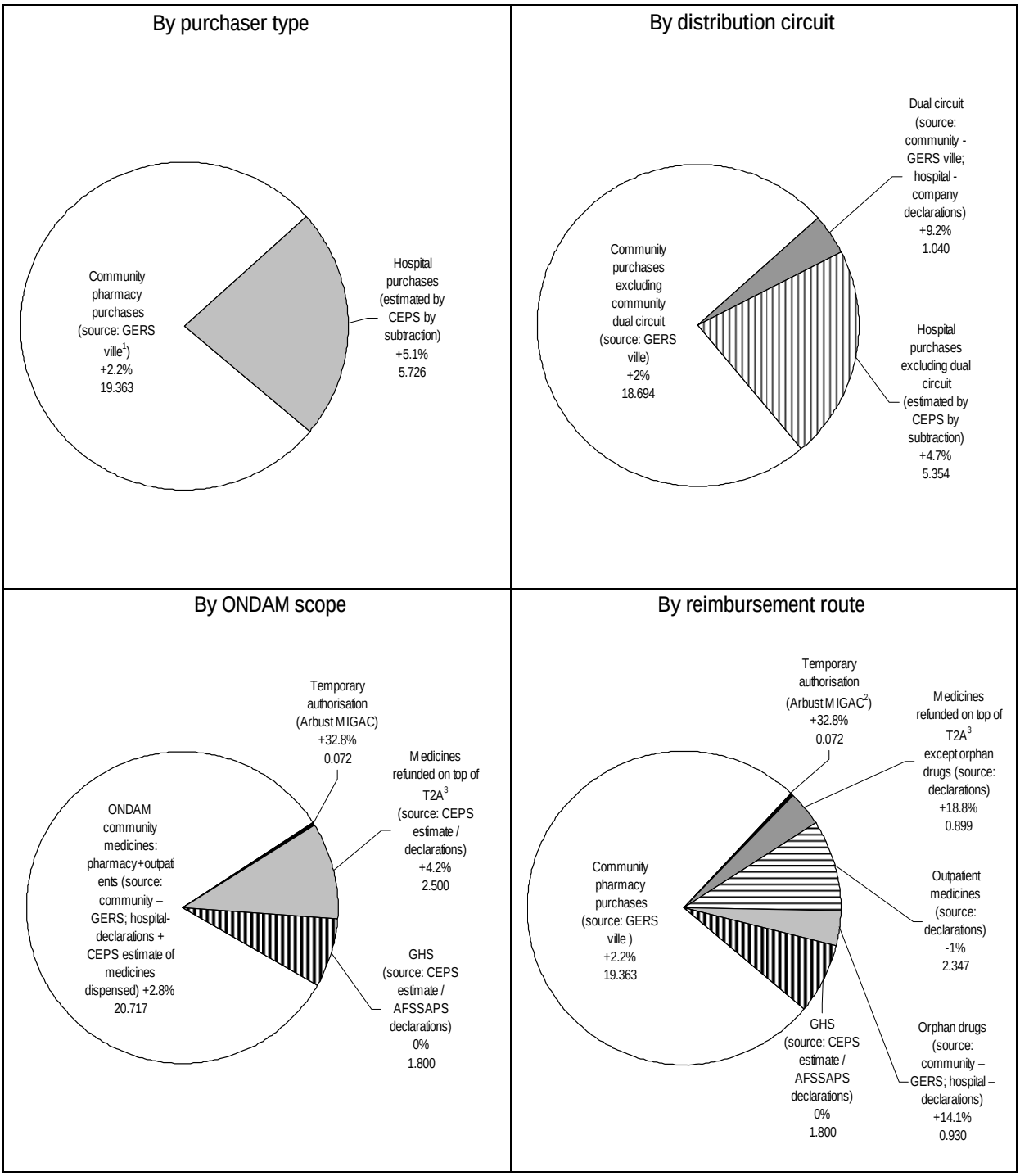
Sales of medicines covered by *l'Assurance maladie* (the national health insurance system) totalled €25.089 billion.

As in 2008, CEPS has drawn up a presentation of all medicines sales covered by national health insurance, broken down according to the main possible categories: type of purchaser, distribution circuit, ONDAM[2] scope or reimbursement route. In drawing up this picture, the committee relied primarily on a comparison between sales figures declared in tax return declarations to AFSSAPS[3], sales data gathered by the GERS community pharmacy section, the declarations CEPS receives from companies of their sales to hospitals in the context of the end of year financial adjustment and data gathered by ATIH[4].

The breakdown of hospital medicine sales which can be claimed back from *l'assurance maladie* between medicines dispensed to outpatients and medicines for inpatients which are not covered by the general "GHS" system (funding for hospital stays based primarily on "groupes homogènes de séjour, similar to diagnosis-related groups) are estimated by CEPS on the basis of the type of product and the information it has regarding hospital dispensing practices.

[2] ONDAM = Objectif national de dépenses de l'assurance maladie – the target annual national health insurance budget.
[3] AFSSAPS: see glossary in Appendix 7.
[4] ATIH: see glossary.

Figure 1: Distribution of the €25.089bn medicine sales covered by national health insurance in 2009



Notes:
[1]: GERS: see glossary in Appendix 7; *GERS ville* - statistics compiled by GERS on medicine sales to community pharmacies.
2: MIGAC – See glossary; Arbust MIGAC: software application used by ATIH.
3: T2A – See glossary.

2.1. *Sales within the scope of the ONDAM community target*

2.1.1 *Breakdown of the growth in sales of medicines dispensed by community pharmacies*

After seeing a historically low growth rate in 2008, sales in manufacturer's price excluding VAT of reimbursable medicines sold in community pharmacies were up 2.2% in 2009 compared with 2008, reaching a total of €19.36 billion (see Table 2). Sales in retail price including VAT were also 2.2% higher than in 2008.

Following the build-up of stocks at the end of 2007 in the wake of the abolition of pharmacists' manufacturer discounts pursuant to the "Act for the Promotion of competition for the benefit of consumers" (Law no. 2008-3 of 3 January 2008), known as the *loi Chatel*, the beginning of 2008 saw a running down of stocks. These lower purchase quantities in 2008 are not a reliable reference point as they produce an inflated growth rate for 2008-2009. This effect is estimated to account for 0.6 growth points.

The growth rate can also be partly explained by higher sales of flu-related drugs at the end of the year. Antipyretic drugs alone account for 0.3 growth points, whilst sales of these drugs had gone down in 2008. Broad spectrum penicillins, seasonal flu vaccines and antiviral drugs effective against flu viruses account for 0.1 extra growth points.

Table 2: Growth of community pharmacy sales of reimbursable medicines, 2008-2009

	Sales in manufacturer's price ex VAT (€bn)	Sales in public price inc VAT (€bn)
2008	18.94*	26.53
2009	19.36	27.11
Growth	2.2%	2.2%

Source: GERS community pharmacy sales data, data processed by CEPS.
** The 2008 figure for sales ex VAT of reimbursable medicines which appeared in the 2008 report was €18.95bn. Due to an input error at GERS, this figure included drugs indicated for the treatment of malaria, which are only reimbursable for residents of French Guiana covered by national health insurance.*

Price, pack and class effects

The figure represented by the price effect, which reflects the committee's work on prices in application of ministerial guidelines, is not surprisingly the same as in 2008.

As regards the other components of the growth rate, the situation is quite different from the previous year, since the pack effect has gone from having a strong downward influence due to the removal of venotonic drugs from the reimbursable medicines list to having a strong upward influence due to the epidemic situation. In 2009, 50 million more packs of painkillers will have been sold than in 2008 and approximately 10 million more packs of antibiotics and antiviral drugs specifically for flu.

The result is an especially low class effect, which primarily reflects the presence of these 50 million packs of painkillers, whose average price is much lower than the average price of all reimbursable packs. There is at least one other circumstantial reason for the net slowdown of the class effect: the receding of sales of human papillomavirus (HPV) vaccines, after two years in which sales were high while catching up with the backlog.

The fact remains that regardless of these circumstantial phenomena, a genuine shrinking of the underlying class effect is probably taking shape, in which the new arrival of a handful of very expensive drugs has not taken over from the dwindling numbers of the major consumption classes.

Table 3: Breakdown of growth in pre-tax community pharmacy sales, 2009

Year	Price effect	Pack effect	Class effect	Total growth
2004	-0.4%	-1.1%	7.8%	6.2%
2005	-1.0%	3.4%	4.4%	6.8%
2006	-3.9%	-5.6%	11.1%	0.8%
2007	-2.1%	0.0%	6.1%	3.8%
2008	-2.2%	-4.9%	8.3%	0.8%
2009	-2.2%	3.1%	1.3%	2.2%

Sources: GERS community pharmacy data, data processed by DSS/6B

Average price of medicines sold in community pharmacies

In 2009, the average prices of reimbursable medicine packs dispensed in community pharmacies fell in both manufacturer's price excluding VAT and public price including VAT. The average manufacturer's price ex VAT was down 0.85%.

The main reason for this was the price reductions implemented by the committee, whose effect on the average price for the first time was not offset by the class effect, which was relatively minor.

Unlike previous years, the markup made by pharmacists was unchanged. This means that their income rose by the same percentage as the rise in medicine sales.

Table 4: Growth in average pack price and distribution markup on reimbursable medicines sold

	2004	2005	2006	2007	2008	2009
Total sales ex VAT (€bn)	16.82	17.97	18.10	18.79	18.94	19.36
Total sales inc VAT (€bn)	24.31	25.83	25.83	26.61	26.53	27.11
Number of packs (in millions)	2,724	2,817	2,658	2,656	2,529	2,607
Average manufacturer pack price ex VAT (€)	6.18	6.38	6.81	7.08	7.49	7.43
Growth / year n-1	*7.40%*	*3.20%*	*6.70%*	*3.89%*	*5.90%*	*-0.85%*
Average public pack price inc VAT (€)	8.93	9.17	9.72	10.02	10.49	10.40
Growth / year n-1	*6.10%*	*2.70%*	*6.00%*	*3.05%*	*4.73%*	*-0.86%*
Average markup (€)	2.57	2.60	2.71	2.74	2.78	2.76
Growth / year n-1	*2.80%*	*1.20%*	*4.10%*	*1.10%*	*1.72%*	*-0.88%*
Markup rate	44.50%	43.80%	42.70%	38.70%	37.13%	37.12%

Sources: GERS community pharmacy sales data, data processed by CEPS.

Table 5: Prices and distribution markups of substitution list and non-substitution list medicines in 2009

Market	Average manufacturer price (AMP) ex VAT	Average public price inc VAT	Average markup[1]	Markup rate[2]
Generics[3]	€3.92	€6.46	€2.417	61.4%
Original drugs	€8.00	€11.31	€3.08	38.5%
Whole substitution list	€5.29	€8.10	€2.63	49.8%
Non-substitution list	€8.56	€11.639	€2.827	33.0%

Sources: GERS community pharmacy sales data, CEPS and data processed by DSS/6B.

1. Distribution markup = wholesaler's markup + pharmacy's markup (Manufacturer's price ex VAT + markup + VAT = Public price inc VAT).

2 Markup rate = average markup on AMP ex VAT.

3. On a like-for-like basis; operational substsitution list for 2009.[5]

[5] The operational substitution list for a year is defined as all generic groups in which at least one generic has been sold during the course of that year

Market share of generics

In 2009, the market share of generics on the operational substitution list was 71.2 % in terms of pack numbers and 62.2 % in terms of sales total excluding VAT. These figures were 70.8% and 57.2% respectively in 2008 (see Table 6).

Table 6: Market share of generic medicines 2008-2009

	2008[1]		2009[1]	
	Units	Value	Units	Value
Proportion of generic groups in overall market	30.98%	19.07%	33.70%	22.54%
Proportion of generic groups in generics group market	70.83%	57.17%	71.20%	62.24%
Proportion of generics in overall market	21.94%	10.90%	24.00%	14.03%

Source: GERS community pharmacy sales data, data processed by DSS/6B.
On a like-for-like basis; operational substsitution list for 2008 and 2009.

In 2009, the generics included on the substitution list accounted for sales worth €2.7bn, a 31.5% increase on the figure for the generics included on the list in 2008. With the significant expansion of the list caused by both *Plavix* (clopidogrel) and *Eupantol/Inipomp* (pantoprazole) going off patent, the market share represented by generics reached 14% of the total sales figure before VAT and 24% of the reimbursable medicine packs sold in community pharmacies in 2009 (see Table 7).

Around fifteen manufacturers launched their generic versions of clopidogrel during the last quarter of 2009. The market share of these generics after only their first three months on the market[6] reached 66.2 % (equivalent to a market share of 22.2 % for the year). *Plavix* was one of the biggest blockbusters. Before its genericisation, it accounted for annual pre-tax sales totalling €540M, representing 2.8% of all pre-tax sales of reimbursable medicines in community pharmacies, and 0.5% of all packs sold.

The market share of generic versions of *Effexor* (venlafaxine), which went off patent in 2008, reached 72 % in terms of units and 60 % in terms of value. Before it was genericised, the drug accounted for annual sales before tax of €115M.

Table 7: Growth in market share of generics in community pharmacies 2008-2009

	2008[5]		2009[5]		Growth 2009/2008	
	Units	Value	Units	Value	Units	Value
Community pharmacy market:	2,529	18,945	2,607	19,365	3.1%	2.2%
non-generics market	1,974	16,880	2 006	17,009	1.7%	0.8%
generic group market[5]	783	3,613	905	4,792	15.5%	32.6%
generics market	555	2,066	601	2,357	8.3%	14.1%

Source: GERS community pharmacy sales data, data processed by DSS/6B.
Units: millions of packs; value: sales ex VAT in EUR millions. Annual sales to date for all products and product formats listed on the 2008 & 2009 operational substitution lists. Like-for-like basis.

Analysis of growth by pharmacotherapeutic class group

The group which contributed most to the growth in sales of medicines dispensed by community pharmacies were the antivirals. This high growth can be explained by the replacement of free combinations with set combinations, due to their greater ease of use, and by the increased volumes connected with the use of second-line treatments (*Isentress* and *Prezista*) where first-line treatments had failed. The availability of *Isentress* in community pharmacies in 2009, where previously it had only been available on prescription to outpatients by hospital pharmacies, led to a €32M increase in

6 Figure to date for the three months to December 2009.

pre-tax sales for this group[7]. Sales of *Atripla*, which became available on the dual circuit in 2009, reached €26M. At the same time, sales of *Truvada*, *Prezista* and *Reyataz*, which were already available in community pharmacies in 2008, continued to grow rapidly (+ €44M in total).

Disease-modifying antirheumatic drugs were the group with the second largest growth. Most of this growth can be accounted for by TNF alpha blockers. These are indicated for the treatment of serious diseases: chronic inflammatory rheumatic diseases (such as rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis), chronic inflammatory bowel diseases such as Crohn's disease and plaque psoriasis and the indications for some of these have recently been extended, thus leading to higher growth in sales. These are recent drugs, of which the first to be available in community was *Enbrel*, in 2003. *Enbrel* and *Humira* between them recorded growth in sales of €73M in 2009.

Table 8: Top five groups contributing to sales growth in 2009

Group	Pre-tax sales 2008 (in €M)	Pre-tax sales 2009 (in €M)	Growth (in €M)	Growth rate 2009/2008
J05B1 (hepatitis antivirals) + J05C (HIV antiretrovirals) including Intelence + L03B1 (alpha interferons)	589	669	80	13.6%
M01C (disease-modifying anti-rheumatic drugs) + Acadione + Raptiva	360	434	74	20.6%
N02 (analgesics) excluding Buprenorphine and Methadone + N07C (antivertigo preparations)	1,018	1,073	55	5.4%
R03 (anti-asthma and COPD products)	981	1,035	54	5.5%
C10A (cholesterol and triglyceride regulating preparations) plus C10C (lipid regulating drug combinations)	1,195	1,246	51	4.2%

Source: GERS community pharmacy sales data, data processed by CEPS

After having been the highest contributing group to growth in sales in 2008, vaccines and allergy treatments had the greatest downward influence on this growth in 2009, despite the growth in seasonal flu vaccines[8]. The completion of the backlog of human papillomavirus vaccinations combined with a 10% reduction in the price of *Gardasil* at the end of 2008 led to a €91M reduction in sales of this medicine alone.

Table 9: Top five groups contributing downward to growth in 2009

Group	Pre-tax sales 2008 (in €M)	Pre-tax sales 2009 (in €M)	Growth (in €M)	Growth rate 2009/2008
J07 (vaccines) + V01A (allergy treatments) + Synagis	538	449	-89	-16.6%
N06A (antidepressants) excluding N06A3 and Levotonine	473	441	-32	-6.7%
C01D + E + X (CHD treatments) + C02 (antihypertensives) + C03 (diuretics) + C07 (beta blockers) + C08 (calcium channel blockers) + Caduet	1,045	1,019	-26	-2.5%
A02B2 (proton pump inhibitors)	852	837	-14	-1.7%
B01C (antiplatelet agents) excluding Xagrid	585	576	-9	-1.6%

Source: GERS community pharmacy sales data, data processed by CEPS.

2.1.2 *Medicines issued to outpatients by hospital pharmacies*

CEPS only has the direct figures, obtained via the companies' tax declarations, for total sales of outpatient medicines, regardless of whether or not these were actually issued to patients. As explained above, the committee estimates the total quantities actually sold on the basis of the types of medicines and the information it is able to obtain about practices. Actual pre-tax sales of reimbursable outpatient medicine in 2009 are estimated at €1.350bn.

7 Although in spite of this, no reduction was seen in sales to outpatients by hospital pharmacies.
8 + €4M growth in pre-tax sales, over 10% higher than in 2008.

This figure is consistent with the figure reported by CNAMTS[9], extrapolated to all the insurance schemes and including VAT and sale markups, which was €1.450bn.

Compared with 2008, the growth rate was 12.5 % in pre-tax sales and 11.5 % taking markups and VAT into consideration. This growth is largely due to the increase in orphan medicines.

2.1.3 *The dual circuit: hepatitis and HIV/AIDS drugs*

"Dual circuit" medicines are medicines which patients can buy from either hospital or community pharmacies. The hospital prescription fee and the community pharmacy pre-tax selling price of these medicines are the same. This relates to medicines for hepatitis and HIV/AIDS. Pre-tax sales of these products rose to €1.04bn in 2009, representing a 9% increase in relation to 2008.

Sales of dual circuit products by hospital pharmacies accounted for 36% of all dual circuit sales in 2009. However this percentage can vary considerably from one period to the next as it its dependent on how quickly new drugs come onto the market. New drugs are initially dispensed by hospital pharmacies and later when their use becomes well established, they are sold more widely in community pharmacies. For example in 2009, the actual growth in community pharmacy sales of these medicines was 14%, whereas sales by hospitals barely changed. This is one of the reasons why it is perfectly legitimate to group community and hospital sales together in the context of the agreements with the pharmaceutical companies, for the purpose of assessing whether the 'K' growth rate thresholds set by the *loi de financement de la Sécurité Sociale* (the annual social security funding act) have been exceeded.

Table 10: Growth in dual circuit sales 2008-2009

	2007	2008	Growth
Sales in manufacturer price ex VAT (€M)	954	1,040	9.0%
Proportion of sales by hospitals	38%	36%	-5.3%

Source: GERS community pharmacy sales data and tax declarations of outpatient sales; data processed by CEPS...
** includes a correction of + €2M in relation to the figures given in the 2008 annual report, based on data not available in 2008.*

2.2. *Sales within the scope of the ONDAM hospital target*

2.2.1 *Medicines reimbursed on top of general hospitalisation costs*

Estimated sales of these medicines in 2009 totalled approximately €2.5bn, representing a 4% increase on 2008.

No direct records are kept of these totals. The estimate is therefore arrived at by matching different sources against each other:

- companies' sales declarations (AFSSAPS tax declarations), though these are not comprehensive and do not distinguish between medicines that were actually sold on to outpatients and claimed back from national health insurance and those that were not.
- GERS data: suppliers' sales to healthcare establishments, broken down by UCD (common dispensing unit) code. The tariffs set by CEPS[10] can be applied to these volumes to obtain a theoretical figure, though with the same proviso regarding accuracy as for the tax declaration figures.

[9] See glossary in Appendix 7.
[10] The *tarifs de responsabilité* ("accountability tariffs", the maximum price chargeable) for medicinal products covered by *l'assurance maladie* on top of funding for general hospitalisation costs are set by CEPS and published in the official bulletin in the form of price decrees (NB: the sums reimbursed to the healthcare establishment by *l'assurance maladie* are worked out on the basis of the "accountability tariffs").

- ATIH data covers all medicines invoiced on top of the general "GHS funding". This information covers the total for purchases at the prices actually implemented and the volumes costed according to the "accountability tariffs".
- data on refunds paid out by the national health insurance general plan (*régime général*), which then need to be extrapolated to all the plans and have sale markups and VAT deducted[11].

2.2.2 *Medicines covered by Provisional Authorisations*

In addition to the funding linked directly to the activities carried out, funds are available to support healthcare establishments in "general interest missions" and in setting up contracts covering targets and resources with their regional hospital services planning and coordinating agency (*Agence régional d'hospitalisation*, ARH).

As there is no specific data available on hospitals' purchases of medicines for inpatient use which are under provisional authorisations (ATU) under the terms of the Public Health Code, Article L.5121-12, these are estimated on the basis of funds allocated by the ARH under this MIGAC[12] heading. In 2009, these funds totalled €71.7bn representing a 33% rise compared with 2008.

2.2.3 *Medicines funded under the GHS tariffs*

CEPS estimates that as in 2007 and 2008, the total spent on medicine purchases funded under the "GHS" heading has remained unchanged, hence in 2009 the figure was €1.8bn.

This estimate was produced using the same method as in previous years and is based both on the declarations made by the companies to CEPS for hospital outpatient medicines and hospital inpatient medicines invoiced on top of those included in GHS funding and those made to AFSSAPS, although not all the latter were available at the time of writing this report.

2.3. *Orphan medicines*

Sales of orphan medicines accounted for over €930M in 2009. Hospitals account for two thirds of this figure. Sales of these medicines grew by 14% from 2008 to 2009.

Beyond the unifying factor of the status given to all medicines in this category, the products it contains actually have widely differing economic profiles. In terms of cost, a little over half the category is accounted for by cancer medicines, primarily those for multiple myeloma and chronic myeloid leukaemia. A total of €130M, covering around half a dozen products, was spent on pulmonary arterial hypertension. Sales of enzyme replacement and other protein replacement medicines, such as treatments for Fabry disease or Gaucher disease were worth approximately €180M. The remaining €130M was split between thirty or so medicines with a variety of indications.

If we present the situation from a different angle, we can note that thirteen orphan drugs each account for annual sales in France of over €30M, making a total of €710M, while around fifty others make up the remaining €230M, with average annual individual sales worth under €5M.

The committee is therefore naturally questioning the value of continuing to provide support and special benefits for medicines that make a high turnover when their profitability on the market is at least as firmly guaranteed as that of most non-orphan medicines.

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11 ERRATUM: Table 8 in the 2008 annual report showed figures estimated by CEPS, whereas the sources quoted were PMSI and Erasmus.

12 MIGAC: see glossary in Appendix 7.

3. From reimbursable sales to actual reimbursements

Sales including VAT of reimbursable medicines by community pharmacies rose to €27.11bn in 2009, representing a 2.2% rise on the 2008 figure. Added to this is the figure for hospital outpatient medicine sales, estimated at €1.35bn, or approximately €1.45bn including markup and VAT, compared with €1.30bn in 2008. The total growth in sales of reimbursable medicines within the scope of the ONDAM community target from 2008 to 2009 can therefore be estimated at 2.73%.

To convert the growth in sales to a figure for growth in expenditure, we need to know how the average reimbursement rate grew. According to CNAMTS, this rate remained almost unchanged, since it was calculated as 75.70% in 2009 and 75.58% in 2008. It is useful to note that alongside this very small growth in the average reimbursement rate there was slightly more sustained growth in the theoretical average rate, in other words the rate we would have seen if none of the insured were claiming for chronic medical conditions (see Table 11). It seems to be the case therefore that as the 2007-2008 growth figures had suggested, chronic conditions have stopped pushing up the growth of the average reimbursement rate and the trend may even be reversing. However, the differences are too small at present to draw any firm conclusions from them, for example regarding the use of the two-part prescription (*ordonnance bizone*).

Growth in reimbursements of medicines within the scope of the ONDAM community target was therefore 2.9%.

The remaining costs borne by patients and hence by the top-up health insurance companies (to the tune of 93% of the total after deduction of excesses) therefore represented €6,940M, a 2.13% increase on 2008.

Table 11: Growth of community pharmacy and outpatient sales and theoretical reimbursements (in €M) in 2008-2009 according to cover level

	2008			2009		
Cover level (theoretical)	Sales inc VAT	Theoretical reimbursements	Average theoretical cover level*	Sales inc VAT	Theoretical reimbursements	Average theoretical cover level*
35%	3,649	1,277		3,711	1,299	
65%	20,442	13,287		20,718	13,467	
100%	2,434	2,434		2,680	2,680	
100% reimbursed outpatient sales	1,300	1,300		1,450	1,450	
Total under ONDAM community target	27,825	18,299	65.76%	28,559	18,896	66.16%

Source: CNAMTS and GERS community pharmacy sales data and tax declarations of outpatient sales; data processed by CEPS.

**sales-weighted average including VAT of listed reimbursement levels.*

CHAPTER II – PRICE SETTING WORK IN 2009

1. Methods for setting medicine prices

The price setting methods are essentially as described in Appendix 2, which is taken from the 2008 report. However there are three points on which the committee felt the need to explain its approach.

1.1. *Upgrading of new alternative medicines with no ASMR rating*

The fundamental rule for setting the price of medicines, as explained and discussed in Appendix 2, is that medicines which do not add to the existing medical benefit can only be included on a reimbursable medicines list if they represent savings on treatment costs. On several occasions, CEPS has encountered problems in applying this rule, which relate to the criteria according to which the *Commission de la transparence* (Transparency Commission) grants ASMR ratings (*amélioration du service médical rendu* – added medical benefit) and to how far back the reference products for the medicine submitted for inclusion on the list go, which can be a long way. For some illnesses, it is a long time since any new products have come onto the market and yet the needs relating to the illness are still partly unfulfilled, primarily due to the fact that some patients do not respond or have stopped responding to the available treatments. It can happen that medicines come forward that have a different mechanism of action and are therefore likely to go at least some way towards fulfilling the unmet needs, and yet which are not – and probably cannot be – shown to be superior to the reference products. The Transparency Commission therefore considers that it cannot grant an ASMR rating above V to these products, whilst at the same time sometimes indicating that they are useful alternative treatments. When on top of this, the treatments costs of the old reference products are very low and hence incompatible with the costs required to market more recently developed drugs, the committee is sometimes obliged to make an exception, as it is allowed to do according to the case law, and to grant an ASMR rating in order to make a drug available to patients, without ignoring the fundamental rule of the *Code de la Sécurité Sociale* (Social Security Code).

1.2. *Restricting spending on ASMR-rated drugs in expensive classes*

Conversely, one might say, the committee has sought to put a halt to the uninterrupted rise in prices of the most expensive medicines. In most countries, for a very long time there had been the tacit acceptance that a medicine which was given a high ASMR rating was entitled to ask a higher price than that of the reference medicine, as authorised in France by the Social Security Code. In some drug classes, in particular anti-cancer drugs, in which new products have succeeded each other at a farily sustained rate, this system has sometimes resulted in prices corresponding to considerable treatment costs: up to around €50,000 per year per patient for some products. The committee has therefore let it be known that at these price levels, it considers that access to these highly profitable markets constitutes sufficient benefit for the innovating companies, whilst it is not necessary or justifiable for the national health insurance system to take on further costs.

1.3. *"Risk-sharing" contracts*

In several European countries, so-called "risk-sharing" contracts are currently being used, though in widely differing forms, the purpose of which is to seek an acceptable compromise when taking on the costs of medicines that are likely to involve a considerable extra burden but whose conditions of use or efficacy are still highly uncertain. Most of these contracts are only risk-sharing by name and are in fact simple price-volume contracts or contracts based on posologies or treatment durations in practice, such as those often used by CEPS.

