The Economic Committee for Health Products

Activity Report 2003

July 2004

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In accordance with article D. 162-2-4 of the Social Security Code, the Economic Committee for Health Products presents a report each year on its activities to the ministers responsible for social security, health, the economy and industry. Article L. 162-17-3 of the Social Security Code also makes provision for the submission of this report to Parliament.

This report outlines the main activities of the Committee in 2003.

Part one deals with medicines and deals successively with the medicines market in 2003 (chapter I), with regulatory action taken by the Committee in application of the Social Security Code and ministerial guidelines (chapter II) and with pricing activities (chapter III).

Part two concerns health products other than medicines. Chapter I is devoted to a description of and the trend in the reimbursement of medical devices. Chapter II deals with the reimbursement of medical devices based on the opinions of the Committee and with the setting of tariffs and prices of products and services as defined by article L. 165-1 of the Social Security Code.

PART ONE - MEDICINES

CHAPTER I - THE REIMBURSABLE MEDICINES MARKET

1. Broad market trends

The development in 2003 of the French reimbursable medicines market and compulsory health insurance spending shares many more similarities than differences, compared with the findings for 2002.

The overall growth in sales, pharmacy sales and sales to healthcare establishments combined, will have risen by 6.5%, against 5.7% in 2002, the difference being explained almost entirely by sales in December 2003 due to a less favourable epidemic situation than in 2002. If we add specific factors - especially the 2001 price reductions - exerting a strong impact on the growth rate in 2002, it becomes clear that 2003 confirmed the slowing trend noted in the Committee's previous report.

Sales levels and growth are undoubtedly still too high compared with the collective resources available and diagnosed needs, but the trends observable in 2002 are still continuing: strengthening growth in generics, the relative abatement in the major growth categories of the past two decades, the concentration of innovations on medicines intended for restricted and well-identified populations.

It is true that the distribution of this overall growth in sales of medicines differs from that of 2002: pharmacy sales did in fact rise by 6.1% against 4.2% in 2002. The difference, besides the epidemic effect already mentioned, is however explained by a major shift from hospital to ambulatory - a growth area - the natural corollary of which is a deceleration in hospital sales.

For their part, reimbursements under compulsory health insurance schemes rose by 6.2%, against 6.5% in 2002, yet this slowdown is wholly ascribable to the specific effect of changes in the reimbursement rates occurring in 2003 and therefore does not affect the trend. On the contrary, the 2003 rate confirms, too, the slowdown recorded the year before compared with previous years (10.6% in 2000 and 8.5% in 2001).

This slowdown however is still far from adequate and, overall, public spending on medicines (ambulatory plus hospital) will therefore have reached EUR 20.7 billion in 2003, namely a contribution of 1.3 billion to the growth in health insurance spending and therefore far beyond what would have enabled the general target set for this year by Parliament to be met.

2. Analysis of ambulatory sales of medicines in 2003

2.1 TOTAL SALES

As a consequence of the absence of hospital transfers, the acceleration of sales of generics and price reductions, in addition to a more favourable epidemic cycle, the year 2002 had experienced only limited growth in the sales of medicinal products. Conversely, as a result of significant hospital transfers and more marked epidemic episodes, growth was stronger in 2003.

Until the end of November, sales were growing at a steady rate of 5.5% compared with the previous year. The epidemic episode in December caused them to rise sharply (12.7% in December 2003 compared with December 2002) leading ultimately to a growth in ambulatory sales of reimbursable medicinal products of 6.1% over the year.

