COMITE ECONOMIQUE DES PRODUITS DE SANTE

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HEALTHCARE PRODUCTS PRICING COMMITTEE

ANNUAL REPORT 2008

30 July 2009

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Under the terms of the Social Security Code, Article D. 162-2-4, the *Comité économique des produits de santé*, CEPS (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 2008.

Part one deals with medicines, looking first at the medicines market in 2008 (Chapter I), followed by regulation and agreements between CEPS and the pharmaceutical companies (Chapter II) and price setting (Chapter III).

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

PART ONE - MEDICINES

CHAPTER I – REIMBURSABLE MEDICINE SALES AND EXPENDITURE IN 2008

1. General market trends

In 2008, sales of reimbursable medicines by community pharmacies or taken care of through the hospital system, expressed in manufacturer's price ex VAT, totalled €24.4 billion, a 2.8 % increase on the previous year, following increases of 3.9 % in 2007 and 1.8 %, 5 % and 6.9 % in 2006, 2005 and 2004 respectively.

In the first instance, this indicates that aside from the factor of the unpredictable residual stock levels of generics held by pharmacies at the end of each accounting year, which may explain why the growth rate in their yearly purchases varies by half a percentage point more or less, the overall pattern of growth has slowed compared with the situation pre-2005. Over the five years 2000 to 2004, medicine sales rose by an average of 6.9 % per year. Over the last four years, the average rise has been 3.3%.

The regulatory measures begun in 2004 under the national health insurance reform have certainly contributed in part to this result, through each of their components: price management, increasing substitution and expenditure control requirements of the medical profession.

However, this slower growth is also largely attributable to the changes that have occurred over this period in the makeup of the medicines market, which are likely to last for the long term. There seems to be little room for further expansion in the major growth categories of the last few decades, during which genuine innovations providing potential benefits to large target groups created a strong substitution effect. Any growth in these categories will be at the margins and of course the territory is now open to expansion of generics or cheaper equivalent treatments. This applies in particular, though not exclusively, to treatments for hypertension, hypercholesterolemia, depression, asthma and gastro-intestinal disorders.

There are certainly still many areas of unmet need, but the discovery of medicines to meet these needs is proving an arduous task, added to which, when the research does have positive outcomes, the groups that stand to benefit from these are so small that even at very high prices, these new products generally represent very modest growth potential in the medium term.

The new situation also confirms that in a country such as France which has a universal health insurance system and complete freedom of prescription, advances made in access to care cannot be expected to make any significant or quick contribution to growth in sales. It is also a recognised fact that the ageing of the population has the overall effect of slowing down rather than boosting consumption of treatments. Therefore the only possibility for growth lies in the arrival of innovative medicines.

The 2008 financial year provides a striking illustration of this last point. Total sales rose by approximately €600M over the financial year. But over two thirds of this overall growth was accounted for by the growth in sales of just three recently authorised medicines: an anti-cancer drug, a treatment for age-related macular degeneration and a human papillomavirus vaccine. However, what is more significant is that since these three medicines are aimed at very specific groups, their growth will plateau out relatively soon and in all likelihood, their annual growth rate for 2009 will be zero.

The results would seem to show, therefore, that aside from any unpredictable and time-limited contribution to growth by certain major new high-potential products, the medicines market is reaching a fairly stable pattern, with the influx of generics and expenditure control more or less balancing out market authorisations of new products with a limited financial impact and what remains of the substitution effect in the traditional drug categories.

2. Sales of medicines covered by national health insurance

As mentioned above, sales of these medicines totalled €24.4 billion in 2008. This figure can be estimated by looking at the sales volumes declared by the pharmaceutical companies in their tax declarations to AFSSAPS[1], though these are not exhaustive [medicines under provisional authorisations (ATU) and some orphan medicines are not declared] and they include medicines exported under what the countries have agreed to call 'parallel trade'. To establish the figure by looking at purchases is a complex process in that overall expenditure is broken down according to several different categories and each of these may or may not involve direct discounts.

In order to make the calculations clearer, therefore, and to substantiate the estimates it has put forward, the committee felt it would be useful to draw up the table presented below, which shows 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 method.

It should be noted that these figures cannot be matched directly against the actual refunds paid out by the health insurance system, mainly due to the time difference between the observation period covering sales to pharmacies and hospitals and the accounting period in which the refunds are actually paid out.

[1] AFSSAPS = Agence française de securité sanitaire des produits de santé, the French medicines and healthcare products regulatory agency.
[2] ONDAM = Objectif national de dépenses de l'assurance maladie – the target annual national health insurance budget.

Figure 1: All medicines sales covered by the health insurance system in 2008, by type of purchaser, distribution circuit, ONDAM scope or reimbursement method (in €bn)

<table>
<tr>
<td rowspan="2">Community pharmacy purchases
(source: GERS ville[3])
18.950</td>
<td>Community purchases excluding dual circuit
(source: GERS ville)

18.332</td>
<td rowspan="3">ONDAM community + outpatient medicines
(source: GERS ville + CEPS estimate)

20.150</td>
<td rowspan="2">Community purchases including dual circuit
(source: GERS)

18.603</td>
</tr>
<tr>
<td>Dual circuit
(source: GERS ville + company declarations to CEPS of outpatient medicine sales)

0.952</td>
</tr>
<tr>
<td rowspan="4">Hospital purchases
(estimated by deduction)

5.450</td>
<td rowspan="4">Hospital purchases excluding dual circuit
(estimated by deduction)

5.116</td>
<td rowspan="2">Medicines refunded on top of T2A
(CEPS estimate)

2.400</td>
<td>Outpatient sales
(company declaration to CEPS via GERS)

2.371</td>
</tr>
<tr>
<td>All non-T2A
(sales volume estimate, source: GERS hôpital, CEPS tariffs; CEPS discount rate calculations, source: ATIH[4])

0.757</td>
</tr>
<tr>
<td>Medicines funded under MIGAC[5]
0.054</td>
<td>MIGAC

0.054</td>
</tr>
<tr>
<td>Medicines funded under GHS[6]
(CEPS estimate)

1.800</td>
<td>GHS
(CEPS estimate)
1.800

Orphan drugs
(community, source: GERS; hospital,
source: outpatient medicine declarations; source: c.f. "all non-T2A" for non-T2A)

0.815</td>
</tr>
<tr>
<td>24.4</td>
<td>24.4</td>
<td>24.4</td>
<td>24.4</td>
</tr>
</table>

[3] GERS = Groupement pour l'Élaboration et la Réalisation de Statistiques - an economic interest group of pharmaceutical companies which produces market statistics; GERS ville - statistics on sales to community pharmacies; GERS hôpital - statistics on sales to hospital pharmacies.
[4] ATIH = Agence Technique de l'information sur l'Hospitalisation, the Hospital information agency.
[5] MIGAC = Missions d'Intérêt Général et d'Aide à la Contractualisation - a hospital funding heading on top of general hospitalisation costs.
[6] GHS = Groupes homogènes de séjour – patient groupings similar to diagnosis-related groups.

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

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

In 2008, community pharmacy sales of reimbursable medicines totalled 18.95 billion euros in manufacturer's price ex VAT (see Table 1). Sales growth in this category alone was up 0.8% in 2008, a similar rate to that of 2006 and significantly lower than that of 2007 (+3.8% compared with 2006). This slower growth has occurred in spite of the emergence of high-potential new medicines. Expressed as public price inc VAT, these sales are actually down 0.3% in 2008 compared with 2007.

Table 1: Growth of community pharmacy sales of reimbursable medicines, 2007-2008

	Sales in manufacturer's price ex VAT (€bn)	Sales in public price inc VAT (€bn)
2007	18.79	26.61
2008	18.95	26.53
Growth	0.8%	-0.3%

Source: GERS community pharmacy sales data, CEPS data processing.

Price, pack and substitution effects

Growth in unit prices of medicines already on the market in 2007 was -2.2%. This downward price effect, which is comparable to that of 2007, is a reflection of the committee's action on prices and clearly illustrates the effect of the measures described in Chapter III, 2 below.

Much of the strong downward pack effect (almost 3 percentage points) can be explained by the removal of medicines from the reimbursable lists at the beginning of the year, especially in relation to venotonic drugs. The increased market share of large pack sizes also contributed 1 percentage point to this effect. If the effect of these two items is cancelled out, the pack effect on growth is still negative by one point. The introduction of deductions on refunds paid to patients (*franchise*) and progress in UNCAM's cost control requirements of the medical profession may both explain this negative trend.

The resulting effect is a substitution effect which reflects the strong bias (8.3%) of the sales figure towards the more expensive formats. However, it should be noted that this effect is calculated as the balance of growth minus price effect minus pack effect and therefore at a constant overall growth figure, the value will be pushed down if the pack effect is inflated. If the pack effect elements that are linked to specific circumstances are removed, the value works out at approximately 5.3%, which is in the same region as the previous years' figures.

Table 2: Breakdown of growth in pre-tax community pharmacy sales

Year	Price effect	Pack effect	Substitution 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%

Sources: GERS community pharmacy data, DSS/6B data processing (excluding cancelling the effect of medicines removed from the reimbursable lists and excluding correction for large pack formats).

Average price of medicines sold in community pharmacies

The price of medicines sold in community pharmacies is the average manufacturer's price ex VAT of the packs sold. It is equivalent to the annual sales figure for all reimbursable medicines divided by the number of packs sold that year. The increase in this price is a result of the substitution effect described above.

It reflects the slide in consumption towards new, higher-priced drugs. In 2008, the increase in this average price was strongly influenced by the two circumstances mentioned above in connection with the pack effect. The average price of medicines whose refund status was reclassified at the beginning of the year was less than €2.00, far lower than the average market price. By removing these medicines from the reimbursable list, the average price of medicines still on the list automatically rose. In the same way, replacing three boxes of 30 tablets with one box of 90 which is three times more expensive has also raised the average price of the packs sold. In the therapeutic groups concerned, large packs accounted for approximately 2 % of all packs sold in 2007 and almost 7 % of those sold in 2008. This substitution led to a 10% increase in average pack price in these groups in 2008.

The average pack price increased by 5.9 % overall in relation to 2007, rising to €7.49 in 2008 (see Table 3).