Genuine risk-sharing contracts could be considered when a medicine is put forward accompanied by clinical documentation that does not warrant a high ASMR rating even though it may have strong

potential. In the majority of cases, the committee relies on what has already been proven, at the risk that the medicine may not be registered on a reimbursable medicines list if no price agreement can be reached under the terms of the Social Security Code. However, 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.

2. Statistics

The following statistics relate to applications submitted by companies and to price change case files opened at the committee's instigation.

The case files are defined in terms of a single type of application regarding a single product: first application for registration on the community medicines list only or on the community medicines and public hospital medicines lists but only for products available in community pharmacies, re-inclusion on the lists, price change, extended indications or changed conditions of use.

Several different branded medicines corresponding to the same drug product may be grouped together in one file (for example for dose changes of the same drug product) and some of these may have several different formats (e.g. packed in boxes of 7 x 10mg tablets or 28 x 10mg tablets). Price change case files opened at the committee's instigation may cover several different branded products.

2.1. *Case files opened in 2009*

In 2009, 1,407 case files corresponding to 5,205 different products or product formats, i.e. 3.7 per file on average, were submitted to CEPS by companies or opened by CEPS. Two thirds of these products or product formats were generic medicines.

The total number of case files opened in 2009 was 10% higher than in 2008. This increase in the committee's case load is due in part to the increased number of re-inclusion applications, especially for generics. It is also due to the number of price change files, 94% of which were opened at the committee's instigation in response to ministerial guidelines (which related to fewer products or product formats that in 2008: 2,231 as opposed to 2,566, of which the proportion represented by generics was considerably higher in 2009).

Table 12: Number and type of case files opened in 2009 by type of application

Type of application	Number of cases	Number of products or product formats[1]	Number of files relating to generics	Percentage of files relating to generics
Extended indications	47	156	1	1%
Price change	406	2,231	1,656	74%
First listing	541	1,513	1,144	76%
Re-listing	413	1,305	678	52%
Total	1,407	5,205	3,479	67%

Source: CEPS - from Medimed application, January 2010.

[1]. 94% of these were instigated by CEPS.

2.2. *Case files closed in 2009*

The number of case files closed in 2009 was higher than the number of files opened, mainly due to the clearing of the backlog of re-inclusion applications. The 1,822 cases processed by the committee in 2009 related to 6,392 products or product formats.

The number of products or product formats affected by price changes in 2009 was slightly lower than the number in 2008 and the proportion of these products which were generics was far higher (72% as opposed to 46% in 2008).

Table 13: Number and type of case files closed in 2008 by type of application

Type of application	Number of cases	Number of products or product formats[1]	Number of files relating to generics	Percentage of files relating to generics
Extended indications	33	237	1	0%
Price change	403	2,521	1,810	72%
First listing	544	1,453	1,149	79%
Re-listing	842	2,181	873	40%
Total	1,822	6,392	3,833	60%

Source: CEPS - from Medimed application, January 2010.

[1]. 95% of these were instigated by CEPS.

Of the applications processed in 2009, 96% ended in agreement between the committee and the respective companies, leading to publication in the *Journal Officiel* (JO – the official gazette of the French government). Of the remaining cases, the applications were withdrawn (2%) or abandoned (1%) by the company. Applications are still only rejected by the committee in exceptional circumstances and usually relate either to first listing, extended indications which have not received a favourable opinion from the Transparency Commission, or price increases.

Table 14: Numbers of products or product formats by type of application and decision for drug files closed in 2009

Decision / Type of application	Accepted	Abandoned	Withdrawn	Rejected	Total
Extended indications	192	2	35	8	237
Price change	2,420	37	63	1	2,521
First listing	1,390	25	22	16	1,453
Re-listing	2,144	0	37	0	2,181
Total	6,182	64	157	25	6,392

Source: CEPS - from Medimed application, January 2010.

2.3. *First applications for registration on the reimbursable medicines lists*

As in previous years, the majority of first applications for registration processed in 2009 related to generic products. Of the first-listing applications for generics, 99% resulted in an agreement, compared with 84% for original drugs. The vast majority of applications which did not have a positive outcome were due to applications being withdrawn or abandoned by the pharmaceutical company.

Table 15: Outcome of first listing applications handled in 2009 by numbers and type of product

Decision / Type of product	Accepted		Abandoned		Withdrawn		Rejected		All
generics	1,134	99%	5	0%	2	0%	8	1%	1,149
original drugs	256	84%	20	7%	20	7%	8	3%	304
all	1,390	96%	25	2%	22	2%	16	1%	1,453

Source: CEPS - from Medimed application, January 2010.

2.4. *Case files still in progress at the end of 2009*

For the second year running, the number of applications in progress at the end of the year was considerably lower than the previous year and in this case was 543.

Table 16: Number of case files still in progress on 31 December 2009

Type of application	Total number of files in progress	Percentage of files relating to generics
Extended indications	30	0%
Price change	64	32%
First listing	177	45%
Re-listing	272	48%
Total	543	43%

Source: CEPS - from Medimed application, January 2010.

3. Processing times for registration applications

3.1. *Processing of fast-track price applications*

Three price applications were processed in 2009 under the fast-track procedure.

Only one of these – for Xarelto (rivaroxaban) - was accepted. This is the first case in which the provisions of the framework agreement were applied whereby the fast-track price procedure is allowed for ASMR IV-rated medicines if it can be shown that their use will not lead to increased costs to the national health insurance system compared with the reference products.

Two other fast-track price applications submitted in 2009 were opposed by the committee and transferred to the normal application procedure. The committee's reason for opposing these applications was the inadequacy of the undertakings in relation to the price level requested.

3.2. *Overall processing time of first applications for registration on the reimbursable medicines lists*

The reduction of the backlog of applications in progress at the end of the year (cf. 2.4) is largely due to the reduction in the processing time of first applications for registration, in particular first-listing applications for generics. The average processing time for applications leading to publication in the *Journal Officiel* (JO) in 2009 was 89 days, the average for generics being 65 days and that for original drugs being 213 days.

Table 17: 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 data from Medimed application, January 2010.

3.3. *Interim processing times*

The overall time taken to process a first listing application has been broken down into the following five stages: from submission of the application up to notification of the Transparency Commission's opinion to CEPS; from notification of the TC's opinion up to the committee's first session (examination), from the first to the last of the committee's sessions devoted to the same case (negotiation), from the last session up to the signing of the rider (agreement) and from the signing of the rider by both parties up to publication of the registration decree and price notice in the JO or to closure of the file in cases of withdrawn, rejected or abandoned applications.

Table 18: Average interim processing times for drug listing applications in 2009 (in number of days)

Type of product	TC	Examination	Negotiation	Agreement	JO or closure	TOTAL
Generics	0	19	1	17	29	66
Non-generics	86	28	41	33	68	256
All	NS	21	9	20	37	106

Source: CEPS data based on extract from Medimed, January 2010.

3.3.1 *First stage: Transparency Commission*

Applications must be lodged simultaneously with both CEPS and the Transparency Commission (TC). During this first stage, the TC examines the application and notifies CEPS of its opinion. Only non-generic medicines, with some exceptions (change of packaging from that of the original drug or non-reimbursable original drug), go through this stage of the application.

In 2009, the average time taken for the Transparency Commission's final opinion to be sent to CEPS was 86 days after receipt of the application.

3.3.2 *Second stage: Examination*

For non-generic medicines, this stage runs from the date on which CEPS receives the TC's opinion to the first session during which the committee examines the product or product format. This stage may include the appointment of a rapporteur after receipt of the TC's opinion, who examines the application in liaison with the pharmaceutical company and draws up a report which is presented to the committee, plus the time taken for the application in question to be accommodated on the committee's agenda (at least one clear week after committee members have received the report).

In 2009, the average duration of this second stage was 21 days. These intervals were cut by more than half between 2007 and 2009, especially for applications concerning generic drugs.

3.3.3 *Third stage: Negotiation*

This third stage runs from the first to the last of the sessions at which CEPS examines the application. It corresponds to the time required by the committee to draw up its proposal, where it is not finalised in a single session, plus the time needed for negotiations between the committee and the pharmaceutical company. The committee must examine the company's counter-proposals if the latter rejects the committee's initial proposal following its discussions with the rapporteur.

In 2009, the average duration of the negotiation stage was 9 days. The average duration for generics was 1 day and 41 days for non-generics.

Listing applications for generics, which accounted for 79% of all listing applications, usually require no more than one examination session by the committee. The negotiation period of the few exceptions which required more than one examination was 30 days on average. For one application, the committee met a total of 5 times due to the complexity of the case. It related to the registration and price setting of certain generics whose INN corresponded to two different original drugs, with different indications and different prices.

Fewer than half the listing applications for non-generic medicines required more than one examination session by the committee. On average, 3 sessions were required before an agreement was reached.

3.3.4 *Fourth stage: Agreement*

This is the time between the last of the committee's sessions devoted to an application and the signing of the relevant contract rider. It corresponds to the time needed to draw up the terms of the rider, which may involve several exchanges of correspondence between CEPS and the company and also the time required for the logistics involved in the two parties signing the rider. The fourth stage actually includes a final negotiating period which is difficult to separate from the time required for the practical arrangements.

As in 2008, the average interval between the last of the committee's session and its decision was 17 days in 2009 for generic drugs and 33 days for non-generics.

3.3.5 *Fifth stage: Signing of the decrees and publication in the Journal Officiel.*

This final stage includes the preparation of the price notices by CEPS, the drawing up and signing of the decrees of registration on the reimbursable medicines lists by the relevant health ministry departments, preparation of the rates decisions by the UNCAM Chief Executive, then sending of these documents to the government publications office for entry in the *JO*.

The average time taken for this stage in 2009 was 37 days; the average time for generics was 29 and for non-generics 68.

4. Hospital prices and tariffs

In 2009, 71 new products (or new formats of already listed products) were registered either on the outpatient medicines list only (16), the list of additional medicines reimbursable on top of GHS funding only (22) or on both lists (33).

Each of these new registrations corresponds to an application which may include several tariff entries (one entry per common dispensing unit).

Of the 2009 applications for registration on both lists, 75% were for generics.

New anti-cancer drugs, antifungal agents, blood products and erythropoietin products were registered on the list of additional medicines reimbursable on top of GHS funding (the "additional medicines list"), including the two orphan drugs Vidaza and Firazyr. Anti-cancer drugs, blood products and drugs for the treatment of HIV were registered on the outpatient medicines list. Four proprietary products registered on this list are orphan drugs: Afinitor, Kuvan, Thalidomide and Vidaza.

The prices of 26 (non-generic) branded drugs and those of 9 drug substances (both original drugs + generics) listed on one or other of the two lists were reduced. Details of these price reductions are given in Chapter III 1.2.

4.1. *Application processing times*

The applications processed by CEPS in 2009 led to the setting of either a prescription fee or a *tarif de responsabilité* (the "accountability tariff", the maximum selling price for drugs on the additional medicines list) by the committee and publication in the *JO* of 216 tariff entries (where tariff entries correspond to a common dispensing unit associated with one or other of the lists: 80 on the outpatient medicines list only, 62 on the additional medicines list only and 37 on both lists).

The application processing times were worked out for products registered on either the outpatient medicines list or the additional medicines list for which the prices were published in 2009.

For 64 of the 216 tariff entries processed in 2009, the companies did not make a price submission, contrary to the provisions of Article 8b) of the framework agreement of 25 September 2008 between the *Comité Economique des Produits de Santé* (CEPS) and the pharmaceutical companies, as amended by the rider of 26 October 2009 (see Appendix 1). Most of the drugs concerned were generics. In such instances, the committee sets the price or tariff unilaterally. The average interval before publication was 76 days after registration on one of the lists.

As for the drugs for which the companies in question did make price submissions, the average interval between registration on one or other of the lists and publication of either the prescription price or the "accountability tariff" was 62 days. The average interval between registration on the outpatient medicines list and publication of the public prescription price was 81 days, whilst the interval before publication of tariffs for medicines registered on the additional medicines list was 38 days. This difference can be explained by the fact that for the additional medicines list, the tariffs can be published at the committee's initiative without going through any further procedures. On average, the tariffs are published 12 days after the pharmaceutical company has been notified of the committee's decision. For medicines on the outpatient list however, the price can only be published at the same time the public reimbursement rate is registered, which is an average of 53 days after the pharmaceutical company has been notified of the committee's decision.

The intervals between the company's prices submission[13] and registration on the list are an average of 11 days for outpatient medicines and 5 days for those on the additional medicines list. The time taken between the price submission and the examination by the committee is the same for medicines on both lists: 8 days. The intervals before the company is notified by post of the committee's decision are an average of 9 days for outpatient medicines and 13 days for those on the additional medicines list. The reason for this discrepancy is that the files concerning medicines on the additional list required more examination sessions on average by the committee than those on the outpatient medicines list.

4.2. *Applications opposed by CEPS*

In 2009, CEPS definitively opposed the company's price submission for five different products. For seven other products, the committee opposed the first submission but an agreement was reached after a second submission. In all other instances, the price or tariff published was the one initially submitted by the company.

13 We have adopted the convention of counting the price submissions immediately from the time they are registered on a list, where the company has made its submission before registration and used the same procedure if the committee has examined the price during a session before the registration.

CHAPTER III - REGULATION

1. Expenditure regulation measures

1.1. *Measures relating to the ONDAM community target*

The committee proceeded to implement price reductions, in accordance with the guidelines received from ministers during the planning phase of the 2009 Social Security Funding Act.

All these reductions were implemented in the agreements with the pharmaceutical companies.

The reductions led to savings totalling just over €410M. It should be noted that this total, which is always calculated by the committee according to the same methods, corresponds to the impact of price reductions on the financial year in question – in this case 2009 – regardless of the date on which they came into force. It therefore includes the carry-over effect of reductions which were introduced in the previous or even earlier financial years, calculated on the basis of the increasing or decreasing sales volumes of the medicines in question and the *Assurance maladie* reimbursement rates in force during the relevant periods. For reductions introduced in the financial year in question, it only includes their impact on that year, hence producing a carry-over effect for the following financial year.

For 2009, the €410M savings are the result of a €215M carry-over effect from previous measures and a €195M effect on 2009 of reductions actually introduced in 2009. The value of the carry-over effect to 2010, which will depend on the sales volumes actually recorded in 2010, may be estimated at approximately €185M.

This figure of €410M can also be broken down into €274M from price reductions of on-patent medicines sold in community pharmacies, added to which are a further €40M of savings on these same medicines as a result of the 5% reduction in manufacturer prices systematically applied to three-monthly pack sizes; €90M worth of savings made on generics and through the fixed "accountability tariffs" and €6M worth of savings from price reductions on medicines sold to outpatients. The committee therefore does not include in these figures any savings linked to the reduced prescription price of original drugs resulting from the advent of generics on the market, insofar as its own actions play no part in this effect.

As regards the various grounds for these reductions, there have been no changes in this respect compared with those described in the previous annual report.

These reductions led to savings of €141M on the amount left for patients, and hence primarily the top-up health insurance companies, to pay.

1.2. *Medicines under the ONDAM hospital target*

1.2.1 *Tariff reductions on genericised medicines*

As in the previous year, reductions of genericised drug prices introduced in 2009 were motivated by the wish to reduce the considerable discrepancy between the prescription price or the "accountability tariffs" set by the committee and the price levels actually used in practice.

These reductions mainly concerned products used in chemotherapy for cancer patients. These were antimetabolites (gemcitabine - *Gemzar*), anthracyclines (doxorubicin – *Adriblastina*, epirubicin – *Farmorubicin*), camptothecin derivatives (irinotecan - *Campto*), platinum derivatives (carboplatin - *Paraplatin*, oxaliplatin – *Eloxatin*), taxanes (paclitaxel - *Taxol*) and vinca alkaloids (vinorelbine - *Navelbine*).

In addition to these drugs used in cancer treatment, the price of fluconazole injection (Triflucan) was also reduced in 2009.

As mentioned above in the context of medicines for outpatients, these reductions are not included as savings resulting from the committee's actions, largely due to the fact that specifically for products that are funded on top of general hospitalisation costs, the reduction of tariffs when prices have already fallen due to competitive downward pressure leads to a reduction in hospitals' income from tariff rebates, but has no impact on their expenditure.

1.2.2 *Price reduction decisions for medicines over five years old*

Prescription price reductions and "accountability tariff" reductions for medicines which have been on the market for over five years and are being sold at lower prices in one or more EU country which is party to the framework agreement than in France affected 23 proprietary products.

The savings made in this respect totalled €24M.

2. Post-registration studies

The registration of new medicines on the reimbursable lists, in particular though not exclusively those which have been given an ASMR rating of III or higher, often goes hand in hand with the obligation to carry out a study, known as a "post marketing" or "post registration study".

The purpose and some of the conditions regarding the conduct of these studies are almost always laid down in the rider clauses between the companies and CEPS setting out the medicine prices and other provisions. They therefore constitute legal obligations for these companies. The general conditions governing the performance of these studies are set in Article 11 of the framework agreement, which discusses follow-up of new medicines in real-life clinical practice.

The vast majority of requests to conduct studies come from the Transparency Commission and the remainder from CEPS.

2.1. *Studies requested by the Transparency Commission*

The general purpose of the requests issued by the Transparency Commission is almost always to ascertain whether a product which has shown promise in clinical trials of potential clinical benefits to a particular patient group, either in terms of efficacy or of undesirable effects, actually presents this benefit in real-life practice and whether the benefit is as significant as had been expected.

In 2009, the Transparency Commission requested fifteen or so studies, the same number as in 2008 and slightly fewer than in previous years due to the current slowdown in the discovery of new drugs. Further information on this subject may be found in the annual report of the *Haute Autorité de Santé*.

2.2. *Studies requested by CEPS*

The committee may request studies in three situations.

In exceptional cases, at the initiative of the *Direction générale de la santé* of the ministry of health, the committee requests a study for very similar reasons to those of the Transparency Commission, where the latter has considered a study unnecessary.

In most cases, the studies requested by the committee are for essentially economic purposes and are aimed at assessing the conditions of use of a new drug in real-life practice, such as posology, co-prescription, place in the treatment strategy, type of patient population reached, etc.

Finally, in the rare instances in which the committee has deemed it possible to enter into a "risk-sharing contract", under the circumstances described in Chapter II, the study is an essential element of the contract.

2.3. *Time taken to conduct the studies*

The situation regarding the sometimes excessive delay that had been occurring in starting or carrying out studies led to two types of measure being taken.

The first measure, implemented in the context of the agreements with the companies, entailed amending the framework agreement to stipulate that even in instances where the Transparency Commission must be consulted over the draft protocol, where it is the commission that has requested the study, the absence of approval of the draft protocol does not exempt the company from the starting the study, at its own risk, within the contractually agreed timescale. The aim was to counteract the possibility of stalling tactics, which were especially tempting to use since ISPEP deems that actively contributing to drawing up protocols does not fall within its remit.

This amendment goes back to 2007 and it is too soon to evaluate the impact it has had on how the studies have actually been conducted. However, it appears that studies have been starting more promptly.

The other measure consisted of introducing a system of sanctions into the law in the event of failure to carry out the studies or of carrying them out too late or inadequately. After several unsuccessful attempts, this was achieved with the new Article L. 162-174-4 5° of the Social Security Code, brought in by Article 73 of the Law of 21 July 2009. In the event of failure by companies to comply with their obligations with respect to conducting studies, the committee is now entitled to impose financial sanctions proportionate to these failures. As at the end of 2009, no sanctions had yet been imposed.

3. Measures relating to promotion of medicines

3.1. *Certification of medical sales visits*

Pursuant to Article L. 162-17-4 of the Social Security Code, introduced by the Law of 13 August 2004, companies who have signed agreements with CEPS "must undertake to abide by the medical sales visit charter and to have the sales visits which they organise or sponsor assessed by accredited bodies and certified as being compliant with the charter, in accordance with the procedure laid down by the *Haute Autorité de Santé*."

As at 31 December 2009, 105 pharmaceutical companies selling medicines to community pharmacies and 40 medical sales visit contractors were certified.

With regard to medical sales visits in hospitals, on the basis of the rider to the medical sales visit charter on this subject signed by LEEM and CEPS on 21 July 2008, the *Haute Autorité de Santé* drew up new certification guidelines in 2009.

The committee set 30 November 2010 as the date by which companies carrying out medical sales visits in hospitals must have been certified, failing which their agreements with CEPS would be terminated.

3.2. *Advertising bans*

In 2009, the committee reached definitive decisions on 17 advertising ban case files. The backlog of case files which had accumulated in 2008 was cleared in the first part of 2009.

Of these 17 advertising bans, four did not result in any penalty. The committee considered that the decision to ban the advertisement and the publication of the decision by AFSSAPS were sufficient sanctions in view of the degree of seriousness of the infringement. The other three advertisement bans resulted in fines worth a total of €3.95M.

The penalties imposed were equivalent to between 2.5% and 8% of the companies' pre-tax sales in France of the product in question. The greatest penalties, representing over 5% of the pre-tax sales, were imposed where the committee considered that the infringement represented a loss of opportunity

for patients. The committee used this as a criterion for three of the advertisement bans it dealt with in 2009.

The committee takes into account any aggravating circumstances, the majority being repeat offending, as well as any attenuating circumstances, before pronouncing its decision. The repeat offence criterion is taken into account when a previous advertisement ban for the same product or a product sold by the same company has been pronounced within the previous three years. The speed of the company's response in withdrawing the advertisement may be taken into consideration as an attenuating circumstance. The most significant reductions in penalties are granted when the company decides of its own accord to withdraw the advertisement as soon as it has been informed that AFSSAPS is looking into the possibility of a ban. In these instances, the company is asked to provide proof that the advertisement has been withdrawn.

CEPS is committed to ensuring the companies are given a fair hearing and takes the information they supply into consideration in reassessing the ban and its scope, and in some cases, the size of the fine imposed. Thirteen of the seventeen bans on which the committee made a decision in 2009 took two examination sessions before a decision was reached. In half the cases, the committee revised the penalty payment downwards, by an average of 30% compared with the intended penalty pronounced following the first examination, after taking the company's arguments into consideration.

All the penalty payments imposed have been settled in full.

4. End of year adjustments

4.1. *Agreements between CEPS and the pharmaceutical companies*

In 2009, 181 companies marketing reimbursable drugs sold in community pharmacies or hospital outpatient departments signed agreements with CEPS exempting them from the *contribution de sauvegarde* (the "safeguard contribution", a payment made by companies if their turnover exceeds the "K rate" threshold).

The growth in sales of reimbursable medicines dispensed in community pharmacies or to hospital outpatients reached 1.8% in monetary terms, which was higher than the "K rate" of 1.4% set for both community and hospitals. Since the threshold was exceeded, contributions were payable.

The growth forecasts on which the clawback thresholds set by CEPS were based were slightly above the actual growth rates which occurred. As a result, in the event, the cumulative total of the companies' contributions under the terms of the agreements was higher than the theoretical sum of the safeguard contributions. Pursuant to Article 17, paragraph 1 of the framework agreement, the committee therefore applied a uniform reduction rate of 20.34% to all the clawback payments owing under the terms of the agreement and to all the companies who were owed credits.

4.2. *Clawback credits*

Companies can receive two different types of credits. They can be credits by way of compensation such as credits for any price reductions introduced in 2009 which qualified for credits, or credits awarded under the CSIS[14] system to companies who have invested within Europe in such a way as to maintain or boost research and production activities in the European pharmaceutical sector or as consideration for expenditure incurred by the companies in producing patient information in Braille. Any credits which are not used in one year may be carried over to the following year.

In 2009, the total amount of clawback credits owing to the companies was €169M, of which €66M were carried over from previous years, €54M were CSIS credits awarded in 2009 and €49M were new credits other than CSIS. Two thirds of these clawback credits (€112M) were actually used, the rest (€57M) being carried forward to 2010.

[14] CSIS: see glossary in Appendix 7.

4.3. *Actual clawback payments*

The net clawback payments, quantity clawbacks and specific clawbacks by product owed by the companies for 2009, after deduction of the clawback credits used, came to a total of €236M.

As at 1 July 2010, only €3,656 of these have not yet been paid to URSSAF[15].

[15] URSSAF: see glossary.

PART TWO – MEDICAL DEVICES

CHAPTER I – SALES AND EXPENDITURE ON REIMBURSABLE MEDICAL DEVICES COVERED UNDER THE MEDICAL DEVICES AND SERVICES LIST

1. Sales

Unlike sales of medicines, for which reliable, detailed, standardised and exhaustive statistics are available almost immediately, in most cases there is little information about sales of medical devices.

Rough estimates can certainly be arrived at through *l'assurance maladie*'s reimbursement statistics (cf point 2 below), and this has been made considerably easier by the coding system, but direct information about sales is much more difficult to gather.

CEPS has undertaken in this report to provide information for three device categories to begin with, gathered in the context of its contractual relationships with the companies concerned, or which it is able to draw directly from the reimbursement statistics wherever these are closely representative of sales.

1.1. *Home respiratory aids and oxygen therapy equipment*

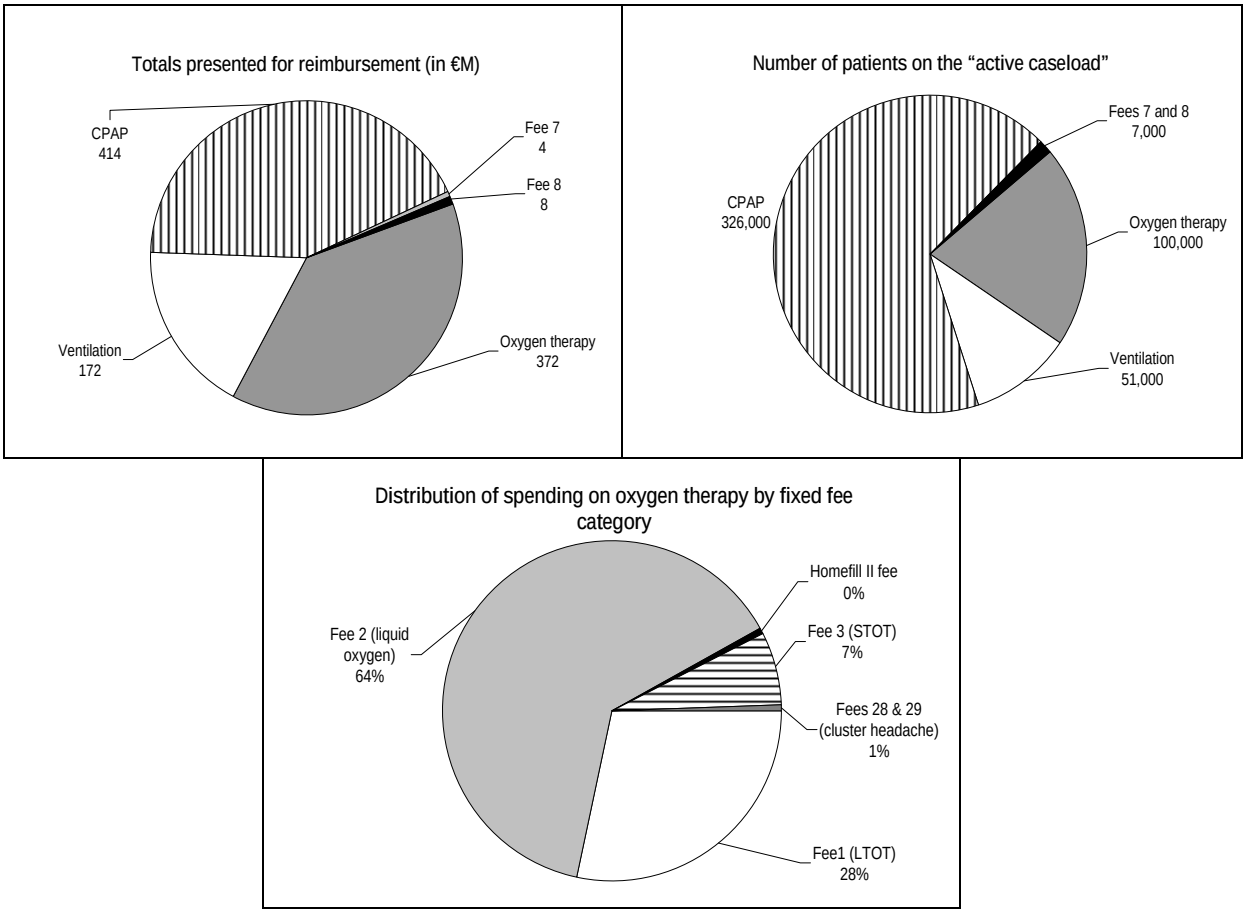
For the purposes of the 2010 tariff reviews, the committee analysed the respiratory equipment market, which has grown considerably over the last ten years or so and which represents almost 15% of spending on medical devices by *l'assurance maladie*.