Table 1: Four-monthly trend in ambulatory sales of medicines in 2003

	1st 4-month period		2nd 4-month period		3rd 4-month period	
	Number	Index	Number	Index	Number	Index
Number of packs sold (10^6)	948 M	100	817 M	86.2	990 M	104.4
Average pre-tax price per pack (€)	5.52 €	100	6.11	110.7	5.67 €	102.7
Turnover (10^6 €)	5,235 M€	100	4,992 M€	95.9	5,613 M€	107.2

Sales at pre-tax ex-factory prices (PFHT) in 2003 stood at €15.84 billion up by €0.9 billion compared with 2002. An acceleration in the growth of sales compared to the previous year (4.2% and €0.6 billion in 2002 compared with 2001) was witnessed. In the main (1% and €150 million), this acceleration is a result of the transfer to ambulatory care of medicinal products previously reserved for hospital use. At the same time, on account of these transfers, hospital purchases experienced a deceleration in growth, from 11.5% in the previous year to 8.2% in 2003, standing at €3.96 billion.

Table 2: Trend from 2002 to 2003 of ambulatory sales of reimbursable medicines

	Number of packs sold - 10^9	Sales at pre-tax ex-factory prices - 10^9 €	Retail sale price after tax (10^9 €)	Average pre-tax ex-factory price, per pack	Average retail sale price after tax, per box
2003	2,755	15,840	23,197	5.75 €	8.42 €
2002	2,738	14,932	22,002	5.45 €	8.03 €
Trend	0.6 %	6.1 %	5.4 %	5.5 %	4.8 %

At public sales prices after tax (PPTTC), the shift in sales towards more expensive products results, on account of the degressivity of margins, in a reduction of nearly one point in the average markup rate and therefore in slower growth in sales and average prices measured at the public sales price than that measured as the pre-tax ex-factory price. It is of course the markup rate and not the markup itself which, in order to adhere to the regulated margin, rose in 2003 by just under 4%.

2.2 THE COMPONENTS OF GROWTH

The 6.1% rise in turnover may be analysed as:

- a reduction of 0.4% in the unit price of packs of medicines compared with the previous year (price effect)[1];
- a growth of 0.6% in the number of packs in 2003 (pack effect);
- a rise of 5.5% in the average price per pack at a constant unit price for presentations (structural effect). This structure effect corresponds to a distortion in the structure of sales towards more expensive presentations, whether it be a shift in sales towards costly therapeutic classes or, within the same therapeutic class, a shift in consumption towards medicinal products marketed at higher prices.

Table 3: The growth components of ambulatory sales

Year	Price effect	Pack effect	Structural effect	Total growth
2003	- 0.4 %	+ 0.6 %	+ 5.5 %	6.1 %
2002	-1.6 %	+ 0.7 %	+ 5.1 %	4.2 %
2001	- 1.3 %	+ 1.2 %	+ 7.3 %	7.2 %
2000	- 0.9 %	+ 2.9 %	+ 6.8 %	8.9 %
1999	- 0.7 %	+ 1.8 %	+ 5.5 %	6.6 %

The price effect, negative as in previous years, is nonetheless less pronounced, in the absence of significant reduction measures in 2002 and 2003.

At + 0.6%, the pack effect is the lowest it has been in the past five years. This increase in volumes of sales is at the same level as the increase in the general population.

Table 4: Trend in number of packs sold

millions of packs

	Volumes 2002	volumes 2003	Trend	Rate of trend
Generics	230	311	+ 81	+ 35.2 %
Non-generics	2,508	2,444	- 64	- 2.5 %
Overall	2,738	2,755	+ 17	+ 0.62 %

The increase in ambulatory sales in 2003 stems primarily, as in previous years, from the structure effect, which alone accounts for 9/10ths of the recorded growth.

2.3 THE GENERIC DRUGS MARKET

Between 2002 and 2003, the number of packs of generic drugs sold (see table 4) rose by 80 billion, from 230 to 311 million packs, whereas sales of non-generic drugs fell by over 6 billion packs. This growth, sustained by substitution, occurred mainly in the period predating the introduction of the first reference prices (*tarifs fofaitaires de responabilité*, TFR).

[1] This price trend is calculated on products sold both in year n and in year n-1.

Compared with 2002, turnover in generic drugs rose by €262 million, namely 43%, which allowed savings of approximately €130 million (namely 0.8 points) on sales in 2003.