Table 3: Growth in average pack price and distribution markup on reimbursable medicines sold

	2004	2005	2006	2007	2008
Total sales ex VAT (€bn)	16.82	17.97	18.10	18.79	18.95
Total sales inc VAT (€bn)	24.31	25.83	25.83	26.61	26.53
Number of packs (in millions)	2 724	2 817	2 658	2 656	2 529
Average manufacturer price ex VAT (€)	6.18	6.38	6.81	7.08	7.49
Growth / year n-1	*7.40%*	*3.20%*	*6.70%*	*3.89%*	*5.90%*
Average public price inc VAT (€)	8.93	9.17	9.72	10.02	10.49
Growth / year n-1	*6.10%*	*2.70%*	*6.00%*	*3.05%*	*4.73%*
Average markup (€)	2.57	2.60	2.71	2.74	2.78
Growth / year n-1	*2.80%*	*1.20%*	*4.10%*	*1.10%*	*1.72%*
Markup rate	41.59%	40.75%	39.79%	38.70%	37.13%

Sources: GERS community pharmacy sales data, CEPS data processing.

The increase in the average price of generics was lower than in 2007. Their average pack price was €3.72 in 2008 as opposed to €3.65 in 2007: an increase of 2%.

Table 4: Prices and distribution markups of medicines on the substitution list and those not on the list in 2008

Market	Average manufacturer price (AMP) ex VAT	Average public price inc VAT	Average markup[1]	Markup rate[2]
Generics	3.72 €	6.17 €	2.32	62.2%
Original drugs	6.77 €	9.77 €	2.80	41.4%
Whole substitution list	4.61 €	7.22 €	2.46	53.3%
Non-substitution list	8.79 €	11.96 €	2.93	33.3%

Sources: GERS community pharmacy sales data, CEPS data processing.

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.

The average official markup was 62% on generics, compared with 41% on original drugs and 33% on other reimbursable medicines. The size of this discrepancy is not only due to the fact that the markup on generics is based on the actual value of the markup on the original drug, which is more

than twice as expensive, but also to the sliding scale of markup rates, as the prices of drugs which are still under patent are usually above the threshold of the lower markup regions.

As we see, the distribution markup rate has fallen again. Even though, in contrast with this drop, the average markup on medicine packs has increased (+1.72% to €2.78), if we bear in mind that the number of packs itself has fallen by almost 5%, the result is a decrease of almost 3 percentage points in the official markup earned by wholesalers and pharmacies. The wholesalers' share of this decrease is proportionally much greater, following the decree of 3 March 2008 which changed the rate of the first manufacturer price bracket and introduced a ceiling of €400 for the third bracket. It is also true that at the same time, the pharmacies' income has been significantly boosted by markups on non-reimbursable medicines, sales of which have gone up by 16%. Finally, it seems that the reduction in the pharmacies' extra profits implemented at the beginning of 2008 (c.f. Chapter III, 2 below) has had nothing like the results that were anticipated and still provides a significant source of income for pharmacies.

Market share of generics

In December 2008, generics accounted for 76.9% of medicines listed in the official AFSSAPS substitution list of 21/01/2009. In terms of total sales of reimbursable medicines by community pharmacies, generics accounted for 10.9% of sales before VAT and 21.9% of packs sold. Sales of generics in 2008 totalled €2.1bn, an increase of 7.1% on the figure for 2007.

The target substitution rate set for 2008 in the UNCAM/Pharmacists agreement was 82.9% of medicines listed in the substitution list in force on 30 June 2008. The share of generics in the overall sales volume in December 2008, calculated on the basis of GERS data, was 83.7% of medicines from the substitution list of 30 June 2008. However, this figure cannot be compared exactly with the target set by the UNCAM/Pharmacists agreement, as the data collected by GERS also reflects stockbuilding. By contrast, CNAMTS[7] data shows a tendency towards stagnation in the proportion of generics sold, albeit at a high level: at the end of December 2008, the share of generics in the official substitution list stood at 82%.

Analysis of growth by pharmacotherapeutic group

In 2008, vaccines were the largest contributor to growth in pre-tax community pharmacy sales of reimbursable medicines (see Table 5). The cervical cancer vaccine Gardasil alone accounted for almost the whole of this growth. The ophthalmic drug Lucentis, indicated in the treatment of age-related macular degeneration, had a comparable effect on sales in its category. Anticancer drugs are still among the top groups contributing outright to overall growth in sales, but this time at a much slower rate of 3%.

Table 5: Top five groups contributing to sales growth in 2008

Group	Pre-tax sales in 2007 (in €M)	Pre-tax sales in 2008 (in €M)	Growth (in €M)	Growth rate
Vaccines and allergy treatments	399	538	139	35%
Sartans and ACE inhibitors	1,304	1,411	107	8%
Anticancer drugs	2,154	2,229	75	3%
AMD treatments	79	150	71	91%
Disease-modifying antirheumatic drugs	289	360	71	25%

Sources: GERS community pharmacy sales data, CEPS data processing.

These high growth effects were counterbalanced by the net decrease in other categories (see Table 6). Venotonics were reclassified on 1 January 2008 and this will be the last time they appear in these

[7] CNAMTS = Caisse nationale de l'assurance maladie des travailleurs salariés: National Health Insurance Fund for Salaried Workers.

categories. Sales of proton pump inhibitors stabilised following the action by UNCAM, the lower value being due to the price reduction on Inexium and to lansoprazole going off-patent. Inroads made by generics, in particular generic amlodipine substitutes, explain the growth trend for anti-hypertensive drugs. And erythropoietins were affected by a price reduction at the end of 2007 and were held back by new recommendations, which led to a pronounced drop in growth.

Table 6: Top five groups contributing to downward growth in 2008:

Group	Pre-tax sales in 2007 (in €M)	Pre-tax sales in 2008 (in €M)	Growth (in €M)	Growth rate
Venotonics	214	14	-200	-84%
Proton pump inhibitors	942	852	-90	-10%
Anti-infective drugs excluding HIV treatments	908	841	-67	-7%
Anti-hypertensive drugs excluding sartans and ACE inhibitors	1,094	1,047	-47	-4%
Erythropoietins	393	349	-44	-11%

Sources: GERS community pharmacy sales data, CEPS data processing.

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 they were actually issued to patients.

Since medicines issued to outpatients are covered 100% by national health insurance, the sales figures for these medicines can be estimated by taking the refunds paid out by the *régime général* [general health insurance plan] and extrapolating these to refunds under all the mandatory plans, after deducting VAT and an estimated figure for the outpatient medicines markup[8].

However, as indicated above, since the dates on which the outpatient sales are claimed back from and accounted for by national health insurance can differ widely from the actual dates on which the medicines are sold, the committee uses various cross-checking methods to estimate these totals. Actual reimbursable outpatient medicine sales in 2008 are estimated at €1.2bn, €340M of which were of "dual circuit" medicines.

This figure is approximately 5% higher than in 2007.

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 €952M in 2008, representing a 7.4% increase in relation to 2007 (see Table 7).

Over one third of dual circuit medicines are sold by hospital pharmacies.

Table 7: Growth in dual circuit sales 2007-2008

	2007	2008	Growth
Sales in manufacturer price ex VAT (€M)	887	952	7.4%
Proportion of sales by hospitals	37%	35%	-6.9%

Source: GERS community pharmacy sales data and tax declarations of outpatient sales; CEPS data processing.

[8] To do this, we apply the key determined by the Social Security Department for extrapolating from the general plan to all the mandatory plans, based on accounting information which is in turn based on estimated expenditure.

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

The overall sales figure for products purchased by healthcare establishments for inpatients (working on the assumption for the sake of simplicity that all purchases of dual circuit medicines by hospital pharmacies are actually issued), totalled €4.254B[9] in 2008. This figure is 8% higher in relation to 2007. Pharmaceutical companies are free to set their own prices for medicines under provisional authorisations (ATU), however these medicines represent a tiny proportion (approx 1%) of this sales total. Over 40% of medicines used in hospitals are funded under GHS (*Groupes Homogènes de Séjour*) tariffs. These tariffs are set on the basis of public procurement rules and therefore CEPS is not involved in setting them. The totals for purchases under this heading do not vary widely from one year to the next.

However, the largest portion of the sales figure, which is also the most variable, is taken up by medicines which are funded on top of general hospitalisation costs[10] and these are subject to an "accountability tariff" (*Tarif de responsabilité*) (see Appendix 1: Framework Agreement, 2.2).

2.2.1. *Medicines funded on top of general hospitalisation costs*

Estimated sales of these medicines in 2008 totalled approximately €2.4bn, representing an increase of almost 16% on 2007.

No direct records are kept in relation to this figure. 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 issued to inpatients and those issued to outpatients and claimed back from national health insurance.
- GERS data: suppliers' sales to healthcare establishments, broken down by UCD (common dispensing units) code. The tariffs set by CEPS[11] can be applied to these volumes to obtain a theoretical figure, though with the same proviso regarding comprehensiveness as for the tax declaration figures.
- ATIH[12] data covers all medicines funded on top of GHS funding, but only for healthcare establishments which were previously under the blanket grant system. This information covers the total for purchases at actual prices and volumes costed at the accountability tariffs.
- data on refunds paid out by the national health insurance general plan (*régime général*), from which VAT needs to be deducted (see Table 8).

[9] Source: Provisional AFSSAPS data as at mid-June 2009, 2008 tax declaration including an estimate for some declarations which have yet to be submitted.
[10] Also known as medicines funded 'on top of T2A' or 'on top of GHS' [T2A = Tarification à l'Activité, or activity-based funding].
[11] The *tarifs de responsabilité* for medicinal products covered by national health insurance on top of T2A 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 national health insurance are worked out on the basis of the accountability tariffs.
[12] ATIH = Agence Technique de l'information sur l'Hospitalisation, the 'Hospital Information Agency'.

Table 8: Growth in expenditure on listed medicines funded on top of T2A

	2006	2007		2008	
	Totals (in €M)	Totals (in €M)	Growth rate	Totals (in €M)	Growth rate
Establishments formerly on blanket grants	1,338	1,575	18%	1,850	17%
Private establishments (formerly under OQN[13] system)	447	500	12%	550	10.0%
Total	1,785	2,075	16%	2,400	16.0%

Scope: General health insurance plan (inc. local mutual health insurance) for whole of France.
Source: PMSI (ATIH medical information system) for former blanket allocation establishments and Erasme V1 for private establishments

2.2.2. *Medicines covered by Provisional Authorisations*

In addition to the funding directly based on the activities carried out, "MIGAC" funds are available for 'general interest missions' which healthcare establishments carry out and to support them 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 the MIGAC heading. In 2008, these funds totalled €54M, representing a 1.1% drop compared with 2007.