The different fixed fees (*forfaits*) for respiratory equipment are divided into three main categories: oxygen therapy (fee categories 1 to 3 + Homefill II and categories 28 and 29 for cluster headaches), ventilation (categories 4 to 6) and continuous positive airway pressure – CPAP (fee category 9). Added to these are two individual fixed fees, category 7 (chest mobilisation and assisted coughing) and category 8 (tracheostomy without ventilation). Fee categories 4 to 9 can be combined with some oxygen therapy categories (10 to 27 and 30 to 35). For the analysis below, combined fees were added to the basic fees, with their corresponding allowance margin. The data shown were extrapolated from data gathered by CNAMTS.

In 2009, the fees claimed back from national health insurance totalled approximately €970M. The reimbursement rate is almost 100%, except for category 9 (75%) and categories 28 and 29 (just under 70%). The cost to *l'assurance maladie* was approximately €840M.

The number of patients on the "active caseload" who received respiratory aids in 2009, averaged out over the year, was almost 460,000 (this is the number obtained by dividing the number of weekly fees recorded during the year by 52) and 25,000 of these benefited from the two-fee combination. Approximately 325,000 patients are on CPAP, of whom 47,000 are on fee category 6 (fewer than 12 hours' ventilation per day), 45,000 on category 2 (liquid oxygen) and 43,000 on category 1 (long-term fixed oxygen). The total number of patients estimated to be on oxygen therapy is 100,000 and the total number on ventilation 51,000.

Figure 2: Home respiratory aids and oxygen therapy in 2009



Reimbursements paid out by *l'assurance maladie* for respiratory aid provision rose 29% overall between 2007 and 2009. Among the largest expenditure categories, those which grew most over this period were category fee 6 (+48.3%) and the CPAP categories (+40.2%). Category 2 grew by 19 % and all the oxygen therapy categories together by 16.8 %.

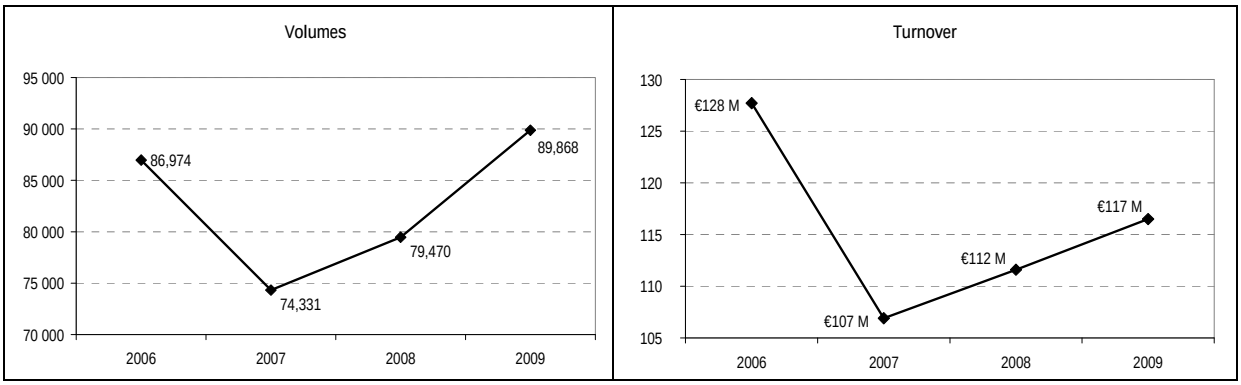
1.2. *Drug-eluting stents*

The drug-eluting stents market has been strongly affected by developments in the medical evaluation of these products. Following the claims regarding the risk of thrombosis which emerged in 2006, the market dropped significantly (-14.5%) from 2006 to 2007. Sales began to pick up again when these claims were disproved. This shows that practitioners take note of the evaluations that are carried out.

In 2006, the market was shared by three product ranges from three different manufacturers. In 2009, there were five product ranges from four manufacturers, with the prospect of two new ranges from two new manufacturers in 2010.

Growth in terms of turnover followed a downward trend alongside the upward trend in growth in volumes, due in the first instance to the introduction of new products at lower prices and in the second instance to the price reductions introduced, mainly in August 2009. This meant that the turnover in 2009 was lower than that of 2006, whilst the sales volumes were higher.

Figure 3: Growth in sales of drug-eluting stents 2006-2009



Source: CEPS - company declarations.

1.3. *Implantable cardioverter defibrillators*

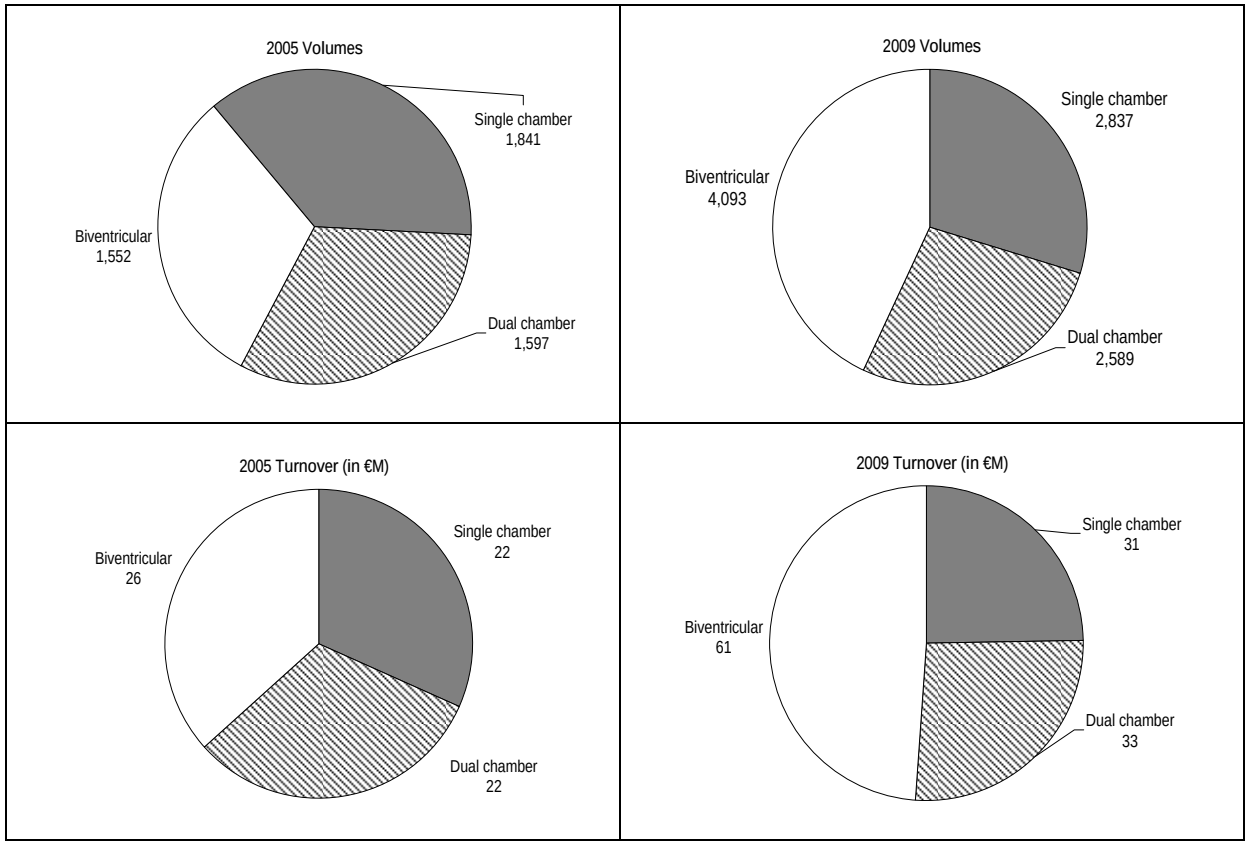
CEPS has information regarding the quantities of reimbursable implantable cardioverter defibrillators (ICDs) sold, from the annual declarations of the five companies who share the market, submitted under the terms of its agreements with the device manufacturers and distributors.

An analysis of the data shows that sales have grown significantly over the last four years. Sales of ICDs rose from 4,990 in 2005 to 9,519 in 2009 (+90.7%). The three categories of defibrillators have grown at the same rate over this period, with especially high growth in biventricular ICDs (see Figure 4).

- From 1,841 to 2,837 for single chamber devices (+54%);
- From 1,597 to 2,589 for dual chamber devices (+62%);
- From 1,552 to 4,093 for bi-ventricular (triple chamber) devices (+164%);

In terms of turnover, the increase between 2005 and 2009 is just as high, due to increased sales of biventricular ICDs and their increasing role, in spite of the 10% price reduction introduced on 13 January 2009. The market grew from €70M to €124M (+77.1%) between 2005 and 2009.

Figure 4: Comparison of defibrillator sales 2005/2009



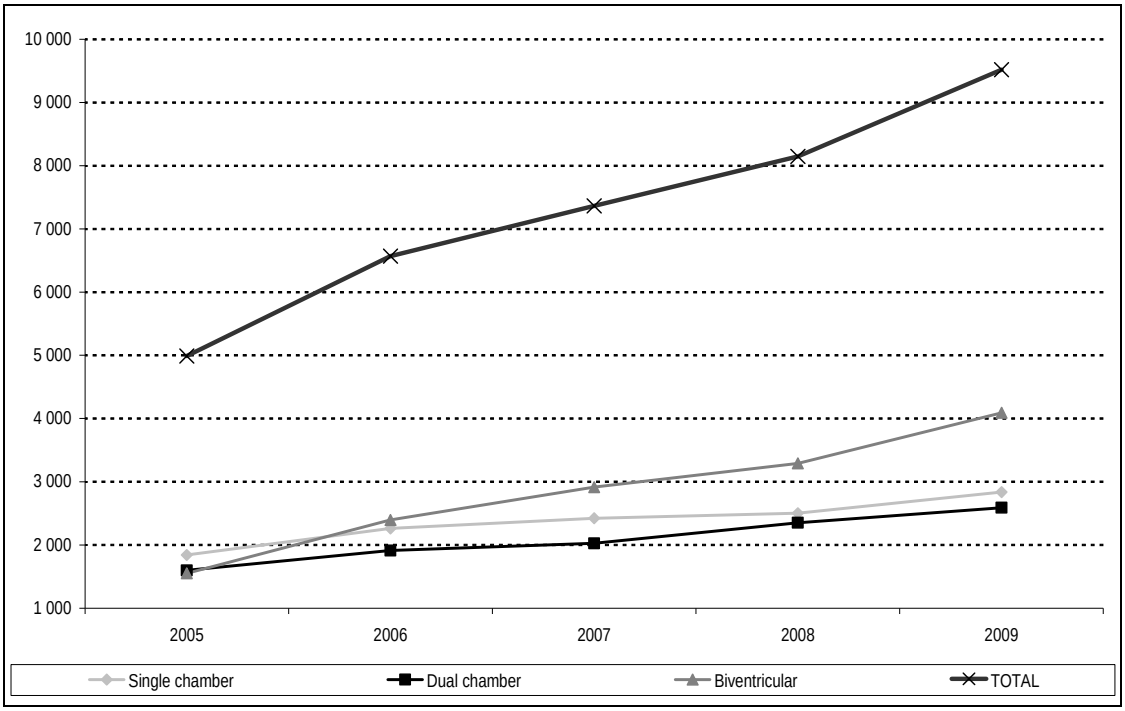
Source: CEPS - company declarations.

Figure 5 traces the growth in sales of implantable cardioverter defibrillators over the last five years. A steady increase can be observed.

This indicates that hospitals and other healthcare establishments widely planned ahead for the extend indication to primary prevention, which was only added to the LPPR list in November 2009.

This forward planning started even before February 2007, which fits in with the delivery by CEPP (*Comité d'évaluation des produits et prestations* – the medical device and services assessment committee) of a positive opinion on this issue.

Figure 5: Growth in sales volumes of defibrillators 2005-2009



Source: CEPS - company declarations.

2. Reimbursement of medical devices

2.1. *Overview*

Spending on medical devices registered on the reimbursable medical devices and products list (LPPR) totalled €5.746bn in 2009 (see Tables 19 and 20).

For the first time, the committee has obtained LPPR data broken down by code and section from each of the three main compulsory health insurance plans (UNCAM): CNAMTS[16], RSI and MSA, plus data from ATIH regarding purchases of implantable medical devices by the healthcare establishments (Implantable Medical Devices, Code III).

Compared with 2008, the reimbursements paid out by the three main plans in 2009 were 0.3% higher (see Table 19).

This represents a significant slowdown in growth compared with previous years, which can be explained by the fact that it was the first full year in which certain medical devices were included in the EHPAD fixed budgets (EHPAD: *Etablissements d'Hébergement pour Personnes Agées Dépendantes* - care homes for the elderly), which took place on 1 August 2008. And indeed, as anticipated, the fall in expenditure related primarily to equipment which came under the new system, such as mobility equipment and home care equipment.

Spending on implantable medical devices (IMDs) by public healthcare establishments must then be added to this. This total was €715M, representing a 12.4 % increase. Total expenditure including spending on IMDs by public healthcare establishments therefore grew by 1.6% in 2009.

[16] Since the data from CNAMTS do not include data for overseas départements, the data were extrapolated to the whole of France including overseas départements on the basis that these represent +3% expenditure, split equally between each code and section.

Table 19: Reimbursements of medical devices in 2009 (in €M)

Name of device or service	2007	2008	2009	Growth rate 2008/2007	Growth rate 2009/2008	Percentage of 2009 total
Code I:						
Home respiratory aids, oxygen therapy equipment	665.4	752.2	838.3	13.0%	11.4%	14.6%
Home care medical aids, nutrition and miscellaneous items	1,826.7	2,025.5	1,913.1	10.9%	-5.5%	33.3%
Casting and splinting equipment	21.4	22.3	22.7	4.0%	1.9%	0.4%
Dressing supplies	394.7	415.1	428.8	5.2%	3.3%	7.5%
Aerosol-generating devices	42.3	43.3	45.9	2.3%	6.1%	0.8%
Code I sub-total	2,950.6	3,258.5	3,248.9	10.4%	-0.3%	56.5%
Code II:						
Orthotic devices (small) (ch 1)	301.8	322.4	340.7	6.8%	5.7%	5.9%
All Opticianry (ch. 2)	179.0	181.5	185.7	1.4%	2.3%	3.2%
Electronic devices for the deaf and hard of hearing (ch. 3)	86.7	91.6	96.8	5.7%	5.7%	1.7%
Non-orthopaedic external orthotic devices (ch. 4)	9.1	9.4	10.7	4.2%	13.1%	0.2%
Eye and face prosthetic devices (ch. 5)	7.4	8.6	8.8	16.0%	2.1%	0.2%
Orthopaedic shoes (ch. 6)	69.7	75.0	77.1	7.6%	2.7%	1.3%
Orthotic prosthetic devices (ch. 7)	158.4	172.2	184.9	8.7%	7.4%	3.2%
Medical devices reimbursement exceptions and 150% LPP occupational accident supplement	0.0	0.3	0.6	ns	ns	0.0%
Code II sub-total	812.1	861.0	905.3	6.0%	5.1%	15.8%
Code III						
Ex-Blanket grant (*dotation globale*) - public hospitals	616.6	636.5	715.2	3.2%	12.4%	12.4%
Ex-"OQN" funding system (private hospitals)	718.7	761.6	762.0	6.0%	0.1%	13.3%
Code III sub-total	1,335.4	1,398.0	1,477.2	4.7%	5.7%	25.7%
Code IV	121.3	137.2	114.9	13.0%	-16.2%	2.0%
Total	5,219.4	5,654.6	5,746.2	8.3%	1.6%	100.0%

Sources: CNAMTS (General plan, with local mutual sections – mainland France), RSI and MSA (all of France), for Code III (medical devices): reimbursable totals – ATIH.
For ATIH statistics: purchases and growth in 2009 include purchases by the Service de Santé des Armées (SSA – army healthcare department) formerly under the blanket grant system, now under the T2A system since 01/01/2009.
Assumption: for overseas territories: +3% on general plan, distributed evenly between all lines.
*ns: *not significant.*

The reimbursable totals presented in Table 20 below correspond to quantities costed at the tariffs set by CEPS. The actual purchase prices can be higher than these tariffs, and for Code II items even much higher, especially adult opticianry and hearing aids.

The average reimbursement rate across all national health insurance plans for medical devices included on the reimbursable medical devices and services list (LPPR) is 89.4%. This high average reimbursement rate actually reflects significant disparities between the different sectors, ranging from 66% for opticianry to 100% for IMDs and mobility equipment.

Table 20: Reimbursement rates for medical devices in 2009

Name of device or service	Reimbursable total 2009 (in €M)	Total reimbursed 2009 (in €M)	Reimbursement rate 2009
Code I:			
Home respiratory aids, oxygen therapy equipment	973.4	838.3	86.1%
Home care medical aids, nutrition and miscellaneous items	2,055.4	1,913.1	93.1%
Casting and splinting equipment	29.8	22.7	76.4%
Dressing supplies	533.4	428.8	80.4%
Aerosol-generating devices	55.9	45.9	82.1%
Code I sub-total	3,647.8	3,248.9	89.1%
Code II:			
Orthotic devices (small) (ch 1)	480.6	340.7	70.9%
All Opticianry (ch. 2)	280.7	185.7	66.1%
Electronic devices for the deaf and hard of hearing (ch. 3)	138.2	96.8	70.1%
Non-orthopaedic external orthotic devices (ch. 4)	11.2	10.7	95.1%
Eye and face prosthetic devices (ch. 5)	8.8	8.8	99.8%
Orthopaedic shoes (ch. 6)	84.9	77.1	90.7%
Orthotic prosthetic devices (ch. 7)	185.0	184.9	100.0%
Medical devices reimbursement exceptions and 150% LPP occupational accident supplement	0.6	0.6	100.0%
Code II sub-total	1,189.9	905.3	76.1%
Code III			
Ex-Blanket grant (*dotation globale*) - public hospitals	715.2	715.2	100.0%
Ex-"OQN" funding system (private hospitals)	762.0	762.0	100.0%
Code III sub-total	1,477.2	1,477.2	100.0%
Code IV	114.9	114.9	100.0%
Total	6,429.9	5,746.2	89.4%

Sources: CNAMTS (General plan, with local mutual sections – mainland France), RSI and MSA (all of France), for Code III (medical devices): reimbursable totals – ATIH.
For ATIH statistics: purchases and growth in 2009 include purchases by the Service de Santé des Armées (SSA – army healthcare department) formerly under the blanket grant system, now under the T2A system since 01/01/2009.
Assumption: for overseas territories: +3% on general plan, distributed evenly between all lines.

2.2. *Analysis by code*

2.2.1 *Code I: Medical devices for home care and daily living aids, dietary foods and dressing supplies*

Code I includes homecare equipment, products and services for patients who are elderly, disabled, require post-operative care or have chronic conditions. Of the spending on medical devices in 2009, 57% was under this category. Spending under this code has decreased slightly (-0.3% compared with 2008), for the reasons explained above.

Self-testing and self-medication devices for diabetic patients also contributed significantly to the growth (+€39M on 2008), which can only be accounted for in very small part by the increased prevalence of type II diabetes and the progress in diagnosis of the disease.

The comments made in the 2008 annual report regarding the worrying rise in home respiratory care and oxygen therapy still apply in 2009. Spending on this category was +€86M compared with 2008 and is still the main category responsible for the growth in spending on medical devices. As in 2007 and 2008, this growth can be accounted for by the high increase in sleep apnea diagnosis and hence in continuous positive airway pressure treatment (CPAP).

2.2.2 *Code II: External orthotic and prosthetic devices*

Unlike 2008, 2009 saw faster growth in spending on external orthotic and prosthetic devices than the average growth of other devices. External orthotic and prosthetic devices account for 16% of total expenditure on medical devices reimbursed by compulsory national health insurance plans, representing a 5% increase on 2008.

The main items contributing to growth under this code were small orthotic devices (€18M) and orthotic prosthetic devices (€13M).

2.2.3 *Code III: Implantable Medical Devices (IMDs), human-derived implants and human-derived tissue grafts*

For implantable medical devices (IMDs) listed under Code III of the LPPR, CEPS sets maximum purchase prices identical to the reimbursement tariffs. The reimbursement rate for these devices is 100%.

Reimbursements under this code were worth a total of €1,477M, representing 5.7% growth compared with 2008. The proportion of this expenditure accounted for by private establishments (formerly on the "OQN funding system") was €762M and has barely changed in relation to 2008. This more or less stable situation is due to the fact that the growth in electrically powered implants (i.e. defibrillators, pacemakers, neurostimulators, etc.) was offset by the decline in inert implants.

Expenditure by public hospitals on LPPR Code III IMDs invoiced in addition to GHS funding (€715M) was lower than that of private hospitals, but the growth rate was much higher (+12.4%). A change made in 2009 to the scope of the IMD heading invoiced in addition to GHS funding in private hospitals (those formerly on "OQN" funding) explains at least in part this difference in the spending growth rates. In fact, some abdominal wall repair implants[17] and urogenitary implants[18] which previously were invoiced on top of GHS funding in private hospitals only have been incorporated since March 2009 into GHS funding, as they are in public hospitals. Changes in the private and public market shares may also be behind these growth differences.

2.2.4 *Code IV: Mobility equipment purchases*

Between 1999 and 2009, spending under Code IV on purchases of mobility equipment (manual and electric wheelchairs, special pushchairs and hand cycles, etc.) grew at an average yearly rate of 10%. Hence the total grew from an overall total of €44M in 1999 to €115M in 2009. During this period, annual growth was always upward, with the exception of 2009, in which it was 14 percentage points down.

This last year was preceded by the reinclusion on 1 August 2008 of the cost of medical devices in the daily care budget of care homes for the elderly (EHPADs), which may have led to the purchase of mobility equipment for individuals and other medical devices for individuals ahead of this change. However, the 13% increase recorded during 2008 is not exceptional in comparison with previous years and should not be overestimated.

In addition to spending associated with purchases of mobility equipment under Code IV, spending on the hire of this equipment under Code I, Chapter II: "medical devices for home care and daily living aids for people with medical conditions and disabilities" was almost €62M and accounts for one third of the overall expenditure.

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[17] Code III, Chapter 1, Section 9: Implants that may affect several body systems (in particular the gastrointestinal, heart, lung, orthopaedic, gynaecological and urinary systems).
[18] Code III, Chapter 1, Section 8

CHAPTER II – PRICE SETTING WORK FOR MEDICAL DEVICES AND SERVICES

1. Tariff and price setting methods

The price setting methods are essentially as described in Appendix 3, which is taken from the 2008 report. However on the following points the committee considered it necessary to explain its approach.

1.1. Price setting based on evaluations

1.1.1 *Innovative devices*

Unlike for medicines, comparisons of medical device prices against other prices in Europe are not covered by any general framework agreement between CEPS and the companies selling the devices. However in practice, the committee regularly has reason to compare the current asking prices against those in force in other countries, especially in Europe, when setting prices for devices which CNEDiMTS (*Commission nationale d'évaluation des dispositifs médicaux et des technologies de santé* – national medical device and technology assessment committee) has granted an "added expected service" (ASA – *amélioration du service attendu*) rating of III or higher.

One particular problem regarding international price comparisons for medical devices relates to the fact that the distribution channels often vary greatly from one country to the next, as does the nature of the services that go along with the sale of the devices themselves. Extreme care therefore needs to be taken when making comparisons, to ensure that the prices under consideration relate to the same items at the equivalent distribution stages.

1.1.2 *Upgrading of new alternative medicines with no ASA rating*

As with medicines, it can happen that in certain fields of care, the devices included on the reimbursement lists do not completely fulfil the needs of the whole patient range. In such cases, the inclusion of a new device on the list can provide a much-needed alternative that goes at least some way towards fulfilling unmet needs, even if the new device does not provide any added service (ASA) in comparison with those already on the lists. Their value and necessity lie not in the fact that they are superior, but that they are different. When these devices cannot be obtained at the same price as the reference products, the committee may accept a higher price, thus de facto granting them an ASA rating.

1.2. *Tariffs and maximum purchase prices*

The committee's principal task with respect to medical devices is to set the tariffs that form the basis for reimbursement by the compulsory health insurance plans. The committee may also consider it necessary to set maximum purchase prices (*prix limite de vente* – PLV), on the basis of sometimes varying considerations.

The committee's aim is to systematically set maximum purchase wherever possible. The committee feels that the contribution made by medical devices to the preservation or restoration of individuals' health or quality of life is as important as that of the other elements of care provision, including medicines. It therefore considers that the percentage left for patients to pay, especially if this is not kept under control, can constitute a threat to their equality of access to care.

In particular, when tariff reductions are introduced, the committee is keen to ensure that these go hand-in-hand with the setting of a maximum purchase price, in order to avoid a situation where savings are made at the patient's expense and turn out in practice to be a reduction in reimbursement, an area over which the committee has no jurisdiction.

It is safe to say that at present, with the notable exception of adult opticianry and hearing aids, the vast majority of devices or services included on the reimbursable medical devices and services list have a maximum purchase price and for those which do not have one or are yet to have one, the prices in force are in any case identical or very close to the tariffs.

This point is confirmed primarily by the data communicated by MSA and RSI regarding all medical devices, divided into LPPR codes and chapters, which provide an indication of the discrepancies between the prices in force and the reimbursement rates. For the majority of medical devices (in terms of quantity) the reimbursement base is over 95% of the sum paid up front by the patient and is often almost 100%.

For the main items under Code I (€3,647bn - 57% of the reimbursable total) there is also a maximum purchase price, with the exception of aerosol therapy and a few minor items). In particular, discrepancies had been identified between the reimbursable tariff and the going prices for adult and paediatric oral nutrition support, leading to an average patient payment of over 10% (whereas for half the sales, there was no percentage left for patients to pay). In 2009, the committee lowered tariffs across the board for adult oral nutrition support by 7%. The tariffs were set after a long series of negotiations with the manufacturers' union. With the exception of certain baby milk substitutes for children allergic to milk proteins, the maximum purchase prices were set at the same level as the tariffs. For paediatric oral nutrition support, the decisions made by the committee in 2009 were published in 2010. They involved introducing maximum purchase prices which would reduce the patient contribution percentage to 20%. The patient contribution percentage for these milk substitutes is now similar to the costs borne by families for the purchase of conventional baby milks.

Within Code II (€1,190bn - 19 % of the reimbursable total), excess patient payments are common and sometimes substantial, with the exception of large orthotic and prosthetic devices. For small external orthopaedic devices, the excess to pay is generally moderate. However for opticianry, the reimbursement rate is equivalent to only 6% and for electronic hearing aids it is only 20%.

All items under Code III (€1.478bn – 23% of the reimbursable total) have a maximum purchase price.

Within code IV (€114M – 1.8% of the reimbursable total) at present there is no maximum purchase price and the patient contribution level can be high, in particular for so-called positioning chairs for the elderly and chairs for people with disabilities.

1.3. *Operation and monitoring of contractual provisions*

The technical constraints that the committee has encountered over the last few years have prevented it from following up the contractual provisions on a yearly basis. In 2009, the time was therefore devoted to catching up on the previous years.

Table 21 below charts the sums charged to the companies under the terms of the contractual price/volume clauses (where the charging periods do not correspond more or less closely to the calendar years, the sums have been broken down on a pro-rata basis for the period in question): the sums were not systematically charged in the year following the period in question.

This table takes any adjustments made after the initial bill and sometimes after the payment into consideration.

Table 21: Sums charged to the companies under the terms of the price/volume clauses regarding medical devices for the period 2003-2008 (in thousands of Euros)

	2003	2004	2005	2006	2007	2008	Total
Drug-eluting stents	1,172	7,211	12,833	8,627	2,976	1,631	34,450
Defibrillators			1,591	5,872	5,771	7,223	20,457
Other			213	879	77	699	776
TOTAL	1,172	7,211	14,637	15,378	9,965	11,131	59,494

Source: CEPS.

From now on, the contractual provisions should be followed up at more regular intervals, to allow the companies concerned to manage any clawback payments they owe more easily.

1.4. *Hire only: therapeutic beds*

During the committee's review of therapeutic bed category listings and tariffs, it decided that for all therapeutic beds, with a few exceptions relating to the types of needs for which they are required, reimbursement by *l'assurance maladie* would apply to hire only, rather than allowing prescribers the choice between hire or purchase. This is what the committee had previously done for insulin pumps.

Here again, the reason for this decision was financial. Regardless of the reimbursement route, it is always *l'assurance maladie* that bears the cost of therapeutic beds. It is therefore beneficial if the beds it funds are used for as long as possible. One can safely assume that on average, hired beds are used for longer before being disposed of than purchased beds, since it is in the hirers' interests to maintain them in order to prolong their life. With purchased beds on the other hand, there is no doubt that even with very careful prescribing many of them will stop being used before they are worn out.

All that remains is to set the tariffs at a level that will ensure this collective benefit is also advantageous for *l'assurance maladie*. This is not a difficult outcome to achieve with a 'hire only' system, as it leaves no room for chance (as the duration of use of purchased beds is dependent on how the patient's condition progresses) or for any opportunistic practices by contractors. The ideal tariff would be made up of a weekly tariff portion to cover the depreciation of the bed over an average duration of use and of a delivery tariff portion to pay for delivery, collection, cleaning and maintenance. This would mean that the duration of hire would be irrelevant for the hirer. The committee has moved in the direction of this kind of tariff by reducing the weekly tariff and increasing the fixed delivery fee. Above all, the committee has ensured that the overall expenditure, which will now only depend on the number of patients who are prescribed a bed and the period for which each patient uses their bed, is slightly lower for the same patients than the expenditure which would have been incurred previously under the combined purchasing and hiring system.

Purchase is still possible in exceptional cases for certain beds for which the demand is low and too unpredictable to make it profitable for contractors to keep a stock of beds for hire. This applies to beds for very tall people, beds specially adapted for particular medical conditions and double beds.

2. The committee's work

2.1. *Work on different case types*

In 2009, the committee received 141 applications from companies. Over half of these were first applications for registration, 35% were applications for re-inclusion, 8% were requests for changes to the registration conditions and 3% applications for tariff increases.

Table 22: Medical device applications examined by the committee in 2009

Type of application	Applications in progress end 2008	Applications submitted in 2009	Applications closed in 2009	Applications in progress end 2009
First listing	120	76	96	100
Re-listing	76	50	55	71
Changes to conditions	33	11	24	20
Tariff change	2	4	4	2
TOTAL	231	141	179	193

Source: CEPS.

As in 2008, the stock of applications in progress at the end of the year was lower, due both to the lower numbers of applications received and to the higher number of applications that were processed.

Of the 96 registration application files closed in 2009, a high percentage (50%) did not result in registration, either because they were rejected (30 cases) or because the company withdrew or abandoned its application (18 cases).

Table 23: Medical device applications dealt with by the committee in 2009

Type of application	Number of applications processed	*Rejected, withdrawn or abandoned**	*Published in the JO*	Average processing time for applications after submission (no. of days)	Average no. of examinations by CEPS
First listing	96	*48*	*48*	398	1.7
Re-listing	55	*2*	*53*	572	1.0
Changes to conditions	24	*5*	*19*	368	1.3
Tariff change	4	*4*	*0*	98	2.0
TOTAL	179	*59*	*120*	440	1.5

Source: CEPS.

** including automatic listing renewals and rejections of registration applications for devices already included in GHS funding at the time of application.*

The majority of the first listing applications that were rejected were decided on the basis of a CNEDiMTS opinion according to which the expected service level was insufficient, mostly in view of the lack of available studies or the poor methodological quality of those available.

Some registration applications, especially those pertaining to abdominal wall repair implants, were automatically rejected because they were processed after March 2009, when the costs of these implants became incorporated into the 'GHS' general hospitalisation funding for both private and public healthcare establishments .

Two of the four price change requests submitted to the committee were accepted.

2.2. *Application processing times*

The average interval between submission of a first listing application and publication was 398 days. For these applications, the opinion of CNEDiMTS was delivered within an average of 154 days and sent to CEPS 19 days later. The first examination by CEPS took place on average 70 days after receipt of CNEDiMTS' opinion. For 57 % of registration applications, only one examination by the committee was required. No examination was carried out at a committee session for 15.3% of them, since they were for cases such as registration requests for products covered under GHS funding. For the remainder, the committee examined applications up to 9 times and 4.1 times on average. The decision was sent to the company or published within an average of 101 days after the committee's final examination.

The overall time taken to examine re-listing applications was longer, with an average of 572 days, and was higher than in previous years. The longer processing times were directly linked to the way in which the committee registers these files. Unlike the system for registering medicine applications, price reduction requests instigated by the committee are dealt with in the same file if they are made at the time the re-inclusion application is being processed. Therefore the files can only be closed once the price negotiations have been finalised. In 2009, the numbers of these price reduction requests were higher.

On average, applications for changes to registration conditions were processed within 368 days, which included 132 days between submission of the application and delivery of CNEDiMTS' opinion.

Tariff change applications were dealt with more quickly: within 98 days on average.

Table 24: Average application processing times (number of days) for medical devices in 2009

Type of application	Interval between submission and CNEDiMTS opinion	Interval before opinion sent to committee	Interval between opinion and 1st examination	Interval between 1st and last examination	Interval between final examination and decision	Total time
First listing	154	19	70	54	101	398
Re-listing	328	28	69	6	142	572
Changes to conditions	132	11	72	36	117	368
Tariff change	54			28	16	98

Source: CEPS.

3. Review of generic list entries

Article 27 of Decree no. 2004-1419 of 23 December 2004 as amended stipulates that each year a decree by the health and social security ministers must determine which generic list entries, by uniform category, must be reviewed, after CNEDiMTS, which replaced CEPP (*Commission d'évaluation des produits et prestations* – medical device and service assessment committee) has issued an opinion. The goal was that all medical device categories, under generic descriptions, should be reviewed once and then again every five years thereafter. The purpose of the review was to refine the details of the indications and the prescription and usage procedures.

However, once CNEDiMTS has issued its opinion, CEPS has a significant amount of complex work to do. Indeed, the opinions do not always translate neatly into tariff categories (in the reimbursable medical device and services list - LPPR) on which reimbursement by *l'assurance maladie* is based. Following this, the negotiations with the manufacturers can be lengthy, as the new definitions proposed by CNEDiMTS can involve reformulating or reconfiguring the products, with the technical adaptations that go along with these. Finally, large numbers of tariff entries may be involved in price negotiations, which can entail new obligations (such as the introduction of a maximum purchase price), and this can take a considerable length of time.

In 2009, the committee worked on the following subjects: mobility equipment for disabled people, self-testing and self-medication devices, oral and enteral nutrition support and dressings and compresses. The review of the reimbursement system for mobility equipment and the review of the generic tariff entries for oral and enteral nutrition support and dressings and compresses are discussed in paragraphs 3.1 to 3.3 below.

3.1. *Review of the reimbursement system for mobility equipment*

During the course of 2009, CEPS conducted reviews of the category listings for mobility equipment, in conjunction with the *Centre d'études et de recherche sur l'appareillage des handicapés* (CERAH – the centre for research and studies into disability living aids) and the *Caisse nationale de solidarité pour l'autonomie des personnes âgées et des personnes handicapées* (CNSA – national independent living fund for elderly and disabled people). This work was based on CEPP's opinion of 11 June 2003, which recommended the following:

that mobility equipment should be registered in the form of modular, cumulative generic list categories;

that reimbursement of the cost of these items should be subject to an inspection by a suitable independent company to ensure they comply with the minimum technical specifications;

that the services associated with the provision of mobility equipment should also be registered on the reimbursable device and services list.

The proposed classification groups together headings relating to the different types of equipment within the same level (the four different types being wheelchairs, pushchairs, wheeled seating shell

frames and hand cycles)[19] with twelve different types of feature: propulsion mode, environment of use of the vehicle, chassis, back, seat, foot-rest unit, arm rests, body support system, driving wheel, steering wheel, immobilisation and braking system and driving and/or control system. These 13 headings are broken down into a total of 183 modules (135 of which were described), in other words between 3 and 23 modules described per feature.

There then follows a proposed categorisation of the associated services, setting out the conditions regarding testing of the equipment, adjustments, adaptations and delivery, and the terms regarding preventive and curative maintenance of the equipment. The CEPP opinion then concludes with a draft form for evaluating needs and monitoring prescriptions of mobility equipment.

CEPS based its work on these recommendations, calling upon the help of organisations such as the national medical technology industry union (Snitem - *Syndicat national de l'industrie des technologies médicales*) and the technical aid manufacturers' union (Ufat - *Union des fabricants d'aides techniques*) when working out the tariffs for the different modules in the mid-2000s.

In 2008, the committee decided to create an extra grouping level, relating to the different types of mobility equipment, whilst still retaining the principle of modules that can be added together. The benefit of this new structure lies in the clearer identification of the equipment and in the fact that only the modules relevant to each type are associated with them, rather than all the modules identified by CEPP. This is an advantage when making recommendations and prescribing in particular. This new classification therefore distinguishes three major types of mobility items, according to whether or not they are modular, and a so-called specific equipment category, making a total of 13 specified equipment categories, as follows:

- two non-modular equipment categories comprising basic chairs, which are estimated to account for 80% of the market: non-modular self-propelled or carer-assisted wheelchairs and non-modular self-propelled or carer-assisted fixed-frame wheelchairs;

- nine modular equipment categories: modular self-propelled or carer-assisted wheelchairs; multi-configurable modular self-propelled or carer-assisted wheelchairs; modular self-propelled sports wheelchairs; modular self-propelled or carer-assisted positioning wheelchairs; electric modular self-propelled wheelchairs; electric modular self-propelled positioning wheelchairs; modular pushchairs; modular wheeled seating shell frames; modular hand cycles;

- one specific equipment category: TOPCHAIR-S special electric stair-mounting wheelchairs.

The routes for obtaining the items, as they are currently envisaged, would differ from one equipment category to the next, depending on the qualifications of the healthcare professionals involved in recommending or prescribing them, as well as on the content and evaluation of the tests carried out by the contractors.

The draft also proposes to amend the hiring procedures for mobility equipment listed under Code I, which currently accounts for one third of annual expenditure on mobility equipment, as well as the possibilities of combining certain medical devices also listed under Code I of the LPPR with those under Code IV.

3.2. *Categorisation of "oral and enteral nutrition support"*

In September 2006, CEPP issued an opinion concerning the review of generic tariff entries for oral and enteral nutrition support[20]. The recommended new approach, which CEPS proceeded to adopt, entailed re-writing the whole section of the list devoted to these products. The specifications for the mixes are more accurate and more varied. For both oral and enteral nutrition support, paediatric products are now also included in separate entries.

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19 For information purposes, the recommendations also mention, without describing them, two other types of vehicle: quadricycles and other cycles, and scooters.

20 http://www.has-sante.fr/portail/upload/docs/application/pdf/cepp-469.pdf

3.3. *Categorisation of "dressings and compresses"*

In March 2007, CEPP issued an opinion concerning the review of dressings[21]. As a result, CEPS reviewed all the generic entries for dressings and clearly defined the respective indications and conditions of use. The committee found it necessary to make a distinction for hydrocellular and hydrocolloid dressings. It created two new generic specialist dressing range entries: alginate dressings and CMC fibrous dressings. The committee decided, for economic reasons and without incurring any risk to patients, not to follow CEPP's opinion regarding the removal of paraffin-coated dressings from the LPPR.

A draft decree notice was published on 30 July 2009.

[21] http://www.has-sante.fr/portail/upload/docs/application/pdf/2010-01/avis_cepp_668_07032007.pdf

CHAPTER III – REGULATION: PRICE AND TARIFF CHANGES IN 2009

1. Price increases

UFOP, the French orthotic and prosthetic device manufacturers' union, submitted an application for a tariff amendment for 2009-2011, motivated by the need to guarantee a 5% net annual profit for the companies operating in the industry. Taking into consideration the overall drop in profits, the committee considered a net profit of 4% to be a workable basis. After having checked up on investment practices in the industry and redistribution levels, the tariffs of large orthotic and prosthetic devices were revised upward 1% on 15 September 2009 under the framework of a three-year agreement for 2009-2011. All the new tariffs and prices were published at the same time in order to avoid any discrepancies and to allow the industry to benefit fully from the effect of the increase for 2010 and 2011.

2. Price reductions

Table 25: Savings made in 2009 from 2008-2009 medical device price/tariff reductions

Medical device reductions	2009 Savings (in €M)
Insulin pump therapy (2008)	3.5
Drug-eluting stents (2008-2009)	8.0
Defibrillators (2009)	13.2
Total	*24.7*

Source: CEPS.

2.1. *Drug-eluting stents*

In 2009, CEPS aligned the tariffs of all drug-eluting stents (Code III) to the tariff of €1,220, which came into force on 1 August. The committee considered that length of time since the registration of the first drug-eluting stent on the reimbursable list in 2003 could no longer justify the discrepancies between the tariffs/maximum purchase prices of the different stents on the market, which all perform equally well.

These reductions, together with reductions decided in 2008, will have produced savings of €8M in 2009 and overall savings of €13.7M for the period 2008-2011.

Added to this, the tariffs for new stents registered since then without a higher ASA rating have been set at the lower level of €1,100.

These price reduction decisions were made before the Economic Evaluation and Public Health Commission of the *Haute Autorité de Santé* had delivered the conclusions of its re-evaluation of drug-eluting stents and comparison of these devices with uncoated stents. Therefore the committee did not take this commission's medico-economic analysis into consideration.

2.1. *Self-testing and self-medication: review of listing categories and tariffs*

In January 2007, CEPP delivered the conclusions of its evaluation of self-testing and self-medication devices (listed under Code I, Chapter 1, Section 3).

A notice of a draft decree amending the registration procedure and the reimbursement terms for self-testing and self-medication devices, was published in June 2009, together with a notice of a draft decree setting the tariffs and maximum public purchase prices in Euros, including VAT, of self-testing and self-medication devices.

The decree was published on 30 December 2009. The amendment of the tariffs and maximum purchase prices of these medical devices therefore formed part of the committee's work in 2009, even though these will not come into force until April 2010.

The main devices affected by these tariff and maximum price reductions were blood glucose self-testing devices, in particular digital automatic blood glucose reading devices, whose tariffs and maximum purchase prices were reduced 10%. The tariffs and maximum purchase prices for lancing device needles were reduced 5%.

The committee agreed to implement prescription prices for single-use lancing devices (applying the same markups as those implemented in the medicines sector for the same prices), while reducing the tariffs and maximum purchase prices of large pack sizes only of these products by 5%.

The tariffs and maximum purchase prices of blood glucose self-monitoring test strips were reduced 2 %.

All of these reductions together should lead to savings of €15.6M, which will take effect in 2010 and 2011.

2.2. *Implantable cardioverter defibrillators*

The blanket 10 % reduction in tariffs/maximum purchase prices of ICDs (Code III) was introduced in 2009. However, since the decision was made and the decree published in 2008, this reduction was mentioned in the committee's 2008 annual report. It has led to savings of €13.2M in 2009 and should lead to total savings of €15.2M in 2009 and 2010.

PART THREE – CONTRIBUTION TO THE COUNTRY'S INVESTMENT ATTRACTION

The implementation of policies in the healthcare products sector aimed at increasing France's attractiveness as a base of industrial or research activities does not fall explicitly within the remit of CEPS as defined in the law. Nonetheless, it is clearly the firm wish of the government authorities whose task it is to provide guidelines for the committee's work, as they have expressed many times, that this work should contribute, within its defined scope, to the implementation of these policies.

There are two separate aspects to this contribution.

The first is the way in which CEPS carries out the regulatory tasks entrusted to it by the relevant statutes, in particular the predictability it can bring through its agreement policies, the way in which it conducts the agreements and consequently the confidence it is able to inspire in the companies as to the continuity of the dialogue between them and the committee.

The second is the way in which it carries out the specific tasks assigned to it within the framework of CSIS (the Health Industries Strategic Council).

ATTRACTIVITY AND REGULATION

As regards price setting, the Social Security Code takes no account whatsoever of the industry's needs. The price setting criteria are linked solely to the actual or anticipated effectiveness of the medicines and their marketing prospects in terms of sales volumes of conditions of use. They do not take into account the nationality or geographical location of the companies which developed or are selling the medicines.

These criteria certainly do not aim at absolute precision, especially with regard to medicines that have been given an ASMR rating. In price negotiations, which are often a complex process, especially when medico-economic arguments are put forward on both sides, the committee is particularly keen to reach a positive outcome when the negotiations are with countries with a strong presence in the European Union.

But the crucial factor remains that price setting, which is done under the scrutiny of the administrative judge, must abide by the principle of equal treatment between companies. This means that the price setting process cannot act as an instrument to attract investment to France on the basis of specific advantages it may offer companies who have invested or are considering investing in France.

On the contrary, the committee believes that it is precisely this equality of treatment, which is implemented within the contractual context defined by the framework agreement, that constitutes a substantial attractive factor, through the legal security it ensures and the opportunity it provides to make long-term plans.

CSIS MEASURES

1. CSIS credits

After the first CSIS council, which met in 2005 under the chairmanship of the Prime Minister, CEPS was entrusted with the task of contributing towards the setting up of production or research facilities within the EU by allocating clawback credit payments to the pharmaceutical companies in question.

In 2005 therefore and every year since, the committee has distributed these credits, which total approximately €50M per year.

These credits are allocated for "concrete" investments, whether these by production plants, research centres, distribution platforms or company offices. It does not award credits for clinical research expenses or for financial investments In the current world climate in which the expiry of patents and mergers are leading to marked reductions in production capacity, the committee is also attentive to the companies' choices in terms of the location of the plants they keep. It is also careful not to reward new sites with credits if they have been built in the wake of demolition of other larger sites.

In principle, the investments rewarded by credits must already have been made. However, for some very large-scale operations which will take several years to complete, the committee may commit to a total sum as soon as the decision to invest is firm, which it will undertake to pay in annual instalments. Such instalments are also decided solely for the purpose of spreading the expense, if it appears that the total sum of the credits to be allocated exceeds an annual sum considered to be reasonable.

The method used by the committee in setting the amounts of the credits is extremely simple. The candidate companies are asked to submit a short file describing the nature of the investments they have made and the sums involved and specifying in which financial years the expenditure was actually incurred. To ensure uniform processing of the decisions and hence equality of treatment of the companies, all the files are examined during a single session, which is usually held in November. By far the most important principle that determines the sum of the credit awarded is the size of the investment. An exception to the rule of the single session is made when the potential allocation of a CSIS credit is a deciding factor for the company concerned when choosing whether or not to invest. It goes without saying that in these cases, the company's decision-making timescale takes precedence.

The credit allocations are genuinely European and operations carried out in other EU countries and awarded credits occupy a significant place.

2. The manufacturing clause

Under the rules currently in force in the European Union, it is a counterfeiting offence to produce or even to stock generic drugs before the date on which the patent of the original drug expires. Whilst this rule is applicable in France and the older EU Member States, exceptions are made for the more recent members. A consequence of this situation is that generic manufacturers are obliged to procure supplies from companies outside France ready for launching their product upon expiry of a patent. There is therefore a high risk that this foreign procurement situation will continue. However, this is not a 'public order' law and the companies owning the intellectual property rights for whose sake it was established, can sign a contract waiving their rights.

To encourage them to do this, one of the decisions made at the CSIS meeting held in 2009 under the chairmanship of the French President was that it should be stipulated, in a rider to the framework agreement signed on 26 October (Appendix 1), that companies which sign an agreement authorising manufacturers to produce and stock generic versions of their drugs before their patent expires would be allocated credit payments in return, the sum of which would naturally depend on the financial scope of the agreements they sign.

APPENDICES

APPENDIX 1: FRAMEWORK AGREEMENT OF 25 SEPTEMBER 2008 BETWEEN THE COMITE ECONOMIQUE DES PRODUITS DE SANTE AND THE PHARMACEUTICAL COMPANIES (as amended by the rider of 26 October 2009)

Having regard to European Union Law, the Social Security Code and national ministerial policy;

Whereas Article L. 162-17-4 of the Social Security Code provides that an agreement may be drawn up setting forth the contractual framework for relations between the Comité économique des produits de santé **(**CEPS – the Healthcare products pricing committee) and each of the companies producing the medicines described in Article L. 162-16-4 of the code;

Whereas, subject to the provisions of the Public Procurement Code, Article L. 162-16-5 of the Social Security Code provides that, with regard to pharmaceutical products which have been granted marketing authorisation and are registered on the list provided in Article L. 5126-4 of the Public Health Code, an agreement should be made setting forth the procedure and conditions governing manufacturers' price submissions, the criteria for opposition by the committee, the conditions under which the declared selling prices may be reviewed and the undertakings to be made by the company;

Whereas Article L. 162-16-6 of the Social Security Code provides that, with regard to the pharmaceutical products mentioned in Article L. 162-22-7 of the same code, an agreement should be made setting forth the procedure and conditions governing manufacturers' price submissions, the criteria for opposition by the committee, the conditions under which the declared selling prices may be revised and the undertakings to be made by the company;

Whereas it is fitting that medicines should be given their rightful place in prevention and healthcare and that this requires both rapid access to innovative medicines, improved efficiency and rationalisation of expenditure on medicines and sustained efforts to avoid excessive consumption and promote responsible usage;

Whereas medicines can be both a source of improvement in quality of care and a source of economies for the public purse when used solely for proven medical purposes, within a competitive market in which generic medicines and self-medication are free to play their part;

Whereas advances in treatments, the demographic situation, epidemiological data and the government's public health plans must be taken into account when appraising growth in the consumption of medicines;

Having regard to the benefits of maintaining and developing a strong, competitive pharmaceutical industry and of protecting intellectual property, trademarks and registration data within European Union territory, as reaffirmed in the work done by the G10;

Whereas the majority of spending on medicines is financed out of the public purse, whose resources are finite by nature, and whereas it is therefore fitting that there should be regulation in place which is proportionate to the contribution made by medicines, in accordance with the law and ministerial policy and under fair, transparent conditions;

Whereas the most desirable means of achieving the goals set forth hereabove is through strengthened cooperation between the public bodies and the pharmaceutical companies;

The Healthcare products pricing committee (CEPS) and the pharmaceutical companies now agree to take their relationship forward within the contractual framework set forth herebelow.

CHAPTER I: EXCHANGING INFORMATION AND MONITORING SPENDING COVERED BY NATIONAL HEALTH INSURANCE

Article 1: Exchanging information

For the sake of transparency, the parties agree on the necessity to improve and share the information they each hold regarding consumption and prescription of reimbursable medicines and the actual reimbursements paid out for medicines.

The representatives of LEEM[22] will facilitate access by members of CEPS, via electronic means in particular, to the commercial information which the companies have available.

They will continue to send the committee, both in hard copy and electronic format, commercial data, of which the companies shall retain ownership, including but not restricted to the statistics produced by the industry's statistics gathering association GERS[23] regarding sales to both community pharmacies and healthcare establishments. Furthermore, to enable CEPS to make the necessary forecasts, at the end of each quarter the committee shall be sent information on the quarterly declarations of sales to healthcare establishments which the companies governed by this agreement undertake to make to GERS, in accordance with the agreement signed between GERS and CEPS.

The companies undertake to send to CEPS upon request the information available to them regarding real-life use of the products for the various indications stated in their marketing authorisations.

The companies also undertake to allow the committee access to information regarding current prices in force in other EU countries and the reimbursement situation and sales volumes in these countries.

CEPS and national health insurance (*l'assurance maladie*) shall make available to LEEMS detailed information regarding the reimbursements paid out by national health insurance and reports of studies conducted into the prescription and consumption of medicines, under the same conditions in which they are made available to the professional healthcare associations, in particular studies regarding statistics derived from the coding of medicines claimed back from national health insurance by the healthcare establishments, as soon as these statistics are available.

CEPS shall inform LEEMS every year of its forecasts regarding growth in sales of reimbursable medicines and its forecasts regarding implementation of the end-of-year adjustments under the terms of Articles 17 and 18 herebelow.

CEPS and LEEMS agree to set up a joint monitoring group which will be responsible for overseeing the implementation of this framework agreement.

Article 2: Monitoring spending covered by national health insurance

a) Termly monitoring

The parties agree to monitor spending on medicines regularly and in consultation with each other, in particular regarding the information mentioned in Article L.162-17-3, paragraph II of the Social Security Code. This consultation shall be organised within the framework of the above-mentioned joint monitoring group.

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[22] LEEM = Les Entreprises du Médicament: the pharmaceutical companies' trade association in France.
[23] GERS = Groupement pour l'Élaboration et la Réalisation de Statistiques - an economic interest group of pharmaceutical companies which produces market statistics.

b) Analysis of sales volume of medicines covered under national health insurance

The joint monitoring group shall also be responsible for analysing variations which take place concerning the scope of the statistical item "reimbursement of medicines dispensed in the community", relating to medicine sales which are covered under national health insurance and are actually reimbursed. Such variations may be brought about by changes in the way the medicine is defined or the scope of community medicine reimbursements or by changes in prescribing, dispensing or insurance cover arrangements both for community-dispensed medicines and medicines issued by hospitals to outpatients.

Article 3: Intellectual property

Companies selling pharmaceutical products to which they hold one or more patent or supplementary protection certificate (SCP) may declare these to the committee along with the respective expiry dates. The committee shall make such declarations accessible to any pharmaceutical company that requests access to them.

Details of the registration of any generic pharmaceutical product on the national health insurance reimbursable medicines lists and where applicable the public hospital approved medicines list shall not be published more than six months before the declared expiry date of the intellectual property rights concerned, where the committee has been notified of such date.

However, any pharmaceutical company which believes that it is able to sell the generic products in question without infringing the declared rights may apply for their product to be registered on the appropriate lists. In this event, the pharmaceutical company must inform the committee, which in turn shall promptly inform the company selling the original medicine as mentioned in the first paragraph hereabove and shall then begin the registration procedure.

Article 3a: Early transfer of rights

The owner of the intellectual property rights to a reference proprietary product may, subject to the provisions of the Intellectual Property Code (*Code de la propriété intellectuelle*), assign the following rights before they have expired to a duly authorised pharmaceutical establishment acting in the capacity of sub-contractor under the terms of Chapter 7 of the Good Manufacturing Practices stipulated in Article L.5121-5 of the Public Health Code (*Code de la santé publique*):

- The right to purchase sufficient quantities of raw materials and generally speaking to carry out any activities that are necessary and essential for the manufacturing process described in the following paragraph:
- To manufacture a generic version, as defined in Article L.5121-1, paragraph 5 of the Public Health Code, of the proprietary product in question, on behalf of a pharmaceutical establishment authorised to use the marketing authorisation for the corresponding generic drug;
- To release batches of the generic product thus manufactured 48 hours before the expiry of the intellectual property rights, for the sole purpose of preparing stocks of the product and to the exclusion of any other act, carried out alone or jointly with the pharmaceutical establishment marketing the generic product, which might lead to the sale or delivery of the generic drug. These batches released at this time may not be delivered until after the expiry of the intellectual property rights pertaining to the original proprietary product. The sub-contractor shall guarantee to the owner of the intellectual property rights to the original proprietary product that the pharmaceutical establishment marketing the generic product will refrain from any actions pertaining to sale or delivery as stipulated above.

The authorisations granted by the intellectual property right owners pursuant to this article shall give rise to clawback credits, the sum of which shall be set, depending on the scope of the authorisations, by mutual agreement between the company and CEPS.

CHAPTER II: MEDICINES SOLD TO COMMUNITY PHARMACIES - AGREEMENTS BETWEEN CEPS AND PHARMACEUTICAL COMPANIES

Article 4: The contractual framework

Any company which sells medicines covered by mandatory national health insurance, provided the company is certified pursuant to Article L.162-17-4 of the Social Security Code, shall be offered the opportunity to enter into a multiannual agreement with the Healthcare products pricing committee (CEPS).