2.2.3. *Medicines funded under the GHS heading*

The forecast made in the 2007 report that the funds devoted to medicines financed under the GHS heading would remain stable appears to have been realistic. On the basis of the available data and previous estimates, we can deduce that sales of medicines financed under GHS totalled around €1.8bn.

2.3. *Orphan medicines*

Sales of orphan medicines accounted for over €800M of the 2008 sales volumes. Hospitals account for two thirds of this figure. Growth in sales of these medicines has been extremely fast, exceeding 30% between 2007 and 2008.

3. From reimbursable sales to actual reimbursements

Total sales including VAT of reimbursable medicines by community pharmacies accounted for €26.5bn in 2008, a drop of 0.3% on the 2007 figure (see Table 9).

In terms of the ONDAM community target, the total for medicines dispensed to outpatients by hospital pharmacies is added on to this, which as seen above, totalled €1.2bn in manufacturer price ex VAT, or approximately €1.2bn including markups and VAT.

The figure for actual reimbursements is essentially arrived at from this total reimbursable sum of €27.8bn on the basis of the average cover level, deducting any sums for medicines which were bought but not claimed for.

The average cover level changes depending on the distribution of reimbursable medicine sales between the different cover levels and from this we can deduce a theoretical average cover level (see Table 9). As shown, the level has increased significantly since 2007. The increase is an explicable phenomenon linked with declining sales of medicines classed in the 35% cover category, combined

[13] OQN = Objectif Quantifié National.

with the increased proportion of expensive medicines classed in the 100% cover category, anticancer drugs in particular. The size of this growth in 2008 is due to the Removal of medicines which had been temporarily classed in the 15% cover category from the reimbursable lists.

Table 9: Growth of community pharmacy and outpatient sales and theoretical reimbursements (in €M) in 2007-2008 according to cover level

	2007			2008		
Cover level (theoretical)	Sales inc VAT	Theoretical reimbursements	Average theoretical cover level	Sales inc VAT	Theoretical reimbursements	Average theoretical cover level
15%	375	56		0	0	
35%	3,772	1,320		3,649	1,277	
65%	20,290	13,188		20,443	13,288	
100%	2,171	2,171		2,434	2,434	
100% reimbursed outpatient sales	1,235	1,235		1,300	1,300	
Total	27,843	17,971	64,60%	27,826	18,299	65.76%

It is also due to the numbers of patient payment exemptions granted for people with chronic medical conditions.

Added to this, the average cover level was strongly influenced in 2008 by the introduction of refund deductions (*franchise*).

CNAMTS estimates that overall, the average level of reimbursement of medicines in 2008 fell to 75.4% from 76.8% in 2007.

Since the specific effect of refund deductions can be estimated at approximately 2.6 percent of the cover level, this would indicate that the factor of exemptions for chronic medical conditions had little effect on the average level in 2008.

As total reimbursable medicine sales falling within the scope of the ONDAM community target were practically stable from 2007 to 2008, growth in actual reimbursements should by rights have reflected the growth in the average cover level, which was minus 1.7%. And this theoretical result is not far off the provisional CNAMTS data on reimbursements, which shows a 0.2% drop in reimbursements, taking refund deductions into account. GERS, which monitors sales to community pharmacies, underestimated growth in sales to individuals covered by health insurance in 2008 by approximately 0.6 percentage points, due to the fact that pharmacies had large stocks of generics built up at the end of 2007, which was not the case in 2008. It also appears that national health insurance paid out an unusually high figure in early 2008 for outpatient medicines which the hospitals had bought in 2007. These two phenomena combined explain the approximate 1.5% gap between actual growth in national health insurance reimbursements and the estimated figure based on recorded sales.

CHAPTER II – PRICE SETTING WORK IN 2008

1. Prices of reimbursable medicines sold in community pharmacies

The committee made no changes to its price setting method in 2008, with the exception of the price setting method for medicines included the generics substitution list, which is outlined in the chapter on expenditure regulation below (Chapter III, 2.1.1).

The price negotiation and setting methods used by the committee are outlined in Appendix 2, which remains unchanged since previous years, with the addition of details concerning price setting for 'me-too' and 'follow-on' medicines which were mentioned in the chapter on price setting in the 2007 annual report.

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 2008*

In 2008, 1,280 case files, of which 56% related to generic medicines, were submitted to CEPS by companies or opened by CEPS.

All the files together covered 4,708 different products or product formats, with an average of 3.7 different products or product formats per file.

Table 10: Number and type of case files opened in 2008 by type of application

Type of application	Number of cases	Number of products or product formats	Number of files relating to generics	Percentage of files relating to generics
Extended indications	44	187	1	2%
Price change[1]	354	2,566	146	41%
First listing	575	1,254	454	79%
Re-listing	307	701	118	38%
Total	1,280	4,708	719	56%

Source: CEPS - from Medimed software application, 23 June 2009.
1: 98% of these were instigated by CEPS.

2.2. *Case files closed in 2008*

In 2008, 1,740 case files covering 5,775 products or product formats were closed. Half of the files closed in 2008 related to generic drugs (see Table 11). Of the price change files which were closed in 2008, 92% were instigated by the committee.

Table 11: 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	59	164	3	5%
Price change	382	2,583	175	46%
First listing	570	1,190	413	72%
Re-listing	729	1,838	272	37%
Total	1,740	5,775	863	50%

Source: CEPS - from Medimed application, 23 June 2009.

1. The same product or product format could be included in more than one application over the course of the year.

2. 92% of these were instigated by CEPS.

Almost all (93%) of the files dealt with in 2008 ended in agreement between the committee and the respective companies, leading to publication in the *Journal Officiel* (JO). Of the remaining cases, the applications were withdrawn (5%) 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 12: Numbers of products or product formats by type of application and decision for files closed in 2008

Decision / Type of application	Accepted	Abandoned or withdrawn	Rejected	Total
Extended indications	79	81	4	164
Price change	2,468	107	8	2,583
First listing	1,056	110	24	1,190
Re-listing	1,796	41	1	1,838
Total	5,399	339	37	5,775

Source: CEPS - from Medimed application, 23 June 2009.

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

A total of 1,190 first listing applications were dealt with by the committee in 2008, most of which related to generic medicines (see Table 13). Applications for generics were accepted in 96% of cases. The rate was lower for original drugs, due to the higher percentage of applications abandoned or withdrawn by companies compared with those for generics (19% versus 3% and 6% versus 0% respectively).

Table 13: Outcome of first listing applications handled in 2008 by numbers and type of product

Decision / Type of product	Accepted	Abandoned	Withdrawn	Rejected	All
generics	812 / 96%	1 / 0%	22 / 3%	12 / 1%	847
original drugs	244 / 71%	21 / 6%	66 / 19%	12 / 3%	343
all	1,056 / 89%	22 / 2%	88 / 7%	24 / 2%	1,190

Source: CEPS - from Medimed application, 23 June 2009.

2.4. *Case files still in progress at the end of 2008*

On 31 December 2008, 958 cases were still in progress. Most of these were relisting applications (see Table 14). The majority of these cases were closed during the first six months of 2009 or are awaiting publication.

In comparison with 2007, this end of year caseload was smaller by 455 cases, nearly all of which corresponded to re-listing applications

Table 14: Number of case files still in progress on 31 December 2008

Type of application	Generics	Genericised originals	Non-substitution list	Total
Extended indications	0	2	14	16
Price change	14	18	29	61
First listing	113	0	67	180
Re-listing	306	12	383	701
Total	433	32	493	958

Source: CEPS - from Medimed application, 23 June 2009.

3. Processing times for registration applications

3.1. *Processing of fast-track price applications*

Fast-track applications were made for four products in 2008 and two of these were accepted.

Both applications accepted in 2008 were submitted in late 2007 and processed during 2008 following the Transparency Commission's final opinion.

The opinion for Tasigna, an orphan medicine used to treat adults suffering from chronic myeloid leukaemia, was delivered on 14 March 2008. Tasigna was given an ASMR[14] rating of II (high) or I (major) depending on patients' clinical profiles. The committee accepted the price one month later.

The second product, Increlex, is an orphan medicine indicated in the long-term treatment of retarded growth in children and adolescents with severe primary IGF-1 deficiency. The Transparency Commission's final opinion was delivered on 4 February 2008, giving the drug an ASMR rating of III. The time taken to notify the company that its price had been accepted was 36 days and the price became effective on 2 April 2008.

The two fast-track price applications opened and processed in 2008 which were opposed by the committee were transferred to the normal application procedure. The committee has stressed that the rules regarding admissibility of fast-track price applications as set in the framework agreement will be strictly applied and all the undertakings required by these rules must be expressly stated in the companies' applications.

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

First listing applications dealt with in 2008 were processed and published in the *Journal Officiel* (official bulletin) within an average of 102 days, which is significantly lower than the 2007 average (172 days), for a similar number of applications processed.

There was therefore a marked improvement in relation to 2007.

For patented medicines, these shorter processing times owe less to faster processing of cases of similar complexity and more to the combination of two specific sets of circumstances. In the first

[14] ASMR = Amélioration de Service Médicale Rendu - improvement in medical benefit compared to existing treatments for the same condition.

instance, the large number of long-standing and even very long-standing cases closed during the 2007 financial year increased the average processing time for that year. This occurred less in 2008. More importantly, in relation to previous years, listing applications in 2008 contained a higher number of simple additions to existing ranges of already listed products and these are of course much simpler to process.

The situation is different for generics, for which the committee has radically changed the processing arrangements, including among other things the introduction of a facility for companies to produce their own riders to the framework agreement, based on the pro-forma rider provided by the committee and to send them to the committee ready-signed.

The average time taken to process abandoned, withdrawn or rejected cases was 260 days and this average was strongly influenced by a few cases which were abandoned de facto as neither the committee nor the company had formally declared them abandoned.