The agreements shall be drawn up with a view to ensuring that this framework agreement is implemented, whilst taking into account each company's individual situation and future development prospects and working within the rules set forth in the Social Security Code and the policy guidelines passed on to the committee each year by the relevant ministers.

Within this framework and save for any exceptions warranted by any specific aspect of the French market, for medicines given an ASMR rating of I to III, these agreements shall guarantee that the price set will be no lower than the lowest price in force in the 4 main comparable EU markets mentioned in Article 7 herebelow, for a period of five years starting from the date the medicines become available to patients by virtue of their registration on the community or hospital reimbursable medicines list. This guarantee also applies to medicines which have been given an ASMR price rating of IV in relation to medicines recently rated at ASMR levels I to III, where the Transparency Commission's opinion indicates that this rating is more beneficial to them than a rating which would have placed them at the same ASMR level as these reference products. An extra year shall be added to this guarantee for the paediatric medicines listed in Article 10 herebelow for which studies have been conducted in implementation of the paediatric investigation plan arranged with the AFSSAPS council.

The companies shall inform CEPS should any significant price changes occur in these EU markets.

For medicines which have been under provisional authorisation (ATU), the companies undertake to take the necessary steps to adhere to the deadlines set by AFSSAPS for bringing the medicines into line with the terms of their marketing authorisations and to submit their applications for registration under their new marketing authorisations on the public hospital approved medicines list and/or the national health insurance reimbursable medicines list, no later than 30 days after receiving notification of the MA decision or specific national conditions. Failure to do so shall lead to the period of their European level price guarantee being reduced by a period equivalent to the length of the delay.

When a product covered by a European level price guarantee is approved for extended indications which are rated at ASMR IV or V and concern a significantly larger patient group than the group covered by the ASMR rating which initially warranted the guarantee, the initial period of the European level price guarantee may be shortened.

When a product covered by a European price level guarantee is approved for extended indications rated at ASMR I to III, the initial period of the guarantee may be extended for up to one year, provided that the new indication(s) concern a sufficiently large patient group in relation to the group covered by the existing indications.

Article 5: Format and content of the multiannual agreements.

The agreements must adhere to the pro-forma agreement attached in Appendix 2. They are made up of three parts:

Part one summarises the prices of medicines which the company sells and which are registered on the national health insurance reimbursable medicines list and the special conditions attached to them where applicable, in the form of a price table and a schedule of conditions.

Part two contains, pursuant to Article L. 162-17-4 of the Social Security Code, the company's undertakings with regard to controlling its marketing policy and ensuring responsible use of the medicine, and any conditions setting forth the company's contribution to achieving the objectives described in Chapter IV herebelow and implementing government policy.

Part three establishes the company's acceptance of the provisions of this framework agreement, in particular those stipulated in Articles 17 and 18 herebelow where applicable, under the conditions provided in said Articles.

Companies which decide not to take advantage of the financial regulation mechanism described in Articles 17 and 18 herebelow, or for whom the mechanism is cancelled either the company itself or by the committee, may nonetheless enter into or maintain an agreement with the committee under the terms of Article L. 162-17-4, however the agreement will not exempt the company from the contributions provided in Article L. 138-10.

The agreements may be supplemented by contract riders. Parts one and two shall be renewed each year during the first six months of the calendar year. Part three shall be renewed before 31 December each year.

Article 6: General measures to promote new medicines

a) Pre-application procedure for medicines with centralised marketing authorisations

Subject to any subsequent decision by the European Commission, any pharmaceutical company whose product marketing authorisation dossier has received a favourable opinion from the human medicines committee of the European Medicines Agency may immediately submit a pre-application dossier to CEPS, the Transparency Commission and the ministers responsible for registration, to allow them to examine in advance the issues involved in registering the new product as a reimbursable medicine and to shorten the registration process. This procedure does not exempt the company from the official procedure governing the submission of applications for registration of a product on the reimbursable medicines list and price setting, in accordance with the procedures outlined in Article R. 163-8 of the Social Security Code. Once the official application has been submitted, the committee shall appoint a rapporteur to begin processing any elements of the application which do not require the Transparency Commission's opinion.

b) Special processing times for medicines which have been given an ASMR rating

The parties agree upon the benefit of shortening the usual statutory 180-day listing procedure in the case of medicines which represent an advance in treatment.

For all medicines with an ASMR rating of at least IV but which nonetheless would not fall within the scope of Article 7 herebelow, the committee undertakes to write to the company within 75 days after the date on which the Transparency Commission delivers its final opinion, proposing a draft agreement, or failing this to set out the reasons why it has not yet been able to formulate a proposal.

This same procedure shall be implemented for paediatric medicines which address the list of paediatric needs sent to LEEM by the committee.

c) Statutory processing times

For all proprietary products, CEPS shall ensure that the statutory processing time of 180 days is adhered to, among other ways by keeping track of the intervals before publication of the undertakings which the committee signs.

d) Evaluation

The procedure and the undertaking stated in the above paragraphs shall be subject to a joint annual evaluation by LEEM and CEPS.

Article 7: Fast-track registration for innovative medicines: price submission

The fast-track registration procedure provided in Article L.162-17-6 of the Social Security Code for certain medicines which have been recognised as making an innovative contribution shall be applied under the following terms and conditions:

a) Description of the procedure

No earlier than the day after and no later than one month after it has received the Transparency Commission's final opinion, a company which meets the conditions mentioned in paragraph b) herebelow may apply for a fast-track price-listing procedure for proprietary products which meet the conditions mentioned in paragraph c) herebelow. This application must adhere to the pro-forma sample attached in Appendix 1 and must contain the undertakings stipulated in paragraph d) herebelow. If after two clear weeks following the week in which the committee received the company's application the committee has not informed the company of its opposition to the application under the terms set forth in paragraph e) herebelow, the application shall be deemed to have been accepted. The agreement shall then be signed within 48 hours and the price decree and notice shall be published in the *Journal Officiel* (the official gazette of the French government) at the earliest possible opportunity. No negotiation shall be entered into with the company regarding the application. In the event of opposition by the committee, the price shall be set according to due process.

The first two working weeks of August and the last week of the year shall not be taken into account when calculating processing times. Furthermore, no price submissions may be made during these periods.

b) Companies concerned

This procedure is open to any company which has a multiannual agreement with CEPS, pursuant to the terms of Article L.162-17-4 of the Social Security Code.

c) Medicines concerned

Proprietary products which the Transparency Commission has rated at ASMR level I to III, provided that these ASMR levels are applicable to the main indications specified in the products' marketing authorisations.
Proprietary products which the Transparency Commission has rated at ASMR level IV, subject to the following additional conditions:

1) There must be a reference medicine and the daily treatment cost of the new medicine, based on the submitted price, must be equal to or lower than that of the reference medicine. CEPS reserves the right however to accept price submissions for products where the daily treatment cost would be higher than that of the reference medicine if the applications can demonstrate that the additional cost is outweighed or exceeded by savings on other items of national health insurance expenditure.

2) The medicine must not be not intended to replace a medicine which has been genericised or is soon to be open to genericisation.

d) Undertakings to be made by the companies

- Regarding prices: the company undertakes to submit a price which is consistent with the approved prices in the following countries: Germany, Spain, Italy, and United Kingdom. In the event that the prices in force in one or more of these countries should alter this price consistency at a later date, the company also undertakes to re-establish consistency by accepting a contractual change to the original price.

- Regarding sales volumes: in the event that its sales volumes exceed the volumes in the mandatory forecast for the first four years as stated in the price submission application, the company undertakes to compensate by means of clawback payments for any additional costs to national health insurance which are not justified by public health decisions made later by public bodies.

- Regarding studies which the company may be requested to carry out in application of Article 11 herebelow.

- The company undertakes, subject to general or specific obligations of information governing pharmaceutical companies, to inform both CEPS and the Transparency Commission of any new scientific information which comes to light and which may affect the cost-benefit ratio as assessed during the Transparency Commission's evaluation. Where the company is aware of any such information prior to the deadline for receipt of the committee's opposition, it shall waive the right to the fast-track procedure.

In addition to the above-stated mandatory undertakings, the company may make other undertakings (regarding posology, daily treatment cost, consultations, etc.) which in the light of the characteristics of the product in question it feels will make its application more favourable to the committee.

The company shall have the opportunity to present its case to the committee prior to entering into the contractual obligations.

e) Conditions governing the committee's right to opposition

The committee must present its opposition in writing, providing valid grounds for the opposition. It may oppose an application on the following grounds:

- Due to explicit public health considerations

- If the level of the proposed price is excessive in relation to the prices in force in the four above-mentioned EU Member States.

- If the sales forecasts are inconsistent with the size of the patient group identified by the Transparency Commission.

- Due to obvious inadequacy of the undertakings made by the company.

- If the company has breached any of its undertakings made during a previous application.

- With regard to ASMR IV-rated medicines, where the special conditions regarding these medicines are not met or simply where the product represents additional costs in relation to the reference product.

CHAPTER III: MEDICINES PURCHASED BY HOSPITALS

Article 8: Implementation of Articles L 162-16-5 and L 162-16-6 of the Social Security Code

a) Common procedure

For the purposes of Articles L. 162-16-5 and L. 162-16-6 of the Social Security Code, outpatient prescription fees for the products included on the list provided in Article L.5126-4 of the Public Health Code and "accountability tariffs" (*tarifs de responsabilité*) for products included on the list provided in Article L. 162-22-7 of the Social Security Code shall be determined on the basis of the common procedure outlined in Articles b) to e) herebelow, subject to any specific conditions detailed in these Articles where applicable.

b) Conducting the procedure

Price submissions formulated according to the terms of paragraph c) herebelow should be handed to the committee in return for proof of receipt or sent by registered post within one week after details of the product's inclusion on one of the lists mentioned in paragraph a) hereabove have been published in the *Journal Officiel*, or in the case of products registered on the list provided in Article L. 5126-4 of the Public Health Code before receiving marketing authorisation, within ten days following receipt of the marketing authorisation decision.

The committee may find the submission inadmissible or may oppose the submitted price under the terms stipulated in Article d) herebelow, within two weeks following receipt of the submission. In the event of inadmissibility or opposition, the company shall be given two weeks starting from the date of receipt of the committee's decision within which to draw up a new submission or to amend its initial submission. The committee shall then have ten days within which to find the submission still inadmissible or to oppose the price submitted. In this instance, the committee's decision regarding inadmissibility or opposition shall be final, pursuant to the above-mentioned Articles of the Social Security Code. If after the committee presents its initial opposition the company does not draw up a new declaration or amend its initial declaration within the above-mentioned two-week time limit, the committee's opposition shall be final.

If the committee does not find the submission inadmissible or oppose the submission within the time limits mentioned in the previous paragraph, the committee shall publish the prescription fee or "accountability tariff" in accordance with the price submitted at the earliest possible opportunity.

In the event that the company does not adhere to the time limit for submission stipulated in the first paragraph hereabove, the committee may announce its opposition to the price at its own convenience, provided that it adheres to the overall seventy-five day statutory time limit for the procedure. If the committee does oppose the price, the time which the company shall have to draw up a new submission or amend its initial submission shall be reduced by a length of time equivalent to the initial delay. If this delay is more than ten days, any opposition by the committee shall be final.

In the event of final opposition, or if the company has not drawn up an admissible submission within thirty days after the start of the time limits stipulated in the first paragraph hereabove, the committee shall set the prescription fee or accountability tariff unilaterally.

c) Content of company price submissions

For each product included in the price submission, the company's submission must contain the following, failing which the submission shall be inadmissible:

- The proposed selling price to healthcare establishments per pack type.

- The current prices in force in the main EU Member States and the product's reimbursement status in these states, plus for products which have been on sale for more than one year, the annual sales volumes recorded in these states.

- Where applicable, up to three years' worth of data on the prices at which the products have been sold to French healthcare establishments.

- The Transparency Commission's opinion or opinions, where such opinions have already been delivered.

- An estimated sales forecast for the next three years.

- An undertaking to inform CEPS each year of the prices in force and volumes sold in the main EU Member States, as well as any alterations to the product's official reimbursement status.

Depending on the particular nature of the products in question, price submissions may also contain undertakings by the company, in particular regarding implementation of Article L. 162-18 of the Social Security Code or the conduct of follow-up studies on the products.

d) Criteria for opposition by the committee

The committee must provide explicit, clear grounds for its opposition.

It may oppose the proposed price on the grounds that it is exceptionally high in relation to the prices in force in the main EU Member States, or in relation to prices in force in the French market where directly comparable products are already being sold on the French market.

It may also oppose the price due to the inadequacy of any undertakings made by the company, in particular, in cases where the proposed price is only justified for some of the indications included in the marketing authorisation, if there is a clear risk that the quantities sold will incur exceptionally high national health insurance spending or if, given the current market, the product's inclusion on one of the lists could lead to sales volumes giving rise to volume discounts on the company's proposed price.

e) Reviewing tariffs and prices

Prices and tariffs may be reviewed either at the company's or the committee's request, in particular when a change occurs to any of the factors on which the existing price or tariff and the parties' undertakings were based; or when new information emerges in France or the European Union, especially regarding the product's evaluation or current prices, or when the product's price is closely linked with variable costs, especially those connected with product safety requirements.

Article 9: Implementation of Article L. 162-22-7-1 of the Social Security Code

When the committee intends to apply the terms of Article L. 162-22-7-1 of the Social Security Code to a drug whose price has already been set pursuant to Article L. 162-16-6 of the code, it must consult the company selling the drug about its plans, both regarding the spending threshold above which the tariff will be reduced and regarding the company's preference if any concerning clawback payments.

When the committee has decided to apply Article L. 162-22-7-1 of the Social Security Code when setting a drug price pursuant to Article L. 162-16-6 of the code, it must inform the company selling the drug of its decision. The company shall be given one month within which to present its observations on the committee's decisions or the chosen spending threshold and to inform the committee of its preference if any concerning clawback payments.

Article 9a: Implementation of Article L. 162-16-5-1 of the Social Security Code

The declarations regarding the maximum prices chargeable to healthcare establishments, which the companies are obliged to make under the terms of Article L. 162-16-5-1 of the Social Security Code, must be sent to CEPS within month after the drug has been given provisional authorisation (ATU) by the AFSSAPS Chief Executive.

These prices shall be published on the CEPS website.

If any clawback payment is owing by virtue of the price or tariff published after the drug has obtained marketing authorisation, this payment shall be determined at the time the price or tariff is set. The payment shall take into account the sums actually charged to the healthcare establishments and any quantities which were supplied free of charge.

CHAPTER IV: IMPROVING THE COST-EFFECTIVENESS OF SPENDING ON MEDICINES

Section I: Novel drugs, orphan drugs and paediatric drugs

Article 10: Special advantages for novel drugs, orphan drugs and paediatric drugs

In the context of agreements with CEPS, novel drugs, orphan drugs and paediatric drugs shall benefit from the provisions of Article 18 herebelow, in particular concerning provisional, full or partial exemption from clawback payments per pharmacotherapeutic class grouping.

The parties wish to promote the orphan drugs market in connection with the EU's incentive policy as expressed in regulation (EC) no 141/2000 of the European Parliament and of the Council of 16 December 1999.

The parties also wish to promote steps to bring paediatric drugs onto the market, in line with the EU regulation.

CEPS shall forward to LEEM the list of paediatric needs drawn up by AFSSAPS: new paediatric products or approval of paediatric indications for existing products.

If a drug is included on the list produced by the European Medicines Agency's paediatric committee or appears on the list of paediatric needs drawn up by AFSSAPS, its pre-tax manufacturer price shall be set so as to guarantee a daily treatment cost which is equal to the drug's daily treatment cost for adults. These provisions shall only apply to drugs which are defined as orphan drugs pursuant to regulation (EC) no 141/2000 of the European Parliament and of the Council of 16 December 1999.

Article 11: Real-life monitoring of new drugs in clinical practice

The parties are agreed on the benefits of gathering data on use of new drugs in real-life situations.

This Article relates to studies which are governed by contractual agreements between CEPS and the company concerned. The studies may be initiated at the instigation of either the Transparency Commission or CEPS.

The recommendations of ADELF (Association des épidémiologistes de langue française, the French speaking epidemiologists' association) and good epidemiological practice shall apply to the manner in which the data is gathered and the studies are audited. The relevant public bodies may exercise their right to monitor compliance with these rules.

The aims of these contractual studies, the obligation to set up a scientific committee where applicable and the timescale within which the studies must be conducted and their findings obtained shall be set forth in a rider to the agreement, which may also make provision regarding the consequences of non-compliance with the timescales.

If the company can demonstrate that the findings of the study it has been requested to carry out would fully or partly duplicate the findings which the studies required as part of the marketing authorisation application process and included in the approved risk management plan would produce within the same length of time, the contractual study shall be modified accordingly. In such cases, CEPS and where applicable the Transparency Commission must be given copies of the findings of the studies included in the risk management plan.

Where a scientific committee is formed, information on the committee's composition and its members' declarations of interest must be sent to the Transparency Commission if the Commission instigated the study or to DGS (Direction Générale de la Santé - Health Department of the Ministry of Health) for other contractual studies. The scientific committee shall be responsible for deciding which type of study is best suited to address the issues raised and/or for approving the study protocol; the committee shall also give an independent expert opinion on the team appointed to carry out the study. This opinion must be sent to either the Transparency Commission or the DGS as applicable. The contract rider stipulates that the studies must be published, notwithstanding any intellectual property rights associated with them.

For studies which the Transparency Commission has instigated and for other contractual studies where this is stipulated in the agreement, the study protocol must be submitted to the Transparency Commission, which will give an opinion as to whether the study design is fit to address the issues raised. This procedure involving the Transparency Commission shall not entitle the company to any extension of the agreed schedule for starting the study and producing the findings.

The findings of the contractual studies shall be submitted to CEPS and to the Transparency Commission, where the latter instigated the study. The parties to the agreement shall discuss what action to take on the basis of the findings.

The committee shall oversee regulation of the costs involved in the studies, which must be reasonable in relation to standard industry practice (regarding number of cases, complexity, etc.) and shall ensure that the overall, proven costs to the company of carrying out the study are proportionate to the anticipated pre-tax turnover from sales of the drug. In the event that the costs are disproportionate in this respect or that the scope of the study is extended for public health purposes to include elements other than the use of the product in question, the company may be compensated for the additional costs incurred via a reduction of its clawback payments.

CEPS may request the companies to draw up protocols which could allow the findings to be extended to other drug products with related therapeutic targets.

These provisions do not rule out the possibility that other studies presented at the company's own initiative may be taken into account.

Penalty payments payable in the event of failure to carry out the studies within the agreed timescale, under the terms of Article L. 162-17-4-4bis of the Social Security Code, shall be set according to the procedure provided in Article 15 b) herebelow.

Article 12: Essential medicines

If a company plans to halt production or sale of one of its proprietary products which satisfies a particular medical need that would no longer be fulfilled if the product were removed from the market,

the company undertakes to enter into discussions with CEPS regarding the financial situation involved in keeping the product on the market, failing which the company's status as an approved supplier may be removed.

Section II: Sources of savings

Article 13: Development of generics and fixed accountability tariffs (*tarifs forfaitaires de responsabilité* – TFRs)

The joint CEPS – LEEMS monitoring group shall study the development of the generics market and carry out a critical analysis of how the market is functioning and the prevailing economic conditions for companies affected by the development of this market.

The parties to this agreement agree that the development of the generics drugs market represents a valuable contribution to the funding of medical advances.

The committee shall consult the companies concerned before placing a generic group on a TFR tariff. Prices submitted to the committee for drugs in the generics groups on TFR tariffs shall be published at the earliest opportunity. The committee undertakes to uphold the principle of open competition within the groups. The committee shall take into consideration the logistical pressures which the pharmaceutical companies will be put under by any changes to tariff levels.

Article 14: Development of self-medication not covered by national health insurance

The parties agree that responsible self-medication should be allowed to develop in France, as it will contribute to the responsible use of medicines without affecting the levels of payments made by national health insurance.

Section III: Responsible use of medicines

Article 15: Information for prescribers, promotion and advertising

a) Information for prescribers and promotion of medicines

The parties are agreed upon the view that promotion of medicines, whilst playing an essential informative and educational role for prescribers, can to differing degrees depending on the type of medicine, exert a disproportionate influence on prescribing practices.

The parties also agree on the view that in cases where the primary aim of the promotional activities is to obtain a market share by fair competition, with no proven risk that it will lead to excessive prescription volumes or irresponsible use of the medicine, limiting the companies' corresponding marketing budgets shall not constitute a high-priority issue in the agreements between the committee and the companies.

Conversely, the parties agree that in any circumstances where there is a risk that the drugs could be prescribed in unjustifiable quantities or under unjustifiable conditions, promotional materials must be produced which pro-actively and explicitly promote the responsible use of the drugs.

To this end, for drugs which are specifically identified as being among those described in the paragraph above, the committee may require the individual agreements to contain undertakings by the companies concerned to adapt their publicity materials and the training and materials given to their medical sales personnel so that they promote responsible use of the drugs and are directed only at the appropriate patient groups. The companies must be prepared to prove at the committee's request that they are abiding by these undertakings.

The pharmaceutical companies undertake to produce and promote a sales visit quality charter setting out the training requirements for and role of their sales personnel and emphasising the quality required of the promotional materials used by sales personnel.

b) Advertising bans

For the purposes of Article L. 162-17-4 of the Social Security Code, in particular in relation to advertising bans issued by AFSSAPS and the financial penalties which may arise therefrom, the parties agree that CEPS shall follow the procedure below when making its decisions.

For advertising bans which the committee considers may give rise to financial penalties:
the committee shall designate a rapporteur who will examine the case and present it at a committee session;
the committee shall draw up a draft decision giving its grounds for the decision;
the committee shall send the company the draft decision, asking the company to present any comments in writing;
the company may request a hearing by the committee; it may also enlist the help of experts or legal advisers;
the committee shall then hold fresh discussions and shall notify the company of its decision.

Article 16: Cooperative action to promote responsible use of medicines

The pharmaceutical companies undertake to actively pursue action undertaken with regard to the responsible use of medicines, in liaison with the appropriate social security bodies.

When HAS, UNCAM, INCA or AFSSAPS[24] are planning actions of a public or general nature which may affect the economic balance of the drugs sector, LEEM may request CEPS to arrange suitable consultations, after having applied to the ministers concerned if necessary.

CHAPTER V: ANNUAL FINANCIAL ADJUSTMENTS

Article 17: Annual financial adjustments: principles

Any company wishing to be exempted from the contributions required under the terms of Article L. 138-10 of the Social Security Code must undertake in the form of a contractual clause, to pay clawback payments, known as end-of-year quantity clawbacks, to the relevant URSSAFs[25]

However, regardless of whether or not the company has signed an agreement,, no end-of-year quantity clawbacks shall be payable if the cumulative growth of sales of reimbursable medicines to community pharmacies and sales to healthcare establishments of medicines included on the list provided in Article L. 5126-4 of the Public Health Code (and as of 1 January 2010 "or on the list provided in Article L. 162-22-7 of the Social Security Code") for all the companies put together does not exceed the sales-weighted mean value of the 'K' growth rates set each year by the Social security finance law (LFSS) pursuant to Article L. 138-10 of the Social Security Code. Furthermore, the

[24] HAS = Haute Autorité de Santé: France's independent health advisory body; UNCAM: Union Nationale des Caisses d'Assurance Maladie; INCa: Institut National du Cancer; AFSSAPS = Agence Française pour la Sécurité Sanitaire des Produits de Santé: government medicines and healthcare products regulatory agency.
[25] URSSAF = Union de recouvrement des cotisations de sécurité sociale et d'allocations familiales: main social security body which collects social security insurance contributions and distributes them to ACOSS (agence central des organismes de sécurité sociale), which in turn distributes the money to the various *Caisses*.

committee undertakes to ensure that the total amount of all the end-of-year quantity clawbacks paid by all the companies put together is less than the sum of the contributions which those companies would have had to pay if none of them had entered into the agreement.

At the end of each year, and by 31 January of the following year at the latest, companies which sell products included on the list provided in Article L. 5126-4 of the Public Health Code (and as of 1 January 2010 "or on the list provided in Article L. 162-22-7 of the Social Security Code") must send a declaration to CEPS, in the format of the pro-forma declaration provided in the attached appendix, giving details, for each product and product format, of the volume and actual turnover of its sales to healthcare establishments over the year and identifying among these figures all sales of products which were on the list (as of 1 January 2010, "on either list") on 31 December in the year for which the payments are owing and had been on the list since at least 1 January of the previous year.

The contractual clawback payments shall be paid to the appropriate URSSAF by 30 April the following year, on the basis of an assessment drawn up by CEPS following discussions during which the company may present arguments for a review of the amount of clawback payments calculated.

The end-of-year quantitative clawbacks are made up of payments per pharmacotherapeutic class grouping and payments based on turnover.

a) Clawback payments per pharmacotherapeutic class grouping

Each year, the committee shall draw up a table dividing the medicines concerned into groups for the whole of the sector concerned. These groups are made up of sets of pharmacotherapeutic classes defined using the EPHMRA codes. The committee shall set a growth rate for each group, in such a way that the weighted mean value of the rates is equal to the weighted mean of the 'K' growth rates established for the year in question by the social security finance law.

LEEM shall be consulted before the table is finalised.

The gross clawback payments owed by the companies, before deducting any exemptions as provided in Article 18 herebelow, shall be calculated as follows:

For each of the drug groups in which the annual growth rate is higher than the rate set by the committee, the total amount owing by all the companies who have agreements with CEPS and sell drugs belonging to that group shall be equal to the difference between the two rates multiplied by a given coefficient, which shall be the same for all groups and shall be set the committee in the light of the forecast sales growth for all the drugs concerned. For drugs sold to healthcare establishments, the sales taken into account shall be those corresponding to products included on the list (as of 1 January 2010, " on one of the lists") as at 31 December in the year for which the payments are owing which had been on the list since at least 1 January of the previous year.

The total clawback payment owing for each group shall be split into two portions, and the relative sizes of these portions, which shall be identical for all groups, shall be determined after consultation with LEEM. The first portion shall be split proportionally between all the companies with agreements who are selling drugs belonging to that group, on the basis of their respective sales figures. The second portion shall be split proportionally between those companies whose annual growth rate is higher than the rate set by the committee, on the basis of their respective excess turnover amounts.

Sales to healthcare establishments shall be calculated by multiplying the number of units sold by their prescription price (as of 1 January 2010, "or their *tarif de responsabilité*").

b) Clawbacks based on capped turnover rates

The companies shall also be liable where applicable for a clawback payment based on the difference between their turnover and a fixed threshold stipulated each year in a contract rider. The rate for this clawback is set, unless otherwise stipulated in the contract, at 10%.

For sales to healthcare establishments, the turnover figure used shall be the actual turnover.

When the sum of the safeguard contributions which the company would have had to pay if it had not signed the agreement is used as a basis for working out the threshold mentioned in the paragraph above, this sum is adjusted to cancel out, where applicable, sales of generics and products on fixed accountability tariffs and sales of drugs which were not claimed back from national health insurance.

Article 18: Annual financial adjustments: special implementation conditions

a) Exemptions from clawback payments per pharmacotherapeutic class grouping

1) Medicines which were given an ASMR rating when they were registered on the reimbursable medicines lists.

- ASMR I and II: full exemption for 36 months and 24 months respectively.
- ASMR III: 50% exemption for 24 months.
- ASMR IV: 25% exemption for 24 months.

For medicines sold to community pharmacies, these exemptions shall be effective as of the date they are sold, and for medicines on the list provided in Article L. 5126-4 of the Public Health Code (as of 1 January 2010, "or on the list described in Article L. 162-22-7 of the Social Security Code"), from the date on which the relevant sales are included in calculations for the clawback payments per pharmacotherapeutic class grouping.

Companies may opt for a fixed, non-extendable exemption period which is longer than the periods provided above, up to a period of five years. In such cases, the exemption rate shall be reduced to ensure that the length of the exemption multiplied by the rate remains constant.

Where the ASMR rating only relates to some of the drug's indications or where different indications have different ASMR ratings, the exemptions shall be worked out in proportion to the sizes of the patient groups concerned.

Where a drug has been covered by a provisional authorisation (ATU) or by a temporary treatment protocol for one of its indications which is not included in the marketing authorisation, the agreement may stipulate clawback exemptions on a case-by-case basis, based on a similar method to the one described above. These exemptions shall be deducted from those arising from any ASMR rating given to the indication in question once marketing authorisation has been obtained.

2) Extension of indications with an ASMR rating

The sum of the clawback payments shall be reduced according to the same rates and for the same periods as stipulated in paragraph 1) above, in proportion to the amount of turnover made by virtue of the new indication, starting from the date of the Transparency Commission's final opinion. Likewise, if a drug which has been exempted on the basis of its ASMR rating has one of its non-ASMR rated indications extended, the exemption shall be proportionally reduced, starting from the date of the Transparency Commission's opinion on the extended indication, according to the size of the patient group concerned. The pro-rata rates shall be established in the individual agreements.

3) Orphan drugs and paediatric drugs

Orphan drugs as defined in the legislation shall be exempted from clawback payments, unless otherwise stipulated in the agreements. For the purposes of the agreements, orphan drugs may be taken to include both legally defined orphan drugs and de facto orphan drugs which were marketed before the relevant legislation came into force.

Paediatric drugs included on the list announced by CEPS shall be exempt from clawback payments, under the same conditions as those stated in paragraph 1) above except that their ASMR ratings shall be set one level higher for these purposes than the level set by the Transparency Commission.

4) Low cost drugs

Generic medicines, medicines on generic prices and medicines on fixed accountability tariffs (TFR) whose price is equal to or lower than that of the tariff, shall be exempt from clawback payments.

5) Medicines for which a significant percentage of sales are not presented for reimbursement

The clawback payments owing shall be reduced proportionally in relation to the value of sales which were not presented for reimbursement, calculated from national health insurance reimbursements data.

6) (until 31 December 2009) Where a drug which is listed on the outpatient medicines list but is primarily issued to inpatients represents a significant proportion of the gross clawback figure payable by a company due to the size of its sales or sales growth, the agreement may contain conditions regarding partial exemption from clawback payments due to this drug.

b) Rules governing double clawbacks per pharmacotherapeutic class grouping and for products under special contractual conditions

Where clawback payments are owing under the terms of an individual agreement relating to a specific drug (e.g. daily treatment cost refunds, volume discounts etc.), any clawback payment per pharmacotherapeutic class grouping which the company owes for this drug shall be recalculated to take the sales of this medicine and any excess turnover made on it as the net sales actually earned by the company (GERS turnover data-specific rebates).

c) Clawback credits

1) Clawback credits for price reductions or refund reclassifications

Price reductions proposed by the companies, with the exception of reductions proposed following the creation of generic groups or in groups on fixed accountability tariffs, shall give rise to a clawback credit equivalent, unless otherwise stipulated in the agreements, to the amount of the reduction of the manufacturer price ex VAT multiplied by the number of units sold during the twelve months preceding the reduction.

Price reductions proposed by CEPS under the terms of Article L. 162-17-4 of the Social Security Code and put into practice through the company's agreement with CEPS may give rise, under the terms stipulated in the agreement, to clawback credits.

Refund reclassifications may give rise, under the terms stipulated in the agreements envisaged in Articles 4 and 5 hereabove, to partial compensation in the form of clawback credits.

2) Clawback credits for Braille

Contributions which companies make to funding the production of patient information leaflets in Braille shall be recognised in the form of clawback credits.

3) Carrying over credits

The companies shall be entitled to carry any clawback credits they receive over into subsequent years.

CHAPTER VI: SCOPE OF THE AGREEMENT

Article 19: Scope and term of the framework agreement

This agreement, which replaces the 'community' framework agreement of 13 June 2003 as amended and the "hospital" framework agreement of 23 March 2004 as amended, shall be effective until 31 December 2011.

The agreement constitutes a framework agreement under the terms of Article L. 162-17-4 of the Social Security Code.

Subject to statutory and regulatory provisions relating to the pharmaceutical sector and in particular to the taxes applicable to the sale and marketing of drugs, this agreement sets out the conditions regarding financial regulation of medicines as they apply to companies which enter into an agreement with CEPS pursuant to Article L. 162-17-4 of the Social Security Code.

The agreement may be supplemented by riders.

In the event that one of the parties should withdraw from the agreement before it expires, the terms of the agreement shall be extended for a maximum period of one year until such time as a new agreement is signed or, for the purposes of Article 8 hereabove, until publication of the decrees provided in Articles L. 162-16-5 and L. 162-16-6 of the Social Security Code.

In the event that the overall balance of this agreement should be altered, in particular following amendments to the applicable statutory or regulatory provisions, a major change in government policy or consequences of the enlargement of the European Union, in such a way as to increase the burden of the pharmaceutical companies' obligations, the agreement shall be renegotiated in order to re-establish a balance between the parties. If such negotiations are unsuccessful, the agreement may be terminated by either party.

Done in Paris in two original copies, 25 September 2008

For the pharmaceutical companies	For the Comité économique des produits de santé
Christian Lajoux	Noël Renaudin

APPENDIX 2: METHODS FOR SETTING MEDICINE PRICES

1. Methods for setting the prices of medicines sold in community pharmacies

Article L.162-16-4 of the Social Security Code sets out the rules governing price setting for medicines which are reimbursable under the social security system:

"The public sale price of each of the drugs mentioned in Article L. 162-17 paragraph I, shall be set by means of a contract between the company selling the drug and the *Comité économique des produits de santé* (CEPS), pursuant to Article L. 162-17-4 of the code or failing this, by decree of the ministers for social security, health and the economy after consultation with CEPS. The primary considerations when setting the prices are the improved medical benefit which the drug provides, the prices of other drugs providing the same treatment, forecast or recorded sales volumes of the drug and the foreseeable and actual use of the medicine".

Article R.163-5-I-2 stipulates that "drugs which provide no improved medical benefit as assessed by the commission provided in Article R.163-15 and no savings on medical treatment costs" may not be included on the list provided in Article L.162-17 of the Social Security Code.

In compliance with these provisions, the committee's task is to obtain the most advantageous price and financial conditions for the national health insurance system, whilst taking into consideration both the medicines market as a whole and the limitations of the ONDAM budget, as well as public health needs and the obligation to treat all the companies equally.

Consideration of the medicines market as a whole requires that beyond the bilateral negotiating framework, all discussions about an individual drug price should be informed by an analysis of the economic consequences of the price on development of the market and national health insurance spending: the direct, immediate consequences on price structures within therapeutic groups; indirect consequences on the relative growth among the different groups; medium-term consequences in terms of estimating the financial burden which the associated reimbursements will have on the ONDAM budget and more long-term consequences if the subsequent emergence of medicines with the same indications is foreseeable.

The goal of fulfilling health needs requires the committee to ensure through its actions that patients have access to the medicines they need and in this respect, price setting is merely a means to an end.

Upholding the principle of equal treatment between medicines must apply regardless of which companies are selling them. This principle dictates specifically, among other things, that the committee should not see it as part of its role, regardless of the benefit that this may bring to research and innovation, to finance research up-front through its pricing of medicines that are not themselves the results of this research, and even less so, where novel medicines are concerned, to treat them differently depending on the country of origin of the innovation.

1.1. Medicines with no ASMR rating

With regard to setting prices for medicines with no ASMR rating, implementing the rule in Article R.163-5-I-2 infers that the committee should answer two questions: saving in relation to what? and the size of the saving.

1.1.1. Saving in relation to what?

In some cases, the choice of a reference treatment against which to measure the saving is obvious and indisputable in light of the Transparency Committee’s opinion. However, this is not always the case by any means.

Often, therefore, when a new product in an existing range is registered, the committee must decide whether the most appropriate way to determine the impact of the product's registration on social security expenditure is to compare it against the range to which the new product belongs and which it will, to a certain extent, replace, or to compare it against equivalent products being sold by other companies (possibly at a lower price). In most cases, the committee decides to compare the new

product with cheaper rival medicines, so as not to perpetuate any unjustified price variations between different products which provide the same service. Sometimes, when an agreement cannot be reached at that price, and especially when the new product is intended to replace an existing product en masse, the committee agrees to set a price midway between the price of the product being replaced and that of the cheaper rival product.

Another equally common problem is choosing between daily treatment cost, course of treatment cost, or packaging cost as a measurement instrument. While the daily treatment cost is the one used most often, especially for solid or injectable treatments for chronic conditions, the solution can be less obvious for short-term treatments or when there is no fixed dose (topical applications, liquid forms, etc.). Arguments in favour of the course of treatment cost are rarely accepted by the committee, as it is aware that prescription practices frequently fail to comply with clinical trial protocols or with the SPC (Summary of Product Characteristics). Therefore, in some cases, when it is clearly inappropriate to use the daily treatment cost and the course of treatment cost is much too unclear, the committee decides to compare boxes or bottles, on the basis of comparable average prescriptions.

Finally, the committee very rarely agrees to take into consideration, for purposes of cost comparison, assertions that the number of co-prescriptions with other medicines will fall, even if this seems to be borne out by the clinical trials. Past experience has shown that these assertions are almost always disproved in practice.

1.1.2. Size of the saving

Generally speaking, the price advantage compared with the last medicinal product registered should be relatively greater where the price of the reference product is high and where more time has elapsed between the two registrations.

However, the expected saving is not measured in terms of the difference in unit price between the new medicinal product and the already registered product with which the Transparency Commission is comparing it. It is measured in terms of overall saving, which is obtained by calculating price differentials by volumes. This general observation leads to two main consequences.

The first results from the distinction between classes in which prescription volumes are fixed (definite diagnoses, specific restricted indications) and classes in which there is a risk of unjustified growth in volumes. In the first instance, the only possible effect of a new competitor is to shift market shares, and therefore it is welcome, even if the price advantage is relatively insignificant. In the second instance however, the relative price advantage gained from the arrival of a new competitor could be offset or even cancelled out by the overall increase in volumes resulting from greater promotional pressure on prescribers. Hence the committee is more exacting in this case.

A second consequence is that savings will only really be achieved if the new medicinal product wins a share of the market, and these savings will be proportional to the market share. Given the fact that all prescriptions without exception are based more on the laboratories' promotional efforts than on price differentials, it has to be said that for the same level of service, higher-priced medicines sell more than their cheaper counterparts. Therefore, the committee can accept prices that are equal to or higher than that of the last similar product registered if it believes that a lower price would be such a competitive handicap to the manufacturer of the new product that it would sell only very few.

Finally, in the case of novel pharmaceutical products with no ASMR rating, the committee is careful to make sure that registration of these new products will not inadvertently - or indeed purposely, where products coming to the end of their patents are concerned – prevent the development of generics for commercial or legal reasons. In such a case, in accordance with ministerial guidelines, the committee will only approve the registration at a price equal to or lower than that of the corresponding generics.

1.2. Medicines with an ASMR rating

Registering these medicines on the lists can lead to additional expenditure by national health insurance, however the decision as to what constitutes an acceptable extra cost is a difficult matter and it is impossible to devise a standard formula.

There is no scale of acceptable price differences that corresponds to the ASMR rating scale. Discussions on the price for an ASMR-rated drug are therefore open to negotiation and the company's demands need to be weighed up against the need or urgency in terms of healthcare needs for the drug to be registered on the reimbursable list.

However, ministerial policy does provide a framework for these negotiations on two particular points. The first relates to medicines with an ASMR rating of III or higher, for which the committee should accept an initial listing price that is consistent with the prices in force in the main EU Member States, in accordance with ministerial guidelines and under the terms provided in the framework agreement. This principle does not imply that all medicines with these ASMR ratings should automatically be registered on the reimbursable lists at a European level price, but rather that if they are accepted onto the lists, it should be at this price. If the expenditure which this price level will entail is out of proportion with the anticipated benefit for patients or for public health, it cannot be ruled out that the product will not be accepted onto the reimbursable medicines lists.

One of the main features of these medicines is that more often than not, the discussions regarding their initial listing price go hand-in-hand with a discussion regarding contractual conditions, which are as important as the price itself, since they are usually drawn up to ensure that the medicine is used appropriately in relation to the identified needs, or to anticipate bulk discounts, depending on the size of the sums in question (c.f. 2.3). Registration of these medicines on the respective lists is also often subject to an undertaking to conduct studies, under the terms set out in Article 6 of the framework agreement.

At the other end of the scale, when an ASMR IV-rated medicine is registered with the intention of replacing a medicine that has been or is soon to be genericised, the price or price schedule must be set in such a way that it will not represent any additional cost to national health insurance in the short or medium term.

For other ASMR IV-rated medicines, price negotiations must take into account the nature of the target patient group. For example, where a medicine has the same target patient group as the reference medicine, the committee may quite happily decide that an increased market share will be adequate reward for the company's innovation, without the need for a price advantage on top of this. The decision may be different if the ASMR rating is based on a specific benefit for a limited patient group.

1.3. Setting prices for "me too" and follow-on drugs

With regard to price setting for "me too" drugs and so-called follow-on drugs, it is important in the first instance to clarify what is meant by these terms.

For a drug with no ASMR rating (ASMR V or higher) which a company is applying to have registered on the reimbursable medicines list, it is important to distinguish whether the new drug is sold by the same company that sells the already listed drug which the new drug is compared against in terms of ASMR rating, or by a rival company.

In the first situation, the new drug will act as a substitute in practice for the existing drug where the latter has gone off-patent or will be going off-patent in the near future. In these instances the new drug is referred to as a "follow-on". It is a simple matter of fact and CEPS is not concerned with what the company's intentions may be. The new drug is usually a variation on its predecessor: an enantiomeric form, new pharmaceutical form, prodrug, etc.. Levocetirizine, tamsulosin and pregabalin are some examples. In such cases, the rule set in the ministerial guidelines is straightforward: the price of the new drug must be the same as the price of generic versions of the original drug. The committee applies this rule to daily treatment costs and public price including VAT.

When the new drug is developed a sufficient distance before its predecessor is due to go off-patent, the committee may agree to list it at the same price, under the contractual condition that once the generics of the original drug arrive, if the second drug has not been genericised itself, its price will be reduced to that of the generics of the original. Some examples of this are desloratadine and lansoprazole oral suspension.

When the new drug has been given an ASMR IV rating in relation to the original, it is still classed as a follow-on, but the price-setting rule is more favourable. The price is set in such a way that the prescription costs of the new drug are no higher in public price including VAT than the prescription cost of the original, taking the degree to which it is substituting the original into account. In this case, the registration agreement stipulates that the price will be reduced at a later date to reflect the market share held by generics, where applicable. Esomeprazole and escitalopram are cases in point.

In the latter situation, when the new drug is sold by a rival company to the company which sells the reference drug, a distinction is made on the basis of the length of time since the reference drug came onto the market. If this period is sufficiently short – up to a few years – and even if the modes of action of the two drug products in question are very similar, it indicates that the two drugs are each the product of independent research and the companies have incurred the same level of risk. These are not "me-too" drugs, but competing drugs which have arrived on the market at different times. CEPS considers that restricting the number and diversity of competing drugs in principle would only present disadvantages, both in terms of cost (new drugs represent savings for national health insurance under the terms of the Social Security Code) and for medical reasons (even a product which is not given a ASMR rating can be a preferable choice for a section of the patient group). Another reason is that if all healthcare systems only allowed the first or first few comers access to the market, this would create an unsustainable burden of "all or nothing" on the companies' research work.

The term "me-too" is therefore only used for drugs which have been inspired by the success of their predecessors and have entailed a relatively low level of risk for the company. By definition, marketing authorisation of "me-too" drugs takes place many years after the market leaders were authorised. Olmesartan, rosuvastatin and lercanidipine are some examples. There is no simple price setting rule for these drugs. The committee's aim is to obtain the greatest possible saving, therefore it seeks to find a happy medium between the saving per pack sold, where the lower the pack price the greater the saving, and the number of packs sold instead of a more expensive rival, where the number of packs sold will be greater if the price is set at a level which will produce resources for more intense marketing.

The above principles apply to the initial listing of the drugs in question. Further down the line, market conditions may change, especially due to the growth both in market share and in price of medicines in the generics substitution list. The committee then implements ministerial policy on 'price consistency' and in the therapeutic groups in which generics are emerging and growing, this leads to a gradual reduction in the price differences between the generics and medicines providing the same treatment which are still patent-protected.

1.4. Price review clauses

Price review clauses are introduced at the time of price setting in three main situations:

- Where certain assumptions are made when setting the initial price, which only time and usage will confirm or negate and it is necessary to guarantee that the actual cost per patient of use of the medicine remains consistent with the level that was agreed with the company at the time of registration. In essence, this is the situation that "daily treatment cost clauses" are designed to cover.

- Where it is necessary to ensure that the quantities of a drug sold remain consistent with the drug's medically established target patient group. These situations are covered by "volume clauses".

- Where the price level and the likely sales volumes, especially for drugs which have been listed at a protected European-level price because of their ASMR rating, warrant a price reduction after the period guaranteed by the framework agreement. In these cases, unconditional price reduction clauses may be drawn up to take effect on a set date.

1.4.1. Daily treatment cost clauses

Daily treatment cost clauses are split into two categories: "range of dose" clauses and "posology" clauses. Where a dose-related effect has been established in their use, many medicines are sold in several different dose sizes, either from the time they are authorised or at a later date when additional dose sizes are added. In these cases, the committee decided that the best way to ensure both that the

different dose sizes of the drug were properly used and that rival companies in the therapeutic group in question were treated fairly, was for all dose sizes of the same drug to be sold at the same price per pharmaceutical unit. Uniform prices mean that it is not in the pharmaceutical companies' interest to specifically promote the sale of the highest, most expensive dose sizes. They also mean that the treatment cost and the balance of relative prices between rival companies can be maintained at the same level over time since the actual treatment costs are independent of the distribution of sales volumes between the different dose sizes.

When it is not possible to set uniform prices, in particular for reasons of internationally consistent prices, a "range of dose" daily treatment cost clause is signed instead with a view to producing a more or less similar effect. In these cases, what is agreed with the company at the time of the drug's registration is actually a daily treatment cost reflected in the prices of the different dose sizes on the basis of an assumed distribution pattern of prescriptions. If the statistics show that the actual distribution is different from the assumed distribution, the prices are revised to establish a new agreed treatment cost.

The purpose and the mechanism of "posology" clauses are exactly the same as those for the "range of dose" daily treatment cost clauses. At the time of the drug's registration, a daily treatment cost is agreed on, based on an assumed average posology (as stated in the MA or as demonstrated in studies conducted prior to registration, including in countries where the drug has already been marketed). If the actual posology observed in real life is different than the posology used to establish the selling price, the price is revised to re-establish the agreed daily treatment cost.

1.4.2. Volume clauses

The committee considers that volume clauses are not warranted when their main effect would be to distribute market shares between competing companies. Except in a few cases, they also do not make sense when registering non ASMR-rated drugs on the lists, as sales of these drugs represent savings for national health insurance and the larger the volumes sold instead of more costly drugs, the greater the savings. In these instances, the committee feels that the system of end-of-year quantity clawbacks per pharmacotherapeutic class grouping is more appropriate.

However, volume clauses are essential in the relatively frequent situations where a novel drug's ASMR rating is only applicable to some of its indications or to a small patient group or where, regardless of any financial considerations, public health requirements dictate that a drug should only be used for a limited number of indications for which it is absolutely essential, as is often the case for antibiotics, for example.

The committee has insisted on not signing any more agreements containing daily treatment cost or volume clauses which would only be implemented via volume discounts. However, to prevent minor and potentially reversible excess sales above the contractual thresholds from leading to a series of marginal price alterations entailing high administrative costs, the committee frequently agrees in practice to make the implementation of price reductions subject to exceeding a variation threshold, where price reductions which are not implemented are compensated for by an equivalent amount of bulk discounts. Above all, in accordance with the framework agreement, price variation clauses entered into for drugs rated at ASMR levels III or higher usually stipulate that the reductions will be converted into clawback payments for the drug's first five years on the market.

1.5. Other price changes

In addition to price reductions introduced in implementation of specific clauses, which do not require further commentary, prices may also be reduced at the committee's initiative in three different situations:

- when the drug is due to have its registration renewed, which is the opportunity for looking at the position which the drug has actually gained in the market, which can vary widely from what may have been anticipated at the time of the drug's first listing. This is the case in particular, even where there has been no improper use of the drug, when the drug's prescription volumes have risen significantly

since it was listed, in particular following extension of its indications. A price reduction may also be justified, in accordance with the Social Security Code, when equally effective and less costly rival drugs have come onto the market since the drug in question was first listed.

- or, pursuant to Article L. 162-17-4 of the Social Security Code, when the growth in spending on a drug is clearly inconsistent with the ONDAM target, even if it is consistent with ministerial policy and the provisions of the framework agreement.

- reductions may also be warranted once the findings of the follow-up studies on real-life use of the drugs, conducted in accordance with Article 6 of the framework agreement, are known, and more generally, when the scientific and epidemiological data used as a basis for the agreements changes significantly.

Companies are of course free to propose price reductions themselves. By definition, these are competitive price reductions, which to date have usually been for market leaders of generic groups that have been put on a "fixed accountability tariff" (*tarif forfaitaire de responsabilité*). The committee is not without hope that this type of reduction could be extended to medicines that are still under patent, as prescribers' and patients' price awareness grows and as companies are obliged to use low price as a marketing lever for their drug, where it has no added medical benefit.

CEPS accepts price increases for essential drugs which meet healthcare needs and were listed at a price that did not allow the companies to cover their manufacturing and marketing costs. These are generally long-standing products whose market has progressively diminished, orphan drugs or drugs which though not strictly defined as orphan drugs can be classed along with them for financial purposes.

However, the committee rejects companies' proposals for so-called 'win-win' price changes, since although their immediate effect may be neutral or beneficial for national health insurance, they tend to prove more costly in the long term and always upset the relative price balance within pharmacotherapeutic groups.

2. Determining hospital medicine prices and tariffs

Within the scope of and on the bases set out in the 2004 Social security finance law (LFSS)and the national health insurance law of 13 August 2004, the CEPS-LEEM hospital medicines framework agreement now provides the framework for the procedures, forms and conditions for the setting and reviewing of prescription fees for medicines on the outpatient medicines list and of "accountability tariffs" (*tarifs de responsabilité*) for products on the T2A list.

2.1. Criteria contained in the Social Security Code

For outpatient medicines, Article L. 162-16-5 of the Social Security Code and for T2A list medicines Article L. 162-16-6 of the same code stipulate that the price setting approach for outpatient prescription fees or the accountability tariff for medicines charged on top of general hospitalisation costs should primarily take into account the selling prices currently used for the medicine, the selling prices of medicines which provide the same treatment, the forecast or actual sales volumes, the foreseeable or actual use of the medicine in practice and the improved medical benefit it provides, as assessed by the Transparency Commission.

2.2. Criteria contained in the hospital medicines framework agreement

In accordance with the above-cited Articles of the Social Security Code, Article 8 of the hospital medicines framework agreement of 25 September sets out the criteria governing opposition by CEPS to a company's submitted price.

CEPS may oppose the proposed price on the grounds that it is exceptionally high in relation to the prices in force in the main EU Member States, or in relation to prices in force in the French market where directly comparable products are already being sold on the French market. It may also oppose the price due to the inadequacy of the undertakings made by the company where applicable, in particular if there is a clear risk, where the proposed price is only justified for some of the indications included in the marketing authorisation, that the quantities sold will incur exceptionally high spending

by the national health insurance system or if, taking market conditions into account, the product's inclusion on one of the lists leads to sales volumes which give rise to volume discounts on the company's proposed price.

2.3. The committee's approach

The committee's acceptance of or opposition to the company's submitted price has therefore been based on either the Social Security Code criteria or the criteria contained in the framework agreement, or a combination of the two.

For all the products concerned, the committee has based its examination on two main sets of information, the first being information derived from processing of the companies' tax declarations, which provides a picture of the volumes they have sold in recent years to healthcare establishments, as well as the average prices used and growth in both prices and volumes; the second being information on prices and sometimes sales volumes of some of the medicines, obtained from other countries and primarily from bodies in the main European countries. The committee has compared both sets of information when making its decisions. The committee has also taken into consideration the fact that registration on the T2A list could act as a growth stimulus for the products concerned. It has also paid close attention to avoiding price discrepancies within the various groups of interchangeable medicines.

2.3.1. European prices as a benchmark

Paradoxically, although this benchmark was adopted in order to provide a guaranteed price for companies selling recent original drugs which would be no lower than prices in force elsewhere in Europe, it has often proved to be a basis for opposing the companies' price submissions, in the many cases where the committee noted that the prices used for French healthcare establishments up to that point or being submitted for the first time were actually higher than all the other European prices, whilst the quantities sold in France were higher than elsewhere in proportion to the size of the patient groups. In exceptional circumstances, the benchmark has led the committee to accept price submissions that were higher than those currently practised in France, where for essential medicines it emerged that the French prices were significantly lower than most other European prices.

2.3.2. The general market as a benchmark

As a whole, the committee felt that there was no reason why this new procedure should begin a general practice of setting higher prices than those in force in France up to that point within a framework of free pricing. In view of the fact that prices had risen considerably in 2003 and 2004 for a large number of medicines, the committee frequently opposed price submissions matching these prices, in order to return to 2003 levels.

Attention should be drawn to two particular situations:

- the first concerns "dual circuit" medicines, which patients can buy either from hospital or community pharmacies. These are medicines for hepatitis and HIV/AIDS. For these products, CEPS considered that the prices negotiated in the agreements for sales by community pharmacies, which without exception were set in relation to the European benchmark, should also be applied to hospital sales with no added markup.

- the second concerns products included on the T2A list which are largely interchangeable and for which any discrepancies in the prices accepted by CEPS would lead to companies giving discounts, where the greater the price advantage for them, the higher the discount they could give, and could induce hospital buyers to buy on the basis of the discounts, thus distorting the competitive element and acting as a type of indirect subsidy to healthcare establishments by national health insurance. With this prospect in mind, the committee decided to standardise the accountability tariffs within each of the interchangeable product groups.

More generally, the committee believes that the difference between the tariff which is reimbursed by national health insurance and the prices actually paid by the healthcare establishments could lead to inappropriate buying practices by the hospitals and that therefore the difference should be restricted to

the usual price differences based on the quantities bought by the establishments or specific services they can provide for the sellers.

APPENDIX 3: TARIFF AND PRICE SETTING FOR MEDICAL DEVICES

The first decision to be made when setting medical device tariffs and prices is whether the products should be listed by generic category or by brand name. This choice is down to the Minister, but CEPS is required to formulate proposals, which it bases on the opinions of CEPP (the Medical device and technology assessment committee) (1). Accountability tariffs, and where applicable maximum sale prices, are then set according to general principles (2) which are implemented according to individual circumstances (3 to 6).

1. Registration by generic category or by brand name

The committee's view, which has consistently informed the proposals it has made to the Health Minister regarding the registration conditions governing each individual case, is that registration by generic category should be the rule and registration by brand the exception.

This does not mean that registration by brand represents a particular distinction or, indeed that it signifies superiority in terms of service provided. On the contrary, it goes without saying that requirements regarding level of service provided should be the same for both types of registration, which both relate to products that will be covered by national health insurance and are for use by people with a medical condition or disability.

It also does not suggest that registration by brand should be a rare occurrence and registration under generic categories more frequent.

It simply means that registration by generic category should be chosen unless – and this is where registration by brand constitutes the exception – generic registration is not possible or is clearly undesirable.

In practice, all instances where registration by generic category is not possible come down to the same situation, which is that it is not possible to produce a generic description and, where applicable, technical specifications capable of guaranteeing that any devices which comply with the description will provide the expected service. This is of course often the case for devices which have been recognised as providing an improved service level or expected service level, which can be clinically proven in tests but for which without the necessary experience in practice it may not be possible to define the technical features that determine this.

By contrast, there are two types of reason why registration by generic category is not desirable. The first type of situation relates to public health concerns and essentially comes under CEPP's remit. For example, in 2006 CEPP recommended that gastric bands should routinely be registered by brand, in order to ensure that bands were only used if CEPP had been able to at least examine the available data on their efficacy and safety for use. However, by the end of 2006, the decree translating this guideline into law had not yet been published, as no practice framework that the relevant government bodies found satisfactory had yet been produced.