Table 15: Processing times for listing applications by type (in number of days)

Decision / Type of product	Accepted	Abandoned, withdrawn or rejected	All
Generics	72	255	74
Non-generics	201	264	206
All	102	260	107

Source: CEPS case processing data from Medimed application, 22 July 2009

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 delivery of the Transparency Commission' (TC) opinion to CEPS; from delivery of this 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 additional clause (agreement) and from the signing of the additional clause 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 16: Average interim processing times for listing applications (in number of days)

Type of product	TC	Examination	Negotiation	Agreement	JO or closure	TOTAL
Generics	0	20	1	16	37	74
Non-generics	73	43	31	25	34	206
All	17*	26	8	19	37	107

Source: CEPS case file data based on extract from Medimed, 22 July 2009
*non-significant

3.3.1. *First stage: Transparency Commission*

Applications must be lodged simultaneously with both CEPS and the Transparency Commission. 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 2008, the average time taken for the Transparency Commission's final opinion to be sent to CEPS was 73 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 given to the committee, as well as the time taken to enter the relevant application on the committee's agenda (at least one clear week after committee members have received the report).

In 2008, the average duration of this second stage was 43 days.

For generic medicines, this stage corresponds to the interval between the date the application is submitted and the first session at which it is examined by CEPS.

In 2008, this interval was 20 days, 19 days fewer than in 2007.

3.3.3. *Third stage: Negotiation*

This third stage runs from the first to the last of the sessions during 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 discussions with the rapporteur.

In 2008, over half the listing applications for non-generic medicines processed by CEPS took more than one session to examine. For these medicines, the average length of this negotiation stage was 61 days. Put together with all listing requests for non-generic medicines, the average interval was 31 days.

Only 3% of listing applications for generic medicines required more than one examination at a committee session and the average interval between the first and last sessions was 19 days. For all generic medicine applications processed in 2008 put together, the average interval was less than 1 day.

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 corresponding 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.

The average interval between the committee's final session and its decision was 17 days in 2008 for generic medicines and 33 days for non-generic medicines: 3 and 6 days less respectively than in 2007.

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

This final stage includes preparation and signing of the price notices by CEPS and signing of the decrees of registration on the reimbursable medicines lists by the relevant health ministry departments, followed by sending of the registration notices and price decrees to the government publications office for entry in the JO.

The average time taken for this in 2008 was 37 days: 37 days for generics and 34 for non-generics. This interval was on average 11 days less than in 2007, which is a significant difference.

4. Hospital prices and tariffs

In 2008, 25 new products (some of them new formats of already listed products) were registered either on the outpatient medicines list, the list of medicines reimbursable on top of GHS funding or both, and several generics were also added. These new entries each have two or three times as many tariff entries [one entry per common dispensing unit (UCD)]

New formats of Advate, Alimta, Benefix, Kogenate and generics of epirubicin, fludarabine, gemcitabine, oxaliplatin, paclitaxel and vinorelbine were registered on both lists in 2008.

Seven new products were registered on the reimbursable outpatient medicines list. These were Celsentri (anti-HIV drug), Ferrisat (an iron deficiency treatment), Firazyr (orphan medicine indicated in the treatment of hereditary angioedema), Mycamine (for the treatment of candidiasis and prevention of Candida infections in patients undergoing bone marrow transplants), Riamet (treatment for malaria episodes), Sebivo (treatment for chronic hepatitis B) and Volibris (treatment for pulmonary arterial hypertension).

Fourteen new products were added to the list of medicines reimbursable on top of GHS funding: Abseamed, Binocrit, Mircera and Retacrit (anaemia treatments), Atriance (orphan medicine used to treat a rare form of leukaemia), Torisel (kidney cancer), Vectibix (metatstatic colorectal cancer), Revlimid (multiple myeloma), Prialt (orphan medicine for severe chronic pain) and Privigen (Human normal immunoglobulin), as were new formats of Novoseven (clotting factor), Velcade (multiple myeloma), Busilvex (used during hematopoietic stem cell transplants) and Campto (colorectal cancer). Some generics such as irinotecan were also registered on this list.

4.1. *Application processing times*

In a number of instances, concerning generics in particular and covering 25 different UCDs, companies did not submit a price declaration. In such instances, the committee sets the price or tariff unilaterally. The average interval before publication was 80 days after registration on one of the lists.

The application processing times were worked out for products registered on either the outpatient medicines list or the list of medicines reimbursable on top of GHS funding for which the prices were published in 2008, with the exception of generics if the hospital prescription fee or accountability tariff aligned with the price of the original drug was set before they were registered on one of these lists.

For medicines for which the company had made a price declaration, the average interval between registration on the outpatient list and publication of the public price was 115 days, whilst the interval before publication of tariffs for medicines registered on the list of medicines reimbursable on top of T2A was 44 days. This difference is due to the fact that for the second list, publication of the tariffs at the committee's instigation is not subject to any further procedures, whereas for medicines on the outpatient list, price notices may only be published at the same time as notices regarding their cover level and their inclusion on the public hospitals' authorised medicines list.

4.2. *Applications opposed by CEPS*

In 2008, CEPS definitively opposed the company's price submission for five different products. For five 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.

CHAPTER III - REGULATION

1. The merged community-hospital framework agreement

A new framework agreement was signed on 25 September 2008 between LEEM[15] and CEPS. In essence, this agreement is a combination of the 2007 revision of the 2003 community pharmacy framework agreement and the agreement on products sold to hospitals which was built up in phases between 2004 and 2006. There is one essential addition, which is the unification of the financial regulation arrangements.

Firstly, CEPS was authorised by the relevant ministers to organise the contractual framework for the postponed extension of the annual financial regulation system to medicines refunded on top of GHS funding. The new framework agreement contains provision for this extension starting from the 2010 financial year. This contractual extension has since been incorporated into the Social Security Code by the 2009 annual social security funding law (LFSS).

This scheduled extension was planned alongside the merging of the community and hospital regulations, on a model based largely on the traditional community regulation system, but incorporating certain features specific to the hospital regulation system.

The unified regulation system is essentially based on the general principle of regulation per pharmacotherapeutic class groupings and the table of these (see Appendix 4) has been adjusted to include medicines sold to hospitals. The rule stipulating that no clawback payments would be due unless sales volumes exceeded the 'K' level has been kept, but has been adjusted to take into account the existence in the law of two separate legal K rates and therefore applies to instances where sales to both community and hospital pharmacies do not exceed the mean sale-weighted value of these two K values.

The main feature of the hospital regulation system is the method of calculating sales of medicines to hospitals. Because of commercial confidentiality, actual sales figures cannot be published in principle since they can be used to calculate the prices which the companies propose in their tender bids. However, to ensure that the system for calculating clawbacks by therapeutic group is transparent and fair, the turnover taken into account to work out sales to hospitals is calculated on the basis of the quantities sold[16] costed at the accountability tariffs or published hospital prescription prices.

As regards turnover clawbacks, these are still calculated on the basis of the actual turnover figures declared by each company.

The exemptions which were contained in the hospital pharmacy framework agreement have been kept in the new merged agreement. This applies to drugs under provisional authorisation (ATU) but also to products which are mainly issued to inpatients rather than outpatients However this exemption will no longer be applicable when medicines refunded on top of GHS funding are incorporated into the regulation system in 2010.

2. Expenditure regulation measures

2.1. *Measures relating to community pharmacy medicines*

2.1.1. *Medicines on the generics substitution list*[17]

[15] LEEM: Les entreprises du Medicament – the pharmacetucial companies' representative body.
[16] Available for all companies in the GERS hospital sales data.
[17] The substitution list is a list of generic product and product formats and their reference product (original drug).

The 'Fixed accountability tariffs' (TFR) policy[18] was continued in 2008, according to rules which are strictly the same as those applied in previously years and involve placing under the TFR heading drug groups in the substitution list within which after 12, 18 and 24 months respectively following the marketing of the first generics in the group the generics' market share has not reached 55%, 60% or 65% respectively. However, these decisions were made at the end of the year, which means that the savings resulting from them will not show up until 2009 (approximately €20M). However the effects of the transfers to TFR processed at the end of 2007 were seen in 2008 and represented total savings of €85M.

The most significant work carried out was to lower the price of generics en masse, so that the measures to reduce community pharmacies' extra profits could take full effect. As we know, the unchecked growth in the extra profits derived by pharmacy owners from generics manufacturers, primarily in the shape of considerably overpriced strategic alliance agreements, had led to an initial reform. Following on from the 2005 legislation introducing changes to the Code of Commerce in relation to retailing at a loss and strategic alliances, the aim of this reform was to limit the financial perks which pharmacy owners were receiving on top of the official discounts. It became clear very early on that loopholes were being found in these regulations, primarily in the form of pharmacies benefitting from official wholesale markups via direct sales.

In order to put an end to these abuses without jeopardising the pharmacy owners' legal position, since large numbers of them had exposed themselves to criminal sanctions, the rule was again changed in the hope that the new system would at last be properly implemented. Under this new system, the total amount of benefits received by the pharmacies from the generics manufacturers (including the wholesale markup where applicable) was reduced to halfway between what had previously been permitted and what they had actually been earning. As this was to the generics manufacturers' advantage, they were also required to reduce their prices.

These reductions took effect in April 2008 and represented annual savings of €90M, hence the pro-rata savings in 2008 were €60M.

Of course, these savings are in addition to the savings resulting from the increased market share gained by generics and from further patent expiries. In this respect, the whole of 2008 saw the benefits of the genericization of amlodipine and terbafine which occurred in mid-2007 and those of risperidone and lansoprazole which happened at the end of 2007. Most of the effect of the main genericizations of 2008, in particular that of venlafxine, will appear in 2009.

At the year-end, after consultation with the generics monitoring group, CEPS introduced some new rules, both regarding the automatic price reduction on new generics in relation to the price of the original drug, which has been raised from 50% to 55% and further price reductions on medicines in the substitution list. The rules now state that after the first generics of a product have been on the market for 18 months (previously 24 months), unless the generic group has been under the TFR heading, the price of the original drug should be reduced by 12.5% (previously 10%) and prices of generics by 7% (previously 4%). However, the prices of generics will only be reduced where there is a sufficient supply of generics within that group.

The additional saving resulting from these measures (approximately €40M) will only appear in the 2009 figures.