The other reasons are of a financial nature, and come under CEPS' remit. These situations usually relate to the need to enter into agreements with the companies on other aspects in addition to tariff or price setting, which entails getting to know the companies. This is the case in particular every time the price setting goes hand-in-hand with conditions regarding the payment of clawbacks or price modifications based on quantities sold or actual use of the device in practice.

Registration by brand can also be necessary when an innovative product has done all the work of demonstrating the service provided by a new type of device at a cost to the company in both time and money. This is to avoid a situation, for a certain length of time at least, where mere imitators can come onto the market and be registered under a generic category, without having to go through any formalities other than CE marking.

2. General principles governing tariff and price setting

The approach to tariff and price setting for medical devices is based on three rules.

Two of these relate to tariffs:

Article R. 165-4 of the Social Security Code stipulates that "products and services (...) which represent neither an improvement to the service expected or the service provided, nor savings on treatment costs, or which are likely to entail unjustifiable national health insurance spending, may not be registered on the list provided in Article L. 165-1 of the code.

Article R. 165-14 provides that "the primary considerations when setting tariffs should be the service expected or provided, any improvement to this service, the tariffs and prices of comparable products or services already included on the list, the sales forecasts and the foreseeable actual conditions of use.

As regards prices, they should be determined on the basis of the very broad provisions of Article L. 162-38 of the same code, according to which the setting of prices or markups by decree for products or services which are to be covered by mandatory national health insurance plans "must take into account growth in workload, income and business for the practitioners or companies concerned".

In practice, the committee is often obliged to combine these rules and does so automatically when a tariff and a maximum sale price are simultaneously set at the same sum. In these instances, it goes without saying that this common sum must comply with the both the rules regarding tariffs and those regarding prices.

Applying these rules to medical devices, which are identical to the rules for medicines where tariffs are concerned, does however pose several problems relating to the special conditions governing reimbursement of medical devices, the shape which innovation often takes in this field and the very diverse nature of the different products and services concerned. The following explanations describe the solutions that the committee has adopted.

3. Tariff setting by category

For products or services which do not represent any improved expected service (ASA - *amélioration du service attendu*) or improved service provided (ASR - *amélioration du service rendu*) to be included on the list, they must represent savings in treatment costs, pursuant to Article R. 165-4. However, in practice, this simple, essential rule is difficult to apply to medical devices. The code effectively makes it a rule (Article R. 165-3) that registration of a covered item should in principle be done according to generic descriptions of the product or service and registration by brand or trading name should be the exception. The result of this is that the vast majority of products and services which are registered as covered items are entered under an existing category and therefore at the same tariff, even though they are not ASR rated, as the products or services already registered as covered items.

The committee has dealt similarly by extension with certain categories of device which have been registered under their brand names in implementation of the second exception to the generic registration rule provided in Article R. 165-3, "when the impact on national insurance spending, public health imperatives or the verification of minimum technical specifications require special monitoring of the product". The same applies to device categories which before the reform were listed under the "approval numbers" system and were registered, sometimes temporarily, under their brand names. For these cases, the committee decided that it was appropriate to treat the products in question as if they were under generic categories and for newly included products to be given a tariff and where applicable a maximum sale price identical to those of products already registered in the category. This practice was given a legal basis in the form of the decree of 23 December 2004 amending Article R. 165-4 of the Social Security Code.

The first consequence of this situation is that the rule on treatment cost savings only applies in practice to new devices with no ASA or ASR rating which do not match an existing generic definition, either because the service expected or provided is obtained, for comparable devices already listed, via a different mode of action or technology, or because the comparison is being made with treatment

methods which do not come under the scope of the list, such as surgical procedures, drug treatments, etc.

The second consequence is that for medical devices, a reduction in the average price in a product category over time, which for medicines occurs naturally with the successive registration of new medicines that are each cheaper than the last, can only be obtained, when justified, via a periodic price reduction review of generic categories or standardised tariffs.

4. Recognising innovation

For products which do provide an improved level of service expected or provided (ASA or ASR), whilst the criteria explicitly set out in the regulations provide a framework and guidelines for setting tariffs, they cannot be used on their own to determine them. The rule in Article R. 165-4 authorises a higher price or tariff for these products but without specifying the size of the premium. The most that can be deduced from this is that generally speaking, a low ASA or ASR rating does not justify a major difference in the tariff compared with the reference product, where a reference product exists, which is not always the case in the medical device field. Added to this, the existence of an ASA or ASR rating is a necessary pre-condition but is not enough on its own to warrant extra expense and the rules do not therefore prevent a new ASA or ASR-rate product from being registered at a lower tariff than that of already listed reference products. Aside from the price of the reference product, even if a certain product is given a high ASA or ASR rating with respect to the minimum technical specifications required to sell it under a generic category, this does not constitute a criterion for setting a higher price or tariff than those given to the generic category, even if only because products with an equal ASA or ASR rating may already have been on the market at the prices or tariffs applicable to the generic category, but also because of the need that may exist to create entries under brand names.

In practice, therefore, the committee has to distinguish quite schematically between three main situations when setting tariffs for innovative products.

In the most straightforward cases, it can be demonstrated that the price that the company has proposed or accepted and which it therefore considers to be a just recognition of its innovation work will entail costs for national health insurance which are lower than, or at the worst equal to, the savings that use of the product will lead to. In these cases, registration poses no problems, though this does highlight the importance of having reliable, convincing medico-economic studies.

In the second instance, it often happens, especially in the case of implantable devices, that advances in service provided take place in the shape of so-called "incremental" innovations, which have the dual feature of being both modest and frequent. When it appears that the prospect of the new product's higher market share is not sufficient remuneration for the innovation work and that a price advantage is also required, the committee may propose tariffs that are higher for a limited period of time than those of comparable products already listed. In the event that another equally innovative product is registered some time later, the committee allows the new device the same price or tariff advantage as its predecessor for whatever time remains of the temporary price advantage period. This means that innovation work is rewarded for a certain, usually short, period before being overtaken by a new, more technologically advanced product. This practice, which the committee implemented when setting tariffs for pacemakers, means that the ASA or ASR ratings can be recognised, whilst avoiding spiralling costs. In this context, the minimum technical specifications attached to the generic category must be periodically revised to incorporate the incremental innovations which have accumulated since the previous definition.

This leaves the most difficult cases: innovations that represent both significant advances and high costs and for which the recompense for the sometimes significant extra costs they represent for the public purse will only be in terms of improved patient care that is not financially measurable. Cost-benefit studies can be used as decision-making aids, but they are usually awkward to carry out. In these situations, discussions regarding price, which is under strong pressure if there is an international market, are largely replaced by the issue of limiting the quantities of the product to the patient groups for which the expected advantage of the innovation has been well established. This presupposes that the issue of identifying and measuring the target patient groups has been dealt with, as well as the

matter of all the different resources that need to be put in place to ensure that only those groups are given the benefit of the innovation. In these cases, contractual provisions are made at the time the product is registered, regarding limitation of sales and compensation payable by the companies if they exceed these quantities and regarding the creation of follow-up studies.

For these major innovations, the price or tariff advantage which the market leader is given can pose problems as soon as equally innovative rival products emerge whose price or tariff will need to be lower. If these products are registered on the hospital T2A list, this price differential could skew the competition between the devices in that the choice will no longer depend only on the expected efficacy of the devices or even on their cost/benefit ratio, but also on the size of the discounts which the manufacturer of the product with the highest price or tariff will be able to offer buyers. The issue then is to re-establish normal competition conditions between equivalent products included on the T2A lists as quickly as possible.

5. Discrepancies between prices and tariffs

The reimbursement system for medical devices, unlike the system for medicines that was in force before fixed accountability tariffs were introduced, is such that in general situations, there can be discrepancies between the tariff, which is the national health insurance reimbursement base, and the actual price.

When it is deemed necessary for reasons of equal access to care or disability support to prevent a wide discrepancy from being established, the only means available since the new rules were introduced is to set a maximum selling price (c.f. the committee's 2001 annual report). The committee has often proposed this method. However, setting a maximum selling price presupposes that the issue needs to be resolved of the extra costs charged for services or accessories which go beyond the definition of the reimbursable product or service as stipulated on the list. This is often the case for external prosthetic devices and orthotic devices, where patients may request, and the operators involved may offer extra aesthetic or technical features, but these are not the only cases. For example, in the area of hearing devices for young children, those working in the profession have highlighted the fact that the discrepancy between the tariff and the price gave room to pay the salaries of the hearing device personnel, whose services might be needed over many sessions in order to adapt the appliances to the patients, especially for patients who are very young or have multiple disabilities. In the event, the patient's share of the costs was usually taken care of by universal health cover (CMU), top-up insurance or help provided by regional or municipal aid bodies approached by the support personnel themselves. The difficult, sometimes impossible task of determining a maximum sale price according to logical criteria and the possibilities available for funding the patients' share of the costs led the committee to opt for setting a maximum selling price for these hearing devices that was higher than the reimbursement tariff.

For add-ons of an aesthetic or technical nature, when they are easy to separate from the defined reimbursable product or service per se, there is no reason why the operators involved should not produce separate bills for the patient's extra share, whilst adhering to the maximum selling price for the main element. When these add-ons, especially the aesthetic type, cannot be separated from the reimbursable device, it is important to avoid exemptions, which could gradually lead to a strong risk of all satisfactory products being taken off the reimbursable list and thus to access problems for less well-off patients. In 2003, the *Conseil d'Etat* ruled in the case of orthopaedic shoes that a complete ban on exemptions was illegal. In this instance, after taking advice from the national consumer's association (*Conseil national de la consommation*), the committee swapped the ban for a strict procedure requiring patients to be informed in advance. Whether the add-ons can be separated from the main product or not, if they are legal, patients must be given information regarding the non-reimbursable elements in advance.

6. Price revisions by profession

The medical devices sector covers several different professions, many of which are made up of small or very small businesses whose operations are more comparable to those of private service providers or cottage industries than those of companies carrying out research and industrial-scale

production. A large proportion of the tariffs and maximum selling prices applicable to the reimbursable services provided by these professions often goes towards salary costs.

In these cases, the issue surrounding tariffs is somewhat different than in the other medical device fields. In particular, the criteria provided in Article L. 162-38 of the Social Security Code regarding price setting (workload, income, business operations) are at the forefront.

Regarding the tariff-setting proposals it formulates and above all regarding the periodic review of tariffs, the committee feels it is important to adhere to two objectives:

- the tariff and price levels must be high enough to guarantee a continuous, uniform supply across the whole country and a quality level consistent with the service expected or provided that warranted inclusion on the list.

- these price levels should not however be such as to unduly favour unproductive operations, effectively turning the products of more competitive businesses into a bargain.

The committee has decided that the most effective way of achieving these objectives is by regular tariff revisions and has therefore proposed annual set tariff revision mechanisms in several cases, based on medium-term cost increases. This procedure goes hand-in-hand with regular monitoring of actual costs and profits, so that the fixed rates adopted can be altered if necessary, either at the committee's initiative or that of the trade organisations concerned.

APPENDIX 4: Table of clawback payment thresholds per pharmacotherapeutic class group for 2009-2011

For the 2009 financial year, the coefficient set in Article 17 a) of the framework agreement is 30%. For each class group, the percentages of the overall clawback payments based on turnover and on the amount made in excess of the threshold are set at 65% and 35%. respectively

NB: Products sold on by hospitals to outpatients are shown in italics, except for the following groups : "*L01 + L02 (anti-cancer agents and cytostatic hormone therapy) + L03A (growth factors) excluding Metvixia, Efudix and Copaxone"*, "'*J01 (systemic antibacterials) + J02A (systemic antimycotics) excluding Terbinafine + J03A (systemic sulphonamides) + J05B (antivirals excludingHIV antivirals) excluding J05B1 + Sebivo*" and "'*B02C and D (clotting factors) + Ceprotin and Protexel + J06 (serum and immunoglobulin) excluding Synagis*".

Group	2008 Sales in €K	2009 rate (K rate included = 1.4%)	2009 rate (K rate not included	2010 rate (K rate not included))	2011 rate (K rate not included)	2012 rate (K rate not included)
A02 (antacids and anti-flatulent agents) other than **A02B2**	117,413	1.4%	0.0%	0.0%	0.0%	0.0%
A02B2 (proton pump inhibitors)	851,517	-5.6%	-7.0%	-7.0%	-5.0%	-5.0%
A03 (antispasmodics, anticholinergics and gastro-intestinal sensorimotor modulators) + **Vogalene** *(including Prepulsid and Debridat injection*)	138,299	1.4%	0.0%	0.0%	0.0%	0.0%
A04 (antiemetics) **except Vogalene**	34,551	1.4%	0.0%	0.0%	0.0%	0.0%
A05A1 (bile therapy and cholecystokinin) **+ A05B** (hepatic protectors, lipotropics) **+ A06** (laxatives) including Relistor ₊ **A07** ((anti diarrhoeals) **except A07E + A09** (digestives including digestive enzymes)	196,228	1.4%	0.0%	0.0%	0.0%	0.0%
A05A2 (bile stone therapy) + **A07E** (intestinal anti-inflammatory agents) **+ Entocort (H02A2)**	65,582	3.0%	1.6%	0.0%	0.0%	0.0%
A10 (drugs used in diabetes) + **A08A** (anti-obesity preparations)	693,118	6.4%	5.0%	5.0%	4.0%	4.0%
A11 (vitamins) + **A12A** (calcium products) + **A12B** (potassium products) + **A12C2** (other mineral supplements) **C10B** (anti atheroma preparations of natural origin) **except calcium sorbisterit and Phosphoneuros** (including *un-alfa injection.*)	113,883	1.4%	0.0%	0.0%	0.0%	0.0%
A12C (mineral supplements) **+ A15** (appetite stimulants) **+ A16A** (other gastrointestinal products: Proglicem)	43,674	1.4%	0.0%	0.0%	0.0%	0.0%
B01A (anticoagulants, non-injectable) + **B01B** (anticoagulants, injectable: heparins) + **B01E** (direct thrombin inhibitors) + **B01X** (other anti-thrombotic agents **except Ceprotin and Protexel** (including *Orgaran*)	292,423	1.4%	0.0%	0.0%	0.0%	0.0%
B01C (anti-platelet agents) **except Xagrid**	585,234	1.4%	0.0%	-30.0%	-20.0%	0.0%
B02A and B (systemic antifibrinolytics and anticoagulant antagonists) + **B03** (anti-anaemic preparations) excluding B03C + **A14A1** (anabolic hormones, systemic) **+ Lederfoline, Elvorine and Folinoral** (including *Venofer*)	57,829	1.4%	0.0%	0.0%	0.0%	0.0%
B02C et D (clotting factors) **+ Ceprotin and Protexel + J06** (serum and immunoglobulin) **except Synagis**	700,095	7.4%	6.0%	6.0%	6.0%	6.0%
B03C (erythropoietin products including Retacrit)	349,140	1.4%	0.0%	0.0%	0.0%	0.0%
C01A + B + C (cardiac glycosides, anti-arrythmics and cardiac stimulants)	105,527	1.4%	0.0%	5.0%	0.0%	0.0%
C01D + E + X (coronary heart disease treatments) + **C02** (antihypertensives) + **C03** (diuretics) + **C07** (beta blockers) + **C08** (calcium channel blockers) + **Caduet**	1,045,075	1.0%	-0.4%	0.0%	0.0%	0.0%
C04 (vasodilators) + **N6D** (nootropics) + **Olmifon**	146,360	1.4%	0.0%	0.0%	0.0%	0.0%
C09 (agents acting on the renin-angiotensin system)	1,410,562	-0.6%	-2.0%	-7.0%	-5.0%	-3.0%
C10A (cholesterol and triglyceride regulating preparations) **+ C10C** (Lipid regulating drugs in combination)	1,195,066	0.4%	-1.0%	-7.0%	-2.0%	-5.0%
D (dermatologicals) + **Terbinafine** + **Metvixia + Efudix**	413,870	1.4%	0.0%	0.0%	0.0%	0.0%

Group	2008 Sales (in €K)	2009 rate (K rate included = 1.4%)	2009 rate (K rate not included)	2010 rate (K rate not included)	2011 rate (K rate not included)	2012 rate (K rate not included))
G01 (gynaecological anti-infectives) **+ Florgynal + G04A** (urinary antiseptics and anti-infectives)**+ Enoxor, Logiflox, Monoflocet, norfloxacin, Noroxin, Peflacine, single dose Peflacine and Uniflox**	68,713	1.4%	0.0%	0.0%	0.0%	0.0%
G02 (other gynaecologicals) excluding **Florgynal + G03** (ovulation inhibitors) **excluding G03B, G and J**	204,619	1.4%	0.0%	1.0%	0.0%	0.0%
G03B (androgens), **G04** (urologicals) **excluding G04A**	261,364	-1.6%	-3.0%	-3.0%	-3.0%	0.0%
G03G (gonadotrophins / ovulation stimulants) + **H01C1 and C3** (hypothalamic hormones) (including *Salvacyl*)	115,344	1.4%	0.0%	0.0%	0.0%	0.0%
H01A (ACTH) + **H01C2** (anti hGH antibodies) + **H02** (oral corticosteroids) **excluding Entocort** + **H04A, B and D** (calcitonins, glucagon and antidiuretic hormones) (inc *Minirin injection*)	175,301	0.4%	-1.0%	-2.0%	-1.0%	0.0%
H03 (thyroid therapy) *(including Proracyl*)	42,380	1.4%	0.0%	0.0%	0.0%	0.0%
H4C (growth hormones)	137,376	0.4%	-1.0%	-1.0%	-1.0%	-1.0%
J01 (systemic antibacterials) + **J02A** (systemic antimycotics) **excluding Terbinafine** + **J03A** (systemic sulphonamides) + **J05B** (antivirals excl. anti-HIV products) **excluding J05B1**	1,015,240	-1.6%	-3.0%	-2.0%	-2.0%	-2.0%
J05B1 (hepatitis antivirals) + **J05C** (HIV antiretrovirals) including Intelence **+ L03B1** (alpha interferons)	954,283	6.4%	5.0%	5.0%	5.0%	0.0%
J07 (vaccines) + **V01A** (allergy treatments) + **Synagis**	563,327	1.4%	0.0%	10.0%	0.0%	0.0%
K (solutions for hospital use) + **Nonan, Decan, Tracutil and Tracitrans**	42,345	6.4%	5.0%	0.0%	0.0%	0.0%
L01 + **L02** (anti-cancer agents and cytostatic hormone therapy) + **L03A** (growth factors) **excluding Metvixia Efudix and Copaxone**	1,925,621	3.4%	2.0%	1.0%	1.0%	1.0%
L03B2 (beta interferons) + **Copaxone**	234,633	1.4%	0.0%	0.0%	0.0%	0.0%
L04 (immunosuppressive agents) **excluding Raptiva**	197,515	1.4%	0.0%	0.0%	0.0%	0.0%
M01A1 (Anti-rheumatics, non-steroidal plain) **excluding Art50 and Zondar + M01A3** (Coxibs, plain) + **M04** (anti-gout preparations)	227,744	1.4%	0.0%	0.0%	0.0%	0.0%
M01A2 (antirheumatic, non-steroidal, combined)+ **M02** (topical antirheumatics and analgesics) + **M03** (muscle relaxants)	110,247	-1.6%	-3.0%	-1.0%	0.0%	0.0%
M01C (disease modifying anti-rheumatic agents) + **Acadione** + **Raptiva**	359,943	6.4%	5.0%	2.0%	0.0%	0.0%
M05B (Biphosphonates) **+ G03J** (Oestrogen receptor modulators) **+ Forsteo and Protelos**	394,339	2.4%	1.0%	1.0%	0.0%	0.0%
M05X (other musculo-skeletal products) + **Art 50** + **Zondar excluding Acadione and Protelos**	249,291	0.4%	-1.0%	-2.0%	-5.0%	0.0%
N01 (inc. ***Naropeine*** and *Versatis*)	40,701	1.4%	0.0%	0.0%	0.0%	0.0%
N02 (analgesics) **except Buprenorphine and Methadone + N07C** (antivertigo preparations)	1,018,137	1.4%	0.0%	0.0%	0.0%	0.0%
N03A (antiepileptics) *(inc Taloxa*)	293,533	1.4%	0.0%	0.0%	0.0%	0.0%
N04A (antiparkinson drugs) + **Adartrel**	111,508	1.4%	0.0%	0.0%	0.0%	0.0%
N05A1 (atypical antipsychotics)	324,925	-0.6%	-2.0%	-2.0%	-2.0%	-2.0%
N05A9 (conventional antipsychotics) + **N06A3** (mood regulators)	86,400	1.4%	0.0%	0.0%	0.0%	0.0%
N05B (hypnotics and sedatives) + **N05C** (tranquilisers)	189,807	1.4%	0.0%	0.0%	0.0%	0.0%
N06A (antidepressants) **excluding N06A3 and Levotonine**	472,850	-3.6%	-5.0%	-5.0%	-2.0%	0.0%
N06B (psychostimulants) + **N07E** (drugs used in alcohol dependence) + **N07F** (drugs used in opioid dependence) + **Rilutek, Levotonine, Buprenorphine and Methadone**	149,110	1.4%	0.0%	0.0%	0.0%	0.0%
N07D (anti-Alzheimer products)+ **Mestinon, Prostigmine** and **Mytelase**	250,673	1.4%	0.0%	0.0%	0.0%	0.0%

Group	2008 Sales (in €K)	2009 rate (K rate included = 1.4%)	2009 rate (K rate not included)	2010 rate (K rate not included)	2011 rate (K rate not included)	2012 rate (K rate not included))
P (antiparasitic agents) **+ J04** (antituberculosis and antileprotic drugs) (including *Eskazole, Lamprene and Notezine*)	19,403	1.4%	0.0%	0.0%	0.0%	0.0%
R01A1 + **A6** (nasal corticosteroids without anti-infectives and other topical nasal preparations) + **R06A** (systemic antihistamines)	327,756	-1.6%	-3.0%	-3.0%	-5.0%	-5.0%
R01A4 + **A7** + **A9** + **B** (nasal anti-infectives) + **R02** (throat decongestant preparations) **+ R05** (cough medicines) **+ R07** (other breathing aid products) **+ A01** (stomatology) **+ Pulmozyme**	155,857	0.4%	-1.0%	-1.0%	-1.0%	-1.0%
R03 (anti-asthma and COPD products)	981,334	0.4%	-1.0%	-1.0%	-3.0%	-3.0%
S01 (ophthalmologicals) **excluding S01E and S01P + S02** (otologicals)	128,327	1.4%	0.0%	0.0%	0.0%	0.0%
S01E (miotics and antiglaucoma preparations)	220,686	0.4%	-1.0%	-1.0%	-1.0%	-1.0%
S01P (ocular anti-neovascularisation products)	150,068	11.4%	10.0%	5.0%	0.0%	0.0%
T01 (diagnostic imaging) **+ T02X T02X** (other diagnostic tests*)* **+ Helikit**	148,098	3.4%	2.0%	0.0%	0.0%	0.0%
V03 (other therapeutic products) **excluding Lederfoline, Elvorine, Folinoral et Pulmozyme et Helikit + Mimpara, Phosphorous, Phosphoneuros and Sorbisterit calcium** *(inc Cardioxane, Uromitexan, Ferriprox, Fasturtec and Ethyol*)	82,051	1.4%	0.0%	0.0%	0.0%	0.0%
V06 (dietetic agents) + **V07** (other products)) **+ C05** (anti haemorrhoid and varicose vein preparations)	48,235	-3.6%	-5.0%	-5.0%	-2.0%	-2.0%
Z (orphan medicines)	666,249	1.4%	0.0%	0.0%	0.0%	0.0%
Total	**21,700,776**	**1.4%**	**0.0%**	**0.0%**	**0.0%**	**0.0%**

APPENDIX 5: PRICE AGREEMENTS AND PRO-FORMA CLAUSES

1. Price agreements for medicines

RIDER TO THE AGREEMENT OF .....
between the Comité économique des produits de santé (CEPS)
and *X*

Having regard to the Social Security Code, in particular Articles L 162-16-4 and L 162-17-4,
Having regard to Decree no 99-554 of 2 July 1999 amending the Social Security Code regarding the registration of medicines on the lists provided in Articles L. 162-17 of the Social Security Code and L. 618 of the Public Health Code and the setting of prices for such medicines,
Having regard to the ruling of 4 August 1987 regarding prices and markups on reimbursable medicines,
Having regard to the General Tax Code, in particular Article 281-8,
Having regard to the Public Health Code, in particular Articles L. 5123-1, L. 5121-8, L. 5121-13 and L. 5121-1,
Having regard to the multiannual agreement made on *dd/mm/yy* between the Comité économique des produits de santé (CEPS) and *X*;
The Comité économique des produits de santé (CEPS) and *X* now agree on the following provisions:

ARTICLE 1:

The prices stated in the table below shall be applicable as of the effective date of the decision.

Price registration or price change

Product	EphMRA/ ATC category	Manufacturer price ex VAT	Public price inc VAT	TFR (Fixed accountability tariff)	Effective date
CIP code, name, dose (of active ingredient), pharmaceutical form, packaging, (of company marketing the product)					Date of publication in the *Journal Officiel* or later date

ARTICLE II: (c.f. pro-forma clauses below)

ARTICLE III:

Appendix 3 to the above-mentioned agreement shall be amended in accordance with Article I.
Appendix 4 to the above-mentioned agreement shall be amended in accordance with Article II.

Done in Paris, on

First name, Surname
Position
Company *X*

First name, Surname
Chairman of the Comité économique
des produits de santé

2. Pro-forma clauses regarding medicines

2.1. Pro-forma posology clause

Article 2:

2.1. The price set in Article I (reference manufacturer price ex VAT: $PFHT_R$) is set on condition that the posology established ($Poso_n$) should be equal to or less than ……. (Reference posology: $Poso_R$).

2.2. The posology ($Poso_n$) shall be monitored every year, and on the first occasion, which shall be dd/mm/yy, it shall be monitored with reference to the most recent EPPM[26] published before this date. If the poslogy observed ($Poso_n$) is greater than the reference posology ($Poso_R$), the manufacturer price ex VAT as set in Article I shall be modified ($PFHT_{n+1}$) on the basis of the following formula:

$$PFHT_{n+1} = \frac{\text{Poso}_R}{\text{Poso}_n} \times PFHT_n$$

If there has already been one price change on the basis of this clause, a further price change may only be introduced on the basis of this clause if the posology observed is higher than the posology observed at the time of the first price change.
If ($Poso_n$ - $Poso_R$) / $Poso_R$ is less than *x* %, the $PFHT_n$ shall not be changed and the company shall instead owe a rebate (R_n) calculated according to the formula given in 2.3 herebelow.

2.3 If the poslogy observed ($Poso_n$) is greater than the reference posology ($Poso_R$), the company may also be liable to pay a rebate (R_n), calculated according to the following formula:

$$R_n = CAHT_n - (PFHT_{n+1} \times V_n)$$

where:

- $CAHT_n$ equals the sales figure established by GERS over the 12 months preceding the date given in 2.2 hereabove;
- V_n equals the sales volume of which GERS has been informed for the same period.

2.4. The company shall be notified of the sum of the rebate owing by CEPS, who will inform the relevant local URSSAF of the payment owing (Paris-RP URSSAF for the Ile de France regions and Lyon URSSAF for all other regions). The company shall pay the sum owing upon receipt of the contribution request from the relevant URSSAF office. The company shall inform CEPS by post of the date and actual sum of the payment.

(The sum of the rebate may be deducted by agreement from the sum used to work out the corresponding end-of-year clawback by pharmacotherapeutic class grouping owed by the company).

[26] Étude permanente de la prescription médicale (Ongoing medical prescription monitoring).

2.2. Pro-forma product range daily treatment cost clause

Article 1:

The initial listing prices (or price changes) given in the table below shall be applicable as of the date they are published in the *Journal Officiel* (or shall be effective as of *dd/mm/yy*).
Product

Product	**Category**	**Manufacturer price ex VAT**	**Public price inc VAT**
First listing – CIP code, product aaa, ...	……	€…,..	€…,..
First listing – CIP code, product bbb, …	……	€…,..	€…,..
Price change – CIP code, product ccc, …	……	€…,..	€…,..

Article 2:

2.1. The prices set in Article 1 are set on condition that the established daily treatment cost for the product range ($CTJG_n$), calculated for the range comprising aaa, bbb, ccc, …., should be less than or equal to € ---.--: the reference product range daily treatment cost ($CTJG_R$).