2.1.2. *Reducing prices of patented medicines*

In 2008, the committee continued its work on coordinating price reductions for medicines which are still under patent, whilst adhering to the provisions of the framework agreement on maintaining a European level price for the most innovative medicines during their first five years on the market.

[18] The fixed accountability tariff (*tarif forfaitaire de responsabilité*, or TFR) is a reimbursement tariff. Products listed under the TFR heading are reimbursed on the basis of this tariff rather than their price.

The impact of these price cuts amounted to €228M in 2008 (€124M of which resulted from the carry-over effect of measures introduced in 2007), while the cuts implemented in 2008 should produce a carry-over into 2009 of more than €170M.

As in previous years, the reasons behind these cuts fall into four main categories:

- re-assessment by the Transparency Committee of the ASMR price rating. This affected medicines used in the treatment of Alzheimer's disease among others.

- application of pre-existing clauses, for example in the case of Glitazones, for which it had been stipulated that their listing price would only be maintained if they achieved a higher ASMR price rating.

- consistency within classes that are sufficiently homogenous and include generic competitors. For example, the price of Inexium (in the PPIs class) has been reduced, as has that of Zelitrex, given the price of Aciclovir.

- price reductions on medicines governed by conditions which can give rise to volume or daily treatment cost discounts, where the size of the discounts can justify reducing the listed price at least in part. This was the case with Spiriva among others.

2.1.3. *The development of large pack sizes with the implementation of the refund reduction*

Sales of large pack sizes have developed considerably since the second half of 2007. These new sizes are a replacement for monthly supply packs. In 2008, just under 19 million quarterly supply packs were supplied to pharmacies by pharmaceutical companies: 3.2 times more than in 2007. Larger pack sizes represented theoretical savings of €81M in 2008, compared with a situation with no quarterly supply packs, and €44M of this figure was due to the actual 2008 effect. These theoretical savings were partially counteracted during the 2008 financial year by patients having larger stocks of medicines, which national health insurance pays for. Patients' large pack stocks are equivalent to 1.5 months' treatment on average as opposed to 0.5 months for the monthly supply sizes.

2.2. *Medicines in hospitals*

2.2.1. *Reduction in generic medicine tariffs*

When a medicine on the hospital-only list is genericized, CEPS automatically sets identical accountability tariffs or prescription fees for both the original drug and the generic versions. If it did not do so, because of the way in which prices are formulated in the hospital medicines sector, the drug with the highest price or tariff would have an unfair advantage over its rivals since for the same net price, it would be able to offer higher discounts.

Added to this, the competition which takes place between the original drug and its generic rivals in the hospital sector would lead to much greater price reductions much sooner than under the administered price system. CEPS therefore simply supports these spontaneous reductions by reducing the published prices or tariffs gradually.

However, the process is carried out at appropriate intervals to ensure that the generics do not become less attractive to hospitals' buyers than drugs which still under patent and hence much more costly, which could be used to replace a portion of them.

2.2.2. *Price reduction decisions for medicines over five years old*

In 2008, CEPS announced its intention to request price 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 countries who have signed up to the framework agreement than in France. When these medicines were first registered, their innovative contribution justified a protected European level price and because of the

price submission rules, the committee was able to accept prices which in some instances were higher than the lowest prices in these EU countries. Once this five-year protection period has expired, the committee believes it is justified in requesting a price reduction where applicable, to reflect these lower prices.

A first price reduction was published in 2008 for Herceptin.

2.2.3. *New rules regarding orphan medicines*

Over the last few years, expenditure on orphan medicines has seen extremely high growth and in 2008 reached a combined total of €815M for both medicines supplied to hospitals and the increasing quantities now distributed to community pharmacies put together.

At these expenditure levels, the committee felt it was no longer possible to continue without a regulatory mechanism. In relation to innovative medicines, the mechanism needed to operate within framework of the undertakings regarding internationally consistent prices for innovative products. Above all, it was essential not to close the door to any promising medicines and to allow all patients concerned to benefit from them.

The committee therefore decided to propose agreements to the companies concerned whereby the companies would undertake to supply their medicine to all patients who might benefit from it without restriction, whilst paying back to national health insurance any turnover they make above an agreed fixed ceiling.

The companies should be satisfied with this, as their international price is adhered to and the fixed turnover ceiling is set at a higher level than the market share they would have in France if access to the medicine among the patients concerned was the same in all countries in which the medicine is sold.

From the national health insurance point of view, since the numbers of patients who will benefit from the medicine will naturally be greater than the number which the fixed ceiling would fund, hence ensuring a payback by the companies, the contract guards against unpleasant financial surprises and in practice sets the actual price at a lower level.

This mechanism was implemented on two occasions in 2008: the first involved Naglazyme (treatment for mucopolysaccharide type VI disease) and the second Soliris (for paroxysmal nocturnal haemoglobinuria)

3. Measures relating to promotion of medicines

3.1. *Certification of sales visits*

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

However, the law did not of course stipulate a timescale within which the approval should be carried out. Therefore, in view of the state of progress of the *Haute Autorité de Santé* approval guidelines and the appointment of the accredited bodies, CEPS set 30 June 2008 as the date by which companies were obliged to be certified, failing which their agreements with CEPS would be terminated. The committee also made it clear that it would be prepared to take into account any representations by companies who had not yet received certification by that date, provided that they could demonstrate the measures they had taken to obtain certification and the reasons for the delay (e.g. if they were recently formed, delays by the certifying bodies, etc.).

In the event, no company had its agreement terminated. The committee satisfied itself that of the 80 largest companies, who represent 98% of total reimbursable medicine sales, all those engaged in sales visits in non-hospital settings had been or were about to be certified.

As at 31 December 2008, 94 pharmaceutical companies and 15 sales visit contractors were certified.

3.2. *Reduction in the number of visits*

The charter had provided the facility for CEPS, after conducting various consultations, to lay down rules regarding reducing the number of visits made to prescribers for certain drug groups. The introduction of this facility was reported in the committee's 2007 annual report.

However following an action brought by two of the companies affected by these reductions, the *Conseil d'Etat* nullified the clause in the charter which had introduced the system, in two identical rulings of October 2008 The Council ruled that the law did not give signatories to the sales visit charter jurisdiction to authorise CEPS to take such steps unilaterally.

CEPS acted on these rulings by reimbursing the companies in the form of clawback credits, as the companies had been penalised with temporary price reductions of the products concerned due to the committee's actions.

3.3. *Advertising bans*

CEPS examines all advertising bans issued by the AFSSAPS Chief Executive[19], regarding both reimbursable medicines sold in community pharmacies and those purchased by hospitals.

However, due to internal restructuring, the committee only examined 5 cases in 2008, which was a small proportion of the bans issued. The backlog will have been dealt with completely within the first few weeks of 2009.

Of these five bans, three resulted in fines worth a total of €2.3M.

In the other two cases, the committee considered that the seriousness of the breach was sufficiently minor to warrant the ban on the advertisement itself and its publication acting as sufficient sanction.

It should be pointed out in this respect that in several of its rulings upholding penalty decisions made by CEPS, the *Conseil d'Etat* stated that CEPS itself had jurisdiction to assess the facts to which the ban related and to make a judgement regarding the facts. This confirms that it is possible for the committee to reach different conclusions than those reached by AFSSAPS, including on whether or not there has been a breach.

The same rulings, as well as many other recitals which have now clearly defined the framework of the committee's mission in this respect, have spelt out two major points in particular. The first is that the inherent seriousness of a breach, which for example might lead to an error by a prescriber regarding a medicine's properties or might present a health risk to patients, is enough to justify a financial penalty without needing to prove that the advertisement had led to increased sales. The second is that the committee would have been acting within the law to consider the position of the medicine concerned among all the company's product sales when setting an appropriate penalty.

4. End of year adjustments

4.1. *Agreements between CEPS and the pharmaceutical companies*

Of the 179 companies selling reimbursable medicines sold in community pharmacies or issued to hospital outpatients to which CEPS offered contractual exemptions from the *contributions de sauvegarde* ['safeguard contributions'][20], 166 companies entered into and signed the agreements.

In 2008, none of the companies owed payments under the 'K' growth rate clause. In fact, in 2008, the companies' overall sales volume in France of products falling under the terms of the clause grew

[19] C.f. Article L. 162-17-4 of the Social Security Code.
[20] Contributions paid as a safeguard against exceeding the fixed turnover threshold.

by 1.1%, which is less than the 'K' rate of 1.4% set for both community pharmacy and hospital outpatient medicine sales.

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 2008 which qualified for credits, or credits awarded under the CSIS system (*Conseil stratégique des industries de santé* – Health industry strategy council) 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. Any credits which are not used one year may be carried over to the following year.

In 2008, the total amount of clawback credits owing to the companies was €163M, of which €71M were carried over from previous years, €51M were CSIS credits awarded in 2008 and €41M were new credits other than CSIS. 61% of these clawback credits were actually used, the remainder being carried over to 2009.

4.3. *Actual clawback payments*

The net amount of clawback payments owed by the companies for 2008 and actually paid to ACOSS[21], minus claimed clawback credits, was €260M. The clawbacks related solely to specific products and primarily to medicines sold in community pharmacies.

[21] ACOSS: Agence Centrale des Organismes de Sécurité Sociale – the central social security bodies' agency.

PART TWO – MEDICAL DEVICES

CHAPTER I – EXPENDITURE ON MEDICAL DEVICES COVERED UNDER THE MEDICAL DEVICES AND SERVICES LIST (LPP[22])

The first point to make is that unlike the system for medicines, the government does not have any direct means of measuring sales or sales growth of reimbursable medical devices, since the field covers a wide range of economic sectors whose distribution channels are also very diverse.

The information on reimbursement produced by CNAMTS, which is now very accurate and reliable since the coding system was introduced, can only provide a rough estimate of the device manufacturers' operations, for two main reasons.

The first is that for a large, albeit decreasing proportion of sales, reimbursements are paid on the basis of the tariff set by CEPS, whereas the actual sale prices can be higher than these rates, or even much higher in some cases, such as adult hearing aids.

The second reason is that the CNAMTS figures do not include purchases by public healthcare establishments which are funded under the GHS heading and no other direct tally is kept of these purchases.

The following data therefore relates to reimbursements paid out under the general health insurance plan (*régime général*), bearing in mind that year-on-year trends can generally be assumed to be similar for the other mandatory plans.

In 2008, these expenses totalled €4.1 billion, an increase of 9.2% on the figure for 2007 (see Table 17).

[22] LPP – Liste des Produits et Prestations.

Table 17: Reimbursements paid out under the general plan in €M

	2007	2008	Growth	Percentage of total
Home breathing aids and oxygen therapy equipment	551.4	626.5	13.6%	15.1%
Other home treatment equipment	713.1	823.6	15.5%	19.9%
Medical devices for homecare and daily living aids for people with medical conditions or disabilities	824.8	882.5	7.0%	21.3%
Items for dressings and casting &splinting equipment	333.6	351.2	5.3%	8.5%
Total for Code I: Medical devices for home treatment and daily living aids	2,423.0	2,683.9	10.8%	64.8%
Orthotic devices	257.2	274.7	6.8%	6.6%
Prescription opticianry	157.2	159.5	1.5%	3.9%
Electronic devices for the deaf and hard of hearing	73.4	77.9	6.2%	1.9%
Non-orthopaedic external orthotic devices	7.7	8.1	5.8%	0.2%
Eye and face prosthetic devices	6.3	7.4	17.5%	0.2%
Orthopaedic shoes	59.3	64.1	8.1%	1.6%
Orthotic prosthetic devices	139.6	152.2	9.0%	3.7%
Total for Code II: External orthotic and prosthetic devices	700.6	743.9	6.2%	18.0%
Inert internal implants	446.2	470.5	5.5%	11.4%
Electrically powered implants	118.1	126.5	7.1%	3.1%
Total for Code III: Implantable medical devices (private clinics only)	564.3	597.1	5.8%	14.4%
Code IV – Disability-adapted vehicles	98.3	111.1	13.0%	2.7%
Total	3,786.1	4,135.9	9.2%	100.0%

Source: CNAMTS

This 9.2% growth, which is even higher than that of the previous year (8.1%), certainly reflects the advances made in home treatment, as in previous years, and the costs are no doubt lower than the potential costs which would be involved in the same people being treated in hospital. On a very different level, it also reflects progress in new, less invasive surgical techniques, which have often been proven to be more cost-effective compared with traditional operating methods.

Nonetheless, this is a very high increase in expenditure. It can be explained in part by circumstances which are probably not reproducible, such as the excessive outlays from the non-hospital care budget in June and July 2008 prior to the introduction of the new fixed budget system for certain medical devices in residential homes for the elderly (EPHADs) on 1 August 2008. Other than this, the increase is a signal that in addition to tariff adjustment measures, action needs to be taken to rationalise prescribing practices.

1. Code I: Medical devices for home care and daily living aids, dietary foods and items for dressings

Code I includes homecare equipment, products and services for patients who are elderly, disabled, require post-operative care or have chronic conditions. In 2008, this category accounted for 65% of all reimbursements under the general health insurance plan, an increase of 11% on the figure for 2007.

This code is still the main category responsible for the growth in medical device expenditure (75%). In 2008, this growth was impacted strongly by the (albeit expected) paradoxical effects of the inclusion of certain expenses in the budgets of EHPADs (Residences for Dependent Elderly People) at a flat rate as of 1st August 2008. In anticipation of this measure, many establishments stepped up their purchases of reimbursable items on behalf of their residents such as hospital-type beds. As a result, the corresponding category grew just as quickly in 2008 as in 2007, although reimbursements paid to elderly people living in EHPADs should have come to a stop.

One of the biggest cost increases resulted from the worrying rise in home respiratory care and oxygen therapy (+€75M). There was no circumstantial explanation for this rise, which, as in the previous year, stemmed essentially from the steady strong increase in sleep apnea diagnoses and hence in continuous positive airway pressure treatment (CPAP).

Self-medication and self-testing devices for diabetes patients also contributed significantly to the growth in this category, although it is not certain that the increasing prevalence and more efficient diagnosis of type-2 diabetes explain this in full.

2. Code II: External orthotic and prosthetic devices

Spending on external orthotic and prosthetic devices is growing less quickly than that on most other devices (6.2%). In 2008, the general health insurance plan paid out €744M for this category, i.e. 18% of its total expenditure.

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

Only private healthcare costs relating to IMDs listed under LPP Code III fall within the scope of expenses reimbursed by the general health insurance plan. In 2008 these costs rose 5.8% to reach €597M under the general plan alone. Orthopaedic implants, such as hip and knee prostheses, were primarily responsible for the increase in this category.

As for healthcare establishments formerly under the blanket grant system, separately invoiced costs relating to IMDs listed under LPP Code III stood at €616M in 2008, as opposed to €601M in 2007.

4. Code IV: Disability-adapted vehicles

After a slight slowdown in 2007, reimbursements for the purchase and maintenance of disability-adapted vehicles picked up again in 2008 (13% compared with 2007). As with the beds and other equipment under Code I, this renewed growth is no doubt connected with the inclusion of this expenditure item in the healthcare budget of EHPADs.

CHAPTER II – TARIFF SETTING FOR MEDICAL DEVICES AND SERVICES

1. Work done by CEPS

1.1. *Applications submitted to the committee*

In 2008, 149 applications by companies were submitted to the committee. Of these applications, 87 were first applications for registration, 7 of which were rejected after the *Comité d'évaluation des produits et prestations* (CEPP – the Medical device and technology evaluation committee) assessed the service rendered by the devices at too low a level for inclusion on the list; 26 applications were for changes to the registration conditions, one of which was abandoned by the company, 12 were for tariff reassessments and 24 were for re-inclusion on the list, one of which was submitted twice (see Table 18).

This is bearing in mind that price submissions are only made for products which the manufacturers or distributers wish to have listed by brand (see Appendix 3).

1.2. *Processing of applications*

1.2.1. *Statistics*

The number of applications still in progress at the end of the year was down slightly on the previous year. This improvement is due less to an increase in the numbers of applications processed, which remained more or less the same (159 as opposed to 155 in 2007) and more to a reduction in the number of applications submitted (149 compared with 219 in 2007).

Table 18: Applications examined by the committee in 2008

Type of application	Applications in progress end 2007	Applications submitted in 2008	Applications closed in 2008	Applications in progress end 2008
First listing	135	87	100	122
Re-listing	67	24	16	75
Changes to conditions	36	26	34	28
Tariff change	3	12	9	6
TOTAL	241	149	159	231

Source: CEPS

1.2.2. *Application processing times*

Of the 149 applications processed during 2008, around 100 needed to be examined only once by the committee and five were withdrawn by the company without CEPS having examined them. On average, 1.4 examinations were required, covering an average period of 295 days.

The shortest processing times were for tariff change applications, even though these required the highest number of examinations by the committee (see Table 19). Conversely, applications for re-inclusion on the list, which generally take over a year to process after submission, are only examined 1.1 times on average. First listing applications are examined 1.5 times on average and are closed an average of 313 days after the date of submission.

Table 19: Applications processed by the committee in 2008

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	89	*4*	*85*	313	1.5
Re-listing	24	*1*	*23*	378	1.1
Changes to conditions	23	*1*	*22*	245	1.2
Tariff change	6	*0*	*6*	131	1.7
TOTAL	142	*6*	*136*	295	1.4

Source: CEPS

The average interval between submission of a first listing application and publication was 313 days (see Table 20). CEPP's opinion was delivered within an average of 144 days and sent to CEPS 11 days later. The time before CEPS first examined applications was just under one month on average. For nearly three quarters of registration requests, only one examination by the committee was required. For the remainder, the committee examined applications up to five times and 2.7 times on average. The decision was sent to the company or published within 83 days after the committee's final examination.

The overall time taken to examine re-listing applications was longer, with an average of 378 days. However, the time required for CEPP to deliver its opinion was shorter than for first listing applications. The examination of re-listing applications during the committee's sessions took longer than for first listing applications, in fact twice as long on average. The committee's decision was also delivered later.

On average, applications for changes to registration conditions were processed within 245 days, which included 89 days between submission of the application and delivery of CEPP's opinion.

Tariff change applications were dealt with more quickly: 131 days on average.

Table 20: Average application processing times (in number of days)[1]

Type of application	Interval between submission and CEPP opinion	Interval before opinion sent to committee	Interval before first examination by committee	Interval between 1st and last examination	Interval between final examination and decision	Total time Total
First listing	144	11	28	47	83	313
Re-listing	151	15	77	20	114	378
Changes to conditions	89	14	28	12	103	245
Tariff change	50			24	58	131

[1]Suspension decisions issued by the ministries, which mostly relate to supporting documents for the application sent to CEPP for examination, are not listed by CEPS and the timescales corresponding to these have not been deducted from the overall application processing times.

2. Determining the tariffs and prices

2.1. *General principles*

The principles upon which CEPS bases its price setting decisions have not changed in practice since 2008. The sections in previous annual reports devoted to developments in this area still apply. These are described again in Appendix 3 to this report.

2.2. *Price and tariff changes in 2008*

2.2.1. *Increases*

A tariff increase for intra-uterine contraceptive devices (IUDs) was adopted in June 2008.

The tariffs for large orthotic and prosthetic devices were also increased by 4.1%, under the terms of the multiannual agreement with the profession, which guaranteed a set net markup rate for three years.

2.2.2. *Reductions*

In accordance with the policy guidelines received from the respective ministers and in view of the alert procedure in particular, CEPS finalised three different price reduction operations in 2008.

The first related to home transfusion tariffs (Code I), which were reduced by between 5% and 20% depending on the product. This produced savings of €4.3M.

As part of a contractual agreement, the committee also published a 10% reduction on the tariffs or maximum sale prices for all cardiac defibrillators (Code III) at the same time that the indications for the appliances were extended. The anticipated savings on this count total €10M, but will not show in the accounts until 2009.

The revision of the tariffs applicable to insulin pump therapy (c.f. 2.2.3 below) also produced savings of nearly €6M.

The tariff agreement sometimes includes conditions requiring clawback payments based on sales volumes oractual use of a device in practice (see pro-forma clause in Appendix 5, 3).

The total amount of clawback payments made in 2008 was €8.68M: just under half the total sum in 2007 (which included payments owing from 2005 and 2006).