2.2. The $CTJG_n$ value shall be monitored every year (n) and the first monitoring shall cover the 12-months preceding dd/mm/yy. The value shall be calculated on the basis of the average yearly cost of the number of treatment days (NJT_n) and of the the posologies of each of the products mentioned in 2.1 hereabove which are included in the EPPM (IMS) data published before dd/mm/yy and the 12-month sales figure stated in the most recent GERS data published prior to this date.
$CTJG_n$ shall be calculated by dividing the sales figure for the whole range ($CAHTG_n$) as declared to GERS, by the number of days' treatment using products in the range ($NJTG_n$), or:

$$CTJG_C = CAHTG_n / NJTG_n$$

where $NJTG_n$ equals the sum of the number of days' treatment with each of the products in the range, or:

$$NJTG_n = \Sigma NJT_{in}$$

The number of days' treatment, NJT_{in} is equal to the number of tablets (or doses/units) sold for each product or product format (i) in the range divided by the corresponding posology (P_i) reported in the EPPM (IMS), or:

$$NJT_{in} = (number\ of\ units\ per\ pack\ x\ number\ of\ packs_i) / Poso_{in}$$

If $CTJG_C > CTJG_R$, the manufacturer price ex VAT of each of the products or product formats in the range mentioned in 2.1. hereabove shall be uniformly modified $(PFHT_{n+1})$ with the result that $PFHT_{n+1} = PFHT_n \times CTJG_R / CTJG_n$ and the company shall be liable for a clawback payment R_n, *where* $R_n = NJTG_n \times (CTJG_n - CTJG_R)$.

However, if $PFHT_{n+1} / PFHT_n > x\%$, no price reduction shall be made and the company shall still be liable to make a clawback payment.

2.3. Pro-forma unit volumes clause

Article 2

2.1. The price (manufacturer price ex VAT) mentioned in Article I (reference manufacturer price ex VAT: $PFHT_R$) is set on condition that the annual sales volume (V_n) shall be less than or equal to the reference sales volume (V_R).

2.2. The sales volume (V_n) shall be reported every year in the GERS data for month *M*, the first occasion being the GERS data published in month *M* of year *A*.

2.3 If the annual sales volume reported (V_n) is greater than the reference sales volume (V_R), the manfuacturer price ex VAT shall be modified ($PFHT_{n+1}$) according to the following formula:

$$PFHT_{n+1} = [V_R \times PFHT_n + (V_n - V_R) \times a \times PFHT_n] / V_n$$

$$= [1 + a \times (V_n - V_R) / V_n] \times PFHT_n \text{ where } 0 < a < 1.$$

In addition, the company will be liable for a clawback payment:

$$R_n = (V_n - V_R) \times a \times PFHT_n$$

2.4 However, if $PFHT_{n+1} / PFHT_n > x$ %, no price reduction shall be made and the company shall still be liable to make a clawback payment.

2.5 Subsequent to any price modification introduced pursuant to 2.2 hereabove, the current price in force ($PFHT_n$) shall only be reduced if the annual sales volume reported (V_{n+i}) is both higher than both V_R and than the sales volume which led to the previous price change (V_n).
If $V_{n+i} > V_n > V_R$, the company shall also be liable to pay a new clawback payment:

$$R_n = (V_{n+i} - V_n) \times a \times PFHT_n$$

2.6 The committee reserves the right to revise the price and the above-mentioned provisions in the event of an extension of the product's indications.

2.7 The company shall be notified of the sum of the rebate owing by CEPS, who will inform the relevant local URSSAF of the payment owing (Paris-RP URSSAF for the Ile de France regions and Lyon URSSAF for all other regions). The company shall pay the sum owing upon receipt of the contribution request from the relevant URSSAF office. The company shall inform CEPS by post of the date and actual sum of the payment.

2.3. Pro-forma pooled sales turnover clause

Article 2

2.1. The price (PFHT – manufacturer price ex VAT) mentioned in Article 1, (reference manufacturer price ex VAT: $PFHT_R$) is set on condition that the annual pre-tax turnover ($CAHT_n$) shall be less than or equal to the reference annual pre-tax turnover ($CAHT_R$).

2.2. The annual pre-tax turnover of the product range mentioned in Article 1 ($CAHT_{Xn}$) and the annual pre-tax turnover of this range and new proprietary products sharing the same indications ($CAHT_n$) shall be reported every year (n) in the GERS data for month *M*, the first occasion being the GERS data published in month *M* of year *A*.

2.3 On the basis of the turnover for one year (n), beyond a reference annual turnover ($CAHT_R$) for all the products mentioned in Article 1 and the new proprietary products sharing the same indications, the company shall be liable to pay a clawback payment:

$$R_{Xn} = (CAHT_{Xn} / CAHT_n) \times [(CAHT_n - CAHT_R) / PFHT_n] \times a \times PFHT_n \text{ where } 0 < a < 1$$
$$= (CAHT_{Xn} / CAHT_n) \times (CAHT_n - CAHT_R) \times a$$

where ($PFHT_n$) is the current manufacturer price ex VAT in force per tablet / mg / capsule, etc.
Furhtermore, the manufacturer price ex VAT per tablet / mg / capsule, etc. of the products mentioned in Article 1 shall be changed ($PFHT_{n+1}$) according to the following formula:

$$PFHT_{n+1} = ((CAHT_{Xn} - R_{Xn}) / CAHT_{Xn}) \times PFHT_n$$

2.4 However if $PFHT_{n+1} / PFHT_n > x$ %, no price reduction shall be made and the company shall still be liable to make a clawback payment.

2.5 Subsequent to any price modification introduced pursuant to 2.3 hereabove, the current price in force ($PFHT_n$) shall only be reduced if the turnvoer reported ($CAHT_{n+i}$) is higher than the turnover which led to the previous price change ($CAHT_n$).
If $CAHT_{n+i} > CAHT_n > CAHT_R$, the company shall also be liable to pay a new clawback payment:

$$R_{Xn+i} = (CAHT_{Xn+i} / CAHT_{n+i}) \times (CAHT_{n+i} - CAHT_n) \times a \text{ where } 0 < a < 1.$$

2.6 The committee reserves the right to revise the price and the above-mentioned provisions in the event of an extension of the product's indications.

2.7 The company shall be notified of the sum of the rebate owing by CEPS, who will inform the relevant local URSSAF of the payment owing (Paris-RP URSSAF for the Ile de France regions and Lyon URSSAF for all other regions). The company shall pay the sum owing upon receipt of the contribution request from the relevant URSSAF office. The company shall inform CEPS by post of the date and actual sum of the payment.

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3. Agreement regarding medical devices (including study clause)

This Agreement is made
between the Comité économique des produits de santé (CEPS)
and the company *(X)*

Having regard to the Social Security Code, in particular Articles L 165-2, L. 165-3and L. 165-4;
Having regard to the opinion of the Medical device and technology assessment committee (CEPP);
whereby the Comité économique des produits de santé (CEPS) and *(X)* agree on the following provisions:

Article 1: This agreement is made under the condition precedent that the decree relating to the registration of device(s) (*Y*) shall be signed by the relevant ministers. This agreement shall be effective as of the corresponding effective date of publication of the decree in the *Journal Officiel.*

Article 2: The tariffs and maximum public selling prices including VAT stated in the table below are set as follows:

Code	**Category**	**€Tarif inc VAT**	**€Max, public price inc VAT**
aaa, …	……	€…,..	€…,..
bbb, …	……	€…,..	€…,..
ccc, …	……	€…,..	€…,..

Article 3: (see pro-forma clauses herebelow)

Article 4: The company (*X*) undertakes to conduct and fund a study …. The aim of this study will be: …. The results of the study shall be sent to CNEDiMTS and to CEPS.

Paris, date

MM
Company *XXXX*

Chairman of the *Comité économique des produits de santé*

4. Pro-forma clause for medical devices

4.1. *Pro-forma unit volumes clause*

Article 3:

3.1 The company (*X*) undertakes to inform the committee every year, during the course of month *mm*, for the year finishing in the *mm* month, and for the first time during the month *mm*/*aaaa*, of the total number of devices (*Y*) that is has sold in France during the previous year.

3.2 If the number (*N*) of devices (*Y*) sold in the year exceeds a certain number (*n*), the prices/tariffs (*P*) stated in the decree, which are shown in Article 1 hereabove, shall be modified (P_M) on the basis of hte formulat:
$P_M = (a \times P) + [(1 - a) \times P \times (n / N)]$, where $0 < a < 1$
And the company shall be liable to pay a clawback payment (*R*) which shall be calculated according to the formula:
$R = (P_V - P_M) \times N$
where (P_V) is the current price of the device in question.
However if $P_M / P_V > x$ %, the price shall not be reduced but the company shall still be liable for the clawback payment (*R*).

3.3 Where there has already been one price reduction under the terms of paragraph 3.2 hereabove, no new price reduction may be introduced on the basis of paragraph 3.2, unless the number (*N'*) of devices (*Y*) sold established on this occasion is greater that the number (*N*) on which the previous reduction was based and if $P_M / P_V > x$ %.
If $N' > n$ and $P_V > P_M$, the company shall be liable to pay a clawback payment $R = (P_V - P_M) \times N'$.

3.4 The company shall be notified of the sum of the rebate owing by CEPS, who will inform the relevant local URSSAF of the payment owing (Paris-RP URSSAF for the Ile de France regions and Lyon URSSAF for all other regions). The company shall pay the sum owing upon receipt of the contribution request from the relevant URSSAF office. The company shall inform CEPS by post of the date and actual sum of the payment.

4.2. Pro-forma pooled sales turnover clause

Article 3:

3.1 The company (*X*) undertakes to inform the committee every year, together with all companies selling the devices (*Y*) in France, during the course of month *mm*, for the year finishing in the *mm* month, and for the first time during the month *mm*/*aaaa*, of the total number of devices (Y_x) that is has sold in France during the previous year.

3.2 On the basis of these declarations, the annual sales by company *(X)* of device (*Y*) and those by each of the companies selling (*Y*) in France shall be evaluated by multiplying the number of (*Y*) sold by the current LPPR tariffs in force, giving a theoretical annual turnover including VAT for each of the companies: $CATTTCy_x$ for company (*X*) and *CATTTCy* the sum of the theroetical annual turnovers including VAT of all companies selling (*Y*) in France.

If $CATTTCy > CATTTCy_{Ref1}$, the company shall be liable to pay a clawback payment, calculated according to the formulae in the table below:

CATTTC threshold (turnover after tax)	**Clawback payment owing**
If $CATTTCy \leq CATTTCy_{Ref2}$	$R_x = a \times (CATTTCy - CATTTCy_{Ref1}) \times (CATTTCy_x / CATTTCy)$ where $0 < a < 1$
If $CATTTCy > CATTTCy_{Ref2}$	$R_x = [a \times CATTTCy_{Ref1} + b \times (CATTTCy - CATTTCy_{Ref2})] \times (CATTTCy_x / CATTTCy)$ where $0 < a < b \leq 1$

Furthermore, if $CATTTCy > CATTTCy_{Ref2}$, the prices /tariffs (P_V) stated in the decree, as mentioned in Article 1 shall be changed (P_M) on the basis of hte formula: $P_M = [(CATTTC_y - R_x) / CATTTC_y] \times P_V$.

3.3 However if $P_M / P_V > x$ %, the price shall not be reduced but the company shall still be liable for the clawback payment (R_x).

3.4 In the event that a price reduction is implemented pursuant to 3.2 hereabove, the conditions of the agreement shall be revised.

3.5 The company shall be notified of the sum of the rebate owing by CEPS, who will inform the relevant local URSSAF of the payment owing (Paris-RP URSSAF for the Ile de France regions and Lyon URSSAF for all other regions). The company shall pay the sum owing upon receipt of the contribution request from the relevant URSSAF office. The company shall inform CEPS by post of the date and actual sum of the payment.

APPENDIX 6: COMMITTEE MEMBERS

1. Members of CEPS

Noël RENAUDIN, Chairman

1.1. Medicines section

Bernard TEISSEIRE, Vice-chairman

Representatives of the Director for Social Security, Ministry of Health and Sport:
Jean-Philippe VINQUANT, followed by Katia JULIENNE, Head, Healthcare Finance Department
Marine JEANTET, Deputy Head, Healthcare Finance Department
Lionel JOUBAUD, followed by Hedi BEN BRAHIM, Head, Healthcare Products Office,
Isabelle CHEINEY, Deputy Head, Healthcare Products Office,
Mourad SAM, Healthcare Products Office

Representatives of the Director General for Health, - Ministry of Health and Sport:
Catherine LEFRANC, Head, Healthcare Products Policy Department
Nadine DAVID, Head, Medicines office
Alexandre BARNA, Medicines office
Anne DE SAUNIERE, Medicines office

Representatives of the Director for Hospital Care and Treatment Structure – Ministry of Health and Sport
Yannick LE GUEN, Head, Department for healthcare establishment quality and operations
Paule KUJAS, Hospital Pharmacist, Deputy Head – Healthcare products cluster, Department for healthcare establishment quality and operations

Representatives of the Director General for Competition, Consumer affairs and Combating fraud – Ministry for the Economy, Industry and Employment:
Marie-Thérèse MARCHAND, Head, Health, Industry and Trade Department
Jean-Yves SAUSSOL, Head, Health office
Dominique MONAVON, followed by Nolwenn DELARUELLE-LAPRIE, Health office

Representatives of the Director General for Competition, Industry and Services - Ministry for the Economy, Industry and Employment:
Jean-Marc GROGNET, Officer, Department of Industry and Life sciences, Chemistry and Materials Technology
François LHOSTE, Financial services officer, Department of Industry and Life sciences, Chemistry and Materials Technology
Catherine TRENQUE, Deputy head, Department of Industry and Life sciences, Chemistry and Materials Technology

Representatives of national health insurance bodies appointed by the Director General of CNAMTS (national health insurance fund for employed workers)
Jean-Pierre ROBELET, Director, care provision
Jocelyn COURTOIS, Deputy Director and head of healthcare products department
Thierry DEMERENS, Medical Examiner, head of department and deputy head, healthcare products department
Martine PIGEON, Deputy Director

Representatives of national health insurance jointly appointed by the Director of the Caisse nationale du régime social des indépendants (national health insurance fund for self-employed workers) and the Director of the Caisse nationale de la mutualité sociale agricole (national health insurance fund for agricultural workers)
Brigitte HEULS, Deputy national Medical Examiner, Caisse nationale du RSI (self-employed workers' fund)
Hélène BOURDEL, Senior consulting pharmacist, Caisse nationale du RSI

Representative of the Union des organismes d'assurance complémentaire (union of top-up health insurance companies):
Martine STERN, Policy Officer
Sébastien TRINQUARD, Health Economist

Representative of the Minister for Research:
Isabelle DIAZ, Health department – Directorate General for Research and Innovation

1.2. Medical devices section

André TANTI, Vice-chairman

Representatives of the Director for Social Security – Ministry of Health and Sport:
Jean-Philippe VINQUANT, followed by Katia JULIENNE, Head, Healthcare Finance Department
Marine JEANTET, Deputy Head, Healthcare Finance Department
Lionel JOUBAUD, followed by Hedi BEN BRAHIM, Head, Healthcare Products Office,
Chrystelle GASTALDI-MENAGER, Healthcare Products office
Olivier VERNEY, Healthcare Products office

Representatives of the Director General for Health - Ministry of Health and Sport:
Catherine LEFRANC, Head, Healthcare Products Policy Department
Stéphan LUDOT, Head, Office of Medical Devices and other Healthcare Products
Joëlle SCHACHMANN, followed by Séverine BERGON Office of Medical Devices and other Healthcare Products

Representatives of the Directorate General for Competition, Consumer affairs and Combating fraud – Ministry for the Economy, Finance and Industry:
Marie-Thérèse MARCHAND, Head, Department of Health, Industry and Trade
Jean-Yves SAUSSOL Head, Health office
Daniel MILES, Health Office
Marie-Caroline FURON, Health Office

Representatives of the Director General for Competition, Industry and Services - Ministry for the Economy, Industry and Employment:
Jean-Marc GROGNET, Head, department of Industry and Life science, Chemistry and Materials Technology
Philippe PARMENTIER, Policy Officer, department of Industry and Life science, Chemistry and Materials Technology

Representatives of national health insurance bodies appointed by the Director General of CNAMTS (national health insurance fund for salaried workers):
Jean-Pierre ROBELET, Director, care provision
Jocelyn COURTOIS, Deputy Director and head of healthcare products department
Annie ARPIN-BARBIEUX, Medical Examiner and Head of Department
Monique STEIMLE, Officer for Economic Studies

Representatives of national health insurance jointly appointed by the Director of the Caisse nationale du régime social des indépendants (national health insurance fund for self-employed workers) and the Director of the Caisse nationale de la mutualité sociale agricole (national health insurance fund for agricultural workers):
Brigitte HEULS, Deputy national Medical Examiner, Caisse nationale du RSI (self-employed workers' fund)
Marie-Noëlle DEMATONS, Medical Examiner, followed by Hélène BOURDEL, Consultant Pharmacist and Head of Department, Caisse nationale du RSI (self-employed workers' health insurance fund)

Representative of top-up health insurance bodies:
Martine STERN, Policy Officer
Sébastien TRINQUARD, Economiste de la Santé

Representatives of the Director for Hospital Care and Treatment Structure – Ministry of Health and Sport
Yannick LE GUEN, Head, Department for healthcare establishment quality and operations
Anne L'HOSTIS, Chief Public Health Medical Examiner, Policy Officer

Representative of Minister for Research:
Régis BEUSCART, Health department – Directorate General for Research and Innovation

Representative of the Caisse nationale de solidarité pour l'autonomie (disabled living fund)
Annie RICHARD-LEBRUN, Director for disability support

Representative of the Directorate General for Social Action
Chantal ERAULT, Head, Disabled Living office, Disability Department

2. Committee rapporteurs

Alex ALINE,
Claire OGET-GENDRE,
Philippe LALANDE,
Régine LEMÉE-PECQUEUR,
Catherine PHILIPPE,
Michel ROUSSEAU,
Franck SUDON,
Bruno STALLA.

3. Details of people working for the committee

Name	Position	Phone number	Fax number	Email address
Dominique Babilotte	Recording price and reimbursement requests	01 40 56 46 84	01 40 56 71 79	dominique.babilotte@sante.gouv.fr
Anne-Marie Bouchard	Hospital medicines: following up applications and drawing up & publication of decisions in the *Journal Officiel*	01 40 56 60 70	01 40 56 71 79	anne-marie.bouchard@sante.gouv.fr
Ghislaine Brouard	Secretary to Chairman and Vice-chairmen	01 40 56 73 76	01 40 56 71 79	ghislaine.brouard@sante.gouv.fr
Marie-Josée Calvo	Secretary to medical devices section	01 40 56 69 07	01 40 56 71 79	marie-josee.calvo@sante.gouv.fr
Carine Ferretti	General rapporteur	01 40 56 49 51	01 40 56 71 79	carine.ferretti@sante.gouv.fr
Michèle Guillerm	Medical devices section	01 40 56 57 55	01 40 56 71 79	michele.guillerm@sante.gouv.fr
Sylvette Laplanche	General Secretary	01 40 56 46 95	01 40 56 71 79	sylvette.laplanche@sante.gouv.fr
Yvan Le Manach	Secretary to the medicines section	01 40 56 69 51	01 40 56 71 79	yvan.lemanach@sante.gouv.fr
Marie Lucet	Drawing up & publication of decrees, decisions and opinions in the *Journal Officiel* – Medicines	01 40 56 44 27	01 40 56 71 79	marie.lucet@sante.gouv.fr
Sylvie Marteau	Decrees, decisions and opinions – Medicines	01 40 56 53 70	01 40 56 71 79	sylvie.marteau@sante.gouv.fr
Claire Oget-Gendre	Deputy General Secretary, in charge of the medical devices section	01 40 56 45 60	01 40 56 71 79	claire.oget-gendre@sante.gouv.fr
Anne Thomine-Demazures	Administration of databases and electronic documents	01 40 56 53 46	01 40 56 71 79	anne.thomine-desmazures@sante.gouv.fr
Christophe Trémoureux	Medical devices	01 40 56 71 63	01 40 56 71 79	christophe.tremoureux@sante.gouv.fr

4. Declarations of interest

	Type of interest			
Name (section)	***Employment contract***	***Paid work (participation in clinical trials, studies, consultations, research, etc.)***	***Ownership of company shares***	***Other declared interests***
Members of the committee and persons attending committee meetings				
CEPS				
Noël RENAUDIN	none	none	none	none
Bernard TEISSEIRE (M[27])	none	none	none	none
André TANTI (MD)	none	none	none	none
Sylvette LAPLANCHE	none	none	none	none
Claire OGET-GENDRE (MD)	none	none	none	none
Christophe TREMOUREUX (MD)	none	none	none	none
Carine FERRETTI	none	none	none	none
DSS				
Jean-Philippe VINQUANT	none	none	none	none
Katia JULIENNE	none	none	none	none
Marine JEANTET	none	none	none	none
Lionel JOUBAUD	none	none	none	none
Hedi BEN BRAHIM	none	none	none	none
Isabelle CHEINEY (M)	none	none	none	none
Chrystelle GASTALDI-MENAGER (MD)	none	none	none	none
Mourad SAM (M)	none	none	none	none
Olivier VERNEY (MD)	none	none	none	none
DGS				
Catherine LEFRANC	none	none	none	none
Stéphan LUDOT (MD)	none	none	none	none
Nadine DAVID (M)	none	none	none	none
Alexandre BARNA (M)	none	none	none	none
Anne DE SAUNIERE (M)	none	none	none	none
Joëlle SCHACHMANN (MD)	none	none	none	none
Séverine BERGON (MD)	none	none	none	none
DHOS				
Yannick LE GUEN	none	none	none	none
Anne L'HOSTIS (MD)	none	none	none	none
Paule KUJAS (M)	none	none	none	none
DGCCRF				
Marie-Thérèse MARCHAND	none	none	none	none
Jean-Yves SAUSSOL	none	none	none	none
Nolwenn DELARUELLE-LAPRIE (M)	none	none	none	none
Dominique MONAVON (M)	none	none	none	none
Daniel MILES (MD)	none	none	none	none
Marie-Caroline FURON (MD)	none	none	none	none

[27] Key: M = Medicines; MD = Medical devices

	Type of interest			
Name (section)	***Employment contract***	***Paid work (participation in clinical trials, studies, consultations, research, etc.)***	***Ownership of company shares***	***Other declared interests***
Directorate general for competition, industry and services				
Jean-Marc GROGNET	none	none	none	none
François LHOSTE (M)	none	none	none	Daughter-in-law working in the pharmaceutical industry
Philippe PARMENTIER (MD)	none	none	none	none
Catherine TRENQUE (M)	none	none	none	none
Assurance maladie obligatoire (mandatory national health Insurance)				
Jean-Pierre ROBELET	none	none	none	none
Monique WEBER	none	none	none	none
Jocelyn COURTOIS	none	none	none	none
Thierry DEMERENS	none	none	none	Sister and brother-in-law working n the pharmaceutical industry
Martine PIGEON (M)	none	none	none	Daughter-in-law working in the pharmaceutical industry
Monique STEIMLE (MD)	none	none	none	none
Annie ARPIN-BARBIEUX (MD)	none	none	none	none
Brigitte HEULS	none	none	none	none
Marie-Noëlle DEMATONS (MD)	none	none	none	none
Hélène BOURDEL (M)	none	none	none	none
Caroline BOULANGER (M)	none	none	none	none
Ministry of Research – Directorate General for Research and Innovation				
Isabelle DIAZ (M)	none	none	none	none
Régis BEUSCART (MD)	none	none	none	none
UNOCAM				
Martine STERN	none	none	none	none
Sébastien TRINQUARD	none	none	none	none
Directorate General for Social Action				
Chantal ERAULT	none	none	none	none
Caisse nationale de solidarité pour l'autonomie (disabled living fund)				
Annie RICHART-LEBRUN	none	none	none	none
CEPS rapporteurs				
Alex ALINE	none	none	none	none
Claire OGET-GENDRE	none	none	none	none
Philippe LALANDE	none	none	none	none
Régine LEMEE-PECQUEUR	none	none	none	none
Catherine PHILIPPE	none	none	none	none
Michel ROUSSEAU	none	none	none	none
Franck SUDON	none	none	none	none
Bruno STALLA	none	none	none	none

APPENDIX 7: Glossary of acronyms and abbreviations

AFSSAPS: Agence française de sécurité sanitaire des produits de santé - French healthcare products regulatory agency
AMM: Autorisation de mise sur le marché – marketing authorisation
AMO: Assurance maladie obligatoire – compulsory health insurance
ASA: Amélioration du service attendu – improvement in expected service
ASMR: Amélioration du service médical rendu – added medical benefit
ASR: Amélioration du service rendu – improvement in service provided
ATIH: Agence technique de l'information sur l'hospitalisation - Technical hospital information agency
ATU: Autorisation temporaire d'utilisation – temporary authorisation for use

CEESP: Commission évaluation économique et de santé publique – economic evaluation and public health committee
CEPP: Commission d'évaluation des produits et prestations – medical device and service assessment committee
CEPS: Comité économique des produits de santé – healthcare products pricing committee
CNAMTS: Caisse nationale d'assurance maladie des travailleurs salariés – national employed workers' health insurance fund
CNEDiMTS: Commission nationale d'évaluation des dispositifs médicaux et des technologies de santé – national medical device and health technologies assessment committee (formerly CEPP: *Decree n°2009-1088 of 02 September 2009*)
CSIS: Conseil stratégique des industries de santé – Health industries strategic council
CSP: Code de la Santé publique – Public Health code
CSS: Code de la Sécurité sociale – Social Secuirty Code

DGCCRF: Direction générale de la concurrence, de la consommation et de la répression des fraudes - Directorate General for Competition, Consumer affairs and Combating fraud
DGS: Direction générale de la santé – Directorate General for Health
DHOS: Direction de l'hospitalisation et de l'organisation des soins, devenue direction générale de l'offre de soins (DGOS) - Directorate for Hospital Care and Treatment Structure, now the Directorate General for Care Provision
DSS: Direction de la sécurité sociale – Directorate for Social Security

GAO: grand appareillage orthopédique - Large orthotic and prosthetic devices
GERS : Groupement pour l'élaboration et la réalisation de statistiques - an economic interest group of pharmaceutical companies which produces market statistics
GHS: Groupe homogène de séjours – standard hospital stay group (similar to diagnosis-related group)

HAS: Haute Autorité de Santé – the "High Health Authority"

LEEM: Les entreprises du médicament – the pharmaceutical companies' representative body
LFSS: Loi de financement de la Sécurité sociale – the annual social security funding act
LPPR: Liste des produits et des prestations remboursables – reimbursable medical device and services list

MIGAC: Mission d'intérêt général et d'aide à la contractualisation –funding for work in the "general interest" and for implementing contracts with regional health agencies
MINEFI: Ministère de l'Economie des Finances et de l'Industrie – Ministry for the Economy, Finance and Industry
MSA: Mutualité sociale agricole – a mutual health insurance fund for agricultural workers

ONDAM: Objectif National Dépenses de l'Assurance Maladie - the target annual national health insurance budget

RSI: Régime Social des Indépendants – self-employed workers' health insurance plan

SMR: Service médical rendu – medical service rendered (used in assessment of medical devices and services)
SNITEM: Syndicat national de l'industrie des technologies médicales – national medical technologies industry trade organisation

TAA-T2A: Tarification à l'activité – activity-based funding model
TFR: Tarif forfaitaire de responsabilité – "fixed accountability tariff"

UCD: Unité commune de dispensation - common dispensing unit
UFAT: Union des fabricants d'aides techniques – technical medical aid manfuacturers' union
UFOP: Union française des orthoprothésistes – French union of orthotic and prosthetic device manufacturers
UNCAM: Union nationale des caisses d'assurance maladie – national union of health insurance funds
UNOCAM: Union nationale des organismes complémentaires d'assurance maladie – national union of top-up health insurance organisations (FFSA, FNMF and CTIP)
URSSAF: Union de recouvrement des cotisations de Sécurité sociale et d'allocations familiales – social security contribution collecting body

VPH: véhicules pour personnes handicapées – mobility equipment