2.2.3. *Removal of devices from the list due to insufficient service level*

In February 2008, two named branded medical devices were removed for the first time from the reimbursable devices list after CEPP delivered an opinion assessing their service rendered as insufficiently high for inclusion. These were devices to protect the hips in the event of a fall.

2.2.4. *Revision of generic list entries*

A large proportion of the committee's work is devoted to action based on CEPP's opinions regarding revision of generic list entries. This work produced few visible results in 2008, due to the highly complex nature of the operations. Firstly, the method for transposing opinions which are expressed in terms of service expected or rendered into appropriate tariffs can be complex. Secondly, drawing up the category definitions and tariffs requires ongoing communication with the different professions, whose interests can sometimes be conflicting (for example those of service providers or distributers and those of manufacturers). Finally, when revising tariffs from scratch, which is sometimes required during a comparative review of service rendered, strict precautions are required to prevent the risk of major additional expenses for national health insurance. Indeed, when we begin to change the usual tariff balance that operators have become accustomed to, it is not always easy to predict how people will act in response to the change.

Hence, by the end of 2008, the large number of opinions delivered by CEPP in its implementation of the Health Minister's programmes set out on the basis of the December 2004 decree, were still waiting to be transposed into regulations.

Certain principles have however emerged from the reflections and discussions which the committee has already held.

In the first instance, the committee is keen to set the maximum selling price in as general a way as possible, bearing in mind that for devices which are eligible for cover by national health insurance by

virtue of their actual or expected service rendered, the aim of equal access to prevention, care or disability support means that there should be a very small difference, or no difference wherever possible, between the price paid and the reimbursement tariff.

In the second instance, the committee also wishes to do its utmost to avoid a situation where certain loss-making areas within a company are subsidised by other extremely profitable operations. For operations which are funded by more than one tariff, for example a fixed supply fee plus a regular ongoing payment, the committee aims to set the tariffs as close as possible to the actual costs, to prevent opportunistic actions by the operators.

On the same lines, wherever the reimbursable service involves providing patients with equipment which can be either bought or hired, the committee has decided to remove the buying option, so that only hired items will be reimbursed. It was considered more beneficial overall for the equipment to have as long a life as possible, since it will be funded one way or another by national health insurance. Clearly, this is more likely to be achieved when the equipment remains the property of professional hire companies, as it is in their interest to maintain it in good order for as long as possible. The issue of sharing this benefit between the companies and national health insurance is then simply a matter of setting the right tariff level.

These last two principles were put into practice in the review of insulin pumps, for which CEPP had issued an opinion. The committee first put a stop to the buying option and then introduced a high increase on the payment for setting up, training, maintenance and stand-by services, in return for an equally high reduction in the daily hire rate.

One problem which needs to be solved when implementing these revised practices is how to assess the length of time the companies will need to comply with the new rules and the need for a period during which the old and new category definitions can exist side by side.

APPENDICES

APPENDIX 1: FRAMEWORK AGREEMENT OF 25 SEPTEMBER 2008 BETWEEN THE COMITÉ ECONOMIQUE DES PRODUITS DE SANTÉ AND THE PHARMACEUTICAL COMPANIES

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[23] 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[24] 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.

[23] LEEM = Les Entreprises du Médicament: the pharmaceutical companies' trade association in France.
[24] 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 list 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.

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 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* [Official bulletin] 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, 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. 162-22-7-1 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[25] 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[26]

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 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.

[25] 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.

[26] 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*.

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 for removal of medicines from the reimbursable lists

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.

Removal of medicines from the reimbursable lists 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 "posolgy" 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 GROUPING FOR 2008-2010

Group	2007 Sales in €K	2008 rate (K rate included = 1.4)	2009 rate (K rate not included)	2010 rate (K rate not included)
For the 2008 financial year, the coefficient provided in Article 17a) of the framework agreement is set at 20%. For each group, the portions of the overall clawback figure based respectively on turnover and excess are set at 65% and 35%.				
NB: Products which can be issued to outpatients and were included in the 2007 base are identified in italics, except for categories L01-L02, J01 etc, and B02 +J06.				
A02 (antacids and anti-flatulent agents) other than A02B2	118,142	1.4	0	0
A02B2 (acid pump inhibitors)	942,024	-5.6	-7	-5
A03 (antispasmodics, anticholinergics and gastro-intestinal sensorimotor modulators) + Vogalene *(including Prepulsid and Debridat inj.)*	150,171	1.4	0	0
A04 (antiemetics) except Vogalene	34,045	1.4	0	0
A05A1 (bile therapy and cholecystokinin) + A05B (hepatic protectors, lipotropics) + A06 (laxatives) + A07 (anti diarrhoeals) except A07E + Intercron and Nalcron + A09 (digestives including digestive enzymes)	203,952	1.4	0	0
A05A2 (bile stone therapy) + A07E (intestinal anti-inflammatory agents) except Intercron and Nalcron	58,350	1.4	0	0
A10 (drugs used in diabetes) + A08A (anti-obesity preparations)	635,430	6.4	5	5
A11 (vitamins) + A12A (calcium products) + A12B (potassium products) + C10B (anti atheroma preparations of natural origin) except calcium sorbisterit and Phosphoneuros + Zymaduo (including *un-alfa inj.*)	108,517	1.4	0	0
A12C (mineral supplements) + A13 (tonics) + A15 (appetite stimulants) except Phosphorous, Zymaduo, Nonan, Decan, Tracutil and Tracitrans (including *Proglicem*)	49,999	1.4	0	0
B01A (anticoagulants, non-injectable) + B01B (anticoagulants, injectable: heparins) + B01E (direct thrombin inhibitors) + B01X (other anti-thrombotic agents) (including *Orgaran*)	285,016	1.4	0	0
B01C (platelet aggregation inhibitors) except Xagrid	557,656	1.4	0	0
B02A and B (systemic antifibrinolytics and anticoagulant antagonists) + B03 (anti-anaemic preparations) except B03C + A14A1 (anabolic hormones, systemic) + Lederfoline and Folinoral (including *Venofer*)	54,709	1.4	0	0
B02C and D (proteinase inhibitors and blood coagulation) + J06 (sera and gamma-globulin) except Synagis	640,873	10	7	7
B03C (erythropoietin products)	392,752	1.4	5	0
C01A + B + C (cardiac glycosides, anti-arrythmics and cardiac stimulants)	109,124	1.4	5	0
C01D + E + X (coronary therapy) + C02 (antihypertensives) + C03 (diuretics) + C07 (beta blocking agents) + C08 (calcium antagonists) + Caduet	1,091,310	-2	0	0
C04 (vasodilators) + N6D (nootropics) + Olmifon	173,509	-8.6	0	0
C05 (anti-varicosis / anti-haemorrhoidal preparations)	214,184	-94.6,	0	0
C09 (agents acting on the renin-angiotensin system)	1,307,485	1.4	0	-5
C10A (cholesterol and triglyceride regulating preparations) except C10A1and Ezetrol	117,941	1.4	0	0
C10A1 (statins) except Caduet + Ezetrol + Inegy	1,018,036	1.4	0	0
D (dermatologicals) + Terbinafine + Metvixia	448,073	1.4	0	0
G01 (gynaecological anti-infectives) + G04A (antiseptics and urinary anti-infectives)	68,775	1.4	0	0
G02 (other gynaecologicals) + G03 (ovulation inhibitors) except G03B, G and J	220,225	1.4	0	0
G03B (androgens), G04 (urologicals) except G04A	269,410	1.4	-3	-3

Group	2007 Sales in €K	2008 rate (K rate included = 1.4)	2009 rate (K rate not included)	2010 rate (K rate not included)
G03G (gonadotrophins / ovulation stimulants) + H01C1 and C3 (hypothalamic hormones)	112,428	1.4	0	0
H01A (ACTH) + H01C2 (anti hGH antibodies) + H02 (oral corticosteroids) + H04A, B and D (calcitonins, glucagon and antidiuretic hormones) (inc *Minirin inj*.)	196,302	0.4	1	-1
H03 (thyroid therapy) *(inc Proracyl*)	39,687	1.4	0	0
H4C (growth hormones)	123,018	1.4	-1	-1
J01 (systemic antibacterials) + J02A (systemic antimycotics) except Terbinafine + J03A (systemic sulphonamides) + J05B (antivirals excl. anti-HIV products) except J05B1	1,068,980	-1.6	-3	-2
J05B1 (hepatities antivirals) + J05C (HIV antivirals) + L03B1 (alpha interferons)	882,498	10	5	5
J07 (vaccines) + V01A (allergens) + Synagis	409,391	8.4	5	5
K (hospital solutions) + Nonan, Decan, Tracutil and Tracitrans	37,939	1.4	0	0
L01 + L02 (anti-cancer agents and cytostatic hormone therapy) + L03A (growth factors) except Metvixia and Copaxone + Xagrid	2,250,000	8	6	6
L03B2 (beta interferons) + Copaxone	228,308	1.4	0	0
L04 (immunosuppressive agents) except Raptiva	178,478	6.4	0	0
M01A1 (Anti-rheumatics, non-steroidal plain) except Art50 and Zondar + M01A3 (Coxibs, plain) + M04 (anti-gout preparations)	237,500	1.4	0	0
M01C (specific anti-rheumatic agents) + Acadione + Raptiva	289,044	11.4	5	2
M01A2 (antirheumatic, non-steroidal)+ M02 (topical antirheumatics and analgesics) + M03 (muscle relaxants)	113,522	-1.6	-3	0
M05B + G03J + Forsteo and Protelos	384,396	4.4	3	1
M05X (other musculo-skeletal products) + Art 50 + Zondar except Acadione and Protelos	248,519	1.4	0	-2
N01 (inc *Naropeine*)	34,421	1.4	0	0
N02 (analgesics) except N02C1, Buprenorphine and Methadone + N07C (antivertigo preparations)	881,691	1.4	0	0
N02C1 (antimigraine triptans)	132,991	1.4	0	0
N03A (antiepileptics) *(inc Taloxa*)	282,612	3.4	0	0
N04A (antiparkinson drugs) + Adartrel	111,347	3.4	0	0
N05A1 (atypical antipsychotics)	329,447	-2	-2	-2
N05A9 (conventional antipsychotics) + N06A3 (mood regulators)	86,201	1.4	0	0
N05B (hypnotics and sedatives) + N05C (tranquilisers)	198,063	-3.6	0	0
N06A (antidepressants) except N06A3 and Levotonine	481,039	-3.6	-5	-5
N06B (psychostimulants) + N07E (drugs used in alcohol dependence) + N07F (drugs used in opioid dependence) + Rilutek, Levotonine, Buprenorphine and Methadone	147,898	1.4	0	0
N07D (anti-Alzheimer products)+ Mestinon, Prostigmine and Mytelase	244,237	6.4	0	0
P (anti-parasitic products) + J04 (drugs for the treatment of tuberculosis and lepra) *(inc Eskazole, Lamprene and Notezine*)	14,754	1.4	0	0
R01A1 + A6 (nasal corticosteroids without anti-infectives and other topical nasal preparations) + R06A (systemic antihistamines)	342,968	1.4	-3	-3
R01A4 + A7 + A9 + B (nasal anti-infectives) + R02 (throat decongestant preparations) + A01 (stomatologicals)	88,297	1.4	-1	-1
R03 (anti-asthma and COPD products) except Pneumorel	980,589	1.4	-1	-1
R05 (cough and cold preparations)+ R07 (other respiratory system products)+ Pneumorel	90,808	-15	-2	-1

Group	2007 Sales in €K	2008 rate (K rate included = 1.4)	2009 rate (K rate not included)	2010 rate (K rate not included)
S01 (ophthalmologicals) other than S01E and S01P	117,483	1.4	0	0
S01E (miotics and antiglaucoma preparations)	211,611	1.4	-1	-1
S01P (ocular anti-neovascularisation products)	78,571	40	10	5
S02 (otologicals)	12,718	1.4	0	0
T01 (diagnostic imaging) + Helikit	135,296	1.4	0	0
T02X (other diagnostic tests*) (inc Metopirone*)	2,505	1.4	0	0
V06 (dietetic agents) + V07 (other non-therapeutic products)	41,509	-1.6	-5	-5
V03 (other therapeutic products) except Lederfoline and Folinoral + Mimpara, Phosphorous, Phosphoneuros and Sorbisterit calcium *(inc Cardioxane, Uromitexan, Ferriprox, Fasturtec and Ethyol*)	94,385	1.4	0	0
	21,211,158			

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 XXXX

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 ..... between the Comité économique des produits de santé (CEPS) and XXXX;
The Comité économique des produits de santé (CEPS) and XXXX 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

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

2. Pro-forma clauses regarding medicines

2.1. Pro-forma posology clauses

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[27] 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:

Erreur ! Des objets ne peuvent pas être créés à partir des codes de champs de mise en forme.

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 by CEPS of the sum of the rebate owing. The rebate shall be payable to the relevant URSSAF by the company within one month after receipt of the notice from CEPS. The company shall inform CEPS by courier 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).

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	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 ($CTJG_R$).

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

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 posologies of each of the products mentioned in 2.1 hereabove which are included in the most recent IMS-DOREMA 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 DOREMA data, or:

$$NJT_{in} = (\text{number of units per pack} \times \text{number of packs}_i) / Poso_{in}$$

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 $R_n = NJTG_n \times (CTJG_n - CTJG_R)$.

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 monitored every year, the first occasion being dd/mm/yy, on the basis of the most recent GERS data published before this date.
If the annual sales volume observed (V_n) is greater than the reference sales volume (V_R), the manufacturer price ex VAT shall be modified ($PFHT_{n+1}$) according to the following formula:

$$PFHT_{n+1} = a\,PFHT_n + (1 - a)\,PFHT_n X (V_R / V_n), \text{ where } 0 < a < 1.$$

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 sales volume observed is higher than the sales volume observed at the time of the first price change.

2.3 et sequ. (c.f. posology clause).

3. Pro-forma clause for medical devices

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

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) of dd/mm/yyyy;
whereby the Comité économique des produits de santé (CEPS) and XXXX agree on the following provisions:

Article 1: This agreement is made under the condition precedent that the decree relating to the registration of YYYY 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* (official bulletin).

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

Code	Category	Price before VAT	Tariff inc VAT	Max. public selling price inc VAT
3aaaaaa	YYYYYYYYYY	€ ----.--	€ ----.--	€ ----.--

Article 3: The company XXXX undertakes to inform the committee every year, during the mm month, for the year finishing in the mm month, and for the first time during the month mm/yyyy, of the total number of YYYY devices that it has sold in France during the previous year.

Article 4:

3.1 If the number (N) of YYYY devices sold every 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 the formula $P_M = (a \times P) + [(1-a) \times P \times (n/N)]$ *(where* $0 < a < 1$*)* and the company shall be liable for a clawback payment (R) which will 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.

3.2 Where there has already been one price reduction on the basis of paragraph 3.1. hereabove, no new price reduction may be introduced on the basis of paragraph 3.1. hereabove unless the number N' of YYYYY devices sold established on this occasion is greater than 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 for a clawback payment (R) where $R = (P_V - P_M) \times N'$.

3.3 The company shall be notified by CEPS of the sum of the rebate mentioned in Article 3 hereabove. The rebate shall be payable to ACOSS by the company within one month after receipt of the notice from CEPS. The company shall inform CEPS by courier of the date and actual sum of the payment.

Article 5: The company XXXX undertakes to conduct and fund a study …. The aim of this study will be: …. The results of the study shall be sent to CEPP and CEPS.

Done in Paris, on

MM — Chairman of the Comité

Company XXXX — des produits de santé

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 Social Security:
Jean-Philippe VINQUANT, Head, Healthcare Finance Department
Marine JEANTET, Deputy Head, Healthcare Finance Department
Lionel JOUBAUD, 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 Social Security:
Catherine LEFRANC, Head, Healthcare Products Policy Department
Nadine DAVID, Head, Medicines office
Alexandre BARNA, Medicines office

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

Representatives of the Director General for Companies - Ministry for the Economy, Finance and Industry:
Jean-Marc GROGNET, Head, 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 salaried workers)
Jean-Pierre ROBELET, Director, Health care supply
Jocelyn COURTOIS, Head, Healthcare products departments
Thierry DEMERENS, Deputy Head, Healthcare products departments
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

Representative of the Director for Hospital Care and Treatment Structure – Ministry of Health and Social Security
Dominique LAGARDE, Policy Officer, Directorate for Hospital Care and Treatment Structure

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

1.2. Medical devices section

N…. Vice-chairman

Representatives of the Director for Social Security – Ministry of Health and Social Security:
Jean-Philippe VINQUANT, Head, Healthcare Finance Department
Marine JEANTET, Deputy Head, Healthcare Finance Department
Lionel JOUBAUD, 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 Social Security:
Catherine LEFRANC, Head, Healthcare Products Policy Department
Stéphan LUDOT, Head, Office of Medical Devices and other Healthcare Products
Joëlle SCHACHMANN, Office of Medical Devices and other Healthcare Products

Representative of the Director for Hospital Care and Treatment Structure – Ministry of Health and Social Security:
Anne L'HOSTIS, Chief Public Health Medical Examiner, Policy Officer

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

Representatives of the Director General for Companies – Ministry of the Economy, Finance and Industry:
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, Health care supply
Jocelyn COURTOIS, Head, Healthcare products departments
Annie ARPIN-BARBIEUX, Deputy Head, Healthcare products departments
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, Caisse nationale du RSI

Representative of top-up health insurance bodies:
Martine STERN, 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 LEMEE-PECQUEUR,
Catherine PHILIPPE,
Michel ROUSSEAU,
Franck SUDON,
Bruno STALLA,
André TANTI.

3. Details of people working for the committee

Name	Role	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
Soheila Léger	Follow-up of agreements - Medicines	01 40 56 71 27	01 40 56 71 79	soheila.leger@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
Geneviève Uchida-Ernouf	Collection of international data	01 40 56 72 14	01 40 56 71 79	genevieve.uchida-ernouf@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				
Comité économique des produits de santé (Healthcare products pricing committee)				
Noël RENAUDIN	none	none	none	none
Bernard TEISSEIRE (M[28])	none	none	none	none
Sylvette LAPLANCHE	none	none	none	none
Michèle AUDEOUD-FAURIS (M)	none	none	none	none
Claire OGET-GENDRE (MD)	none	none	none	none
Michel ROUSSEAU	none	none	none	none
Carine FERRETTI	none	none	none	none
Directorate for Social Security				
Jean-Philippe VINQUANT	none	none	none	none
Marine JEANTET	none	none	none	none
Lionel JOUBAUD	none	none	none	none
Isabelle CHEINEY (M)	none	none	none	none
Chrystelle GASTALDI-MENAGER (MD)	none	none	none	none
Sam MOURAD (M)	none	none	none	none
Olivier VERNEY (MD)	none	none	none	none
Directorate General for Health				
Catherine LEFRANC	none	none	none	none
Stéphan LUDOT	none	none	none	none
Nadine DAVID (M)	none	none	none	none
Alexandre BARNA (M)	none	none	none	none
Joëlle SCHACHMANN (MD)	none	none	none	none
Directorate for Hospital Care and Treatment Structure				
Dominique LAGARDE (M)	none	none	none	none
Anne L'HOSTIS (MD)	none	none	none	none
Directorate General for Competition, Consumer affairs and Combating fraud				
Marie-Thérèse MARCHAND	none	none	none	none
Anne DUX	none	none	none	none
Jean-Yves SAUSSOL	none	none	none	none
Nolwenn DELARUELLE-LAPRIE (M)	none	none	none	none
Dominique MONAVON	none	none	none	none
Daniel MILES (MD)	none	none	none	none
Directorate General for Companies				
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

[28] 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*
Members of the committee and persons attending committee meetings				
Assurance maladie obligatoire (mandatory national health Insurance)				
Jean-Pierre ROBELET				
Monique WEBER	none	none	none	none
Jocelyn COURTOIS	none	none	none	none
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
Ministry of Research – Directorate General for Research and Innovation				
Isabelle DIAZ (M)	none	none	none	none
Régis BEUSCART (MD)	none	none	none	none
Union des organismes d'assurance complémentaire (Union of top-up health insurance companies)				
Martine STERN	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
André TANTI	none	none	none	none