Table 5: Trend in the generic drugs market in 2003

units in millions / value in millions €

	2002*		2003**	
	Units	Value	Units	Value
Ambulatory market	2,738	14,932	2,755	15,840
of which the non-generics market	2,508	14,323	2,444	14,969
of which the generic groups market	575	2,190	600	2,219
of which the generics market	230	609	311	871
Share of generic groups in the total market	21.0 %	14.7 %	21.8 %	14.0 %
Share of generics in the generic groups market	39.7 %	27.8 %	50.6 %	39.3 %
Total market share of generics	8.4 %	4.1 %	12.4 %	5.5 %

* On the basis of the AFSSAPS list appearing in the JO of 27 October 2002

** On the basis of the AFSSAPS list appearing in the JO of 9 January 2004 (decision of 23 December 2003).

In terms of volume, sales of generics therefore accounted for most sales in the generic groups and nearly 40% of turnover for these groups.

In 2003, the average pre-tax price per generic pack sold rose by 5.8%, i.e. at a slightly faster rate than the price of medicines as a whole. This increase corresponds to the patent expiry of more costly medicinal products. Nevertheless, the general shift in sales towards the most expensive medicinal products is also beginning to affect the generic groups and is contributing to this rise in the average price.

The average markup rate in 2003 will have been 64% on generic drugs, against 45% for non-generics.

Table 6: Generics and non-generics: volume, prices and margins in 2003

Market	Units (10^6)	Average PFHT	Average PPTTC	Margin	Markup rate
Generics	311	2.80 €	4.6 €	1.80 €	64 %
Non-generics	2,444	6.12 €	8.9 €	2.78 €	45 %
Overall	2,755	5.75 €	8.42 €	2.67 €	46.4 %

2.4 THE PRICE OF MEDICINES

2.4.1 The INSEE price indices

INSEE calculates annually the price indices of pharmaceutical specialities, both reimbursable or non-reimbursable by Social Security.

Table 7: Prices indices of pharmaceutical specialities

(base 100 in 1998)

Year	Reimbursable specialities		Non-reimbursable specialities	
	December	Annual Average	December	Annual Average
1999	99.1	99.5	103.4	102.4
2000	98.2	98.8	105.1	104.7
2001	96.0	97.5	107.7	106.3
2002	95.7	96.0	110.5	109.4
2003	94.6	95.2	116.2	113.3

Source INSEE – Monthly statistical bulletin 2004, n° 2.

The trend in this index, calculated at a constant market on the basis of public prices, shows a continued downward movement in reimbursable pharmaceutical specialities which remains significant in 2003 (-0.8%), despite the absence of significant price reduction measures, owing to the development of the generic drugs market (now taken into account in the index) and alignments in the prices of originator drugs in the groups of medicines subject to the reference price reimbursement system (TFR).

The INSEE index does not however allow account to be taken of newly registered pharmaceutical specialities other than generics or the shift in consumption towards these specialities which are by and large more expensive, allowing instead an examination to be made of the price of packs of medicinal products.

2.4.2 The average price of medicinal product packs

The average price of "packs" sold is obtained by dividing the annual turnover by the number of units (packs) sold that same year. It relates to all products sold in a given year whatever their market share. It therefore incorporates prices and their variation, but equally the "structural" effects.

Table 8: Trend from 1999 to 2003 in the average price of reimbursable medicinal product packs sold and margins (1998 = 100 index)

	1998	1999	2000	2001	2002	2003
Average PFHT per "pack"	4.48 €	4.69 €	4.98 €	5.29 €	5.47 €	5.75 €
Trend / year n-1	-	+ 4.7 %	+ 6.2 %	+ 6.2 %	+ 3.4 %	+ 5.1 %
Index (100 in 1998)	100	104.7	111.2	118.1	122.1	128.3
Average PPTTC per "pack"	6.60 €	6.99 €	7.37 €	7.87 €	8.03 €	8.42 €
Trend / year n-1	-	+ 5.9 %	+ 5.4 %	+ 6.8 %	+ 2.0 %	+ 4.8 %
Index (100 in 1998)	100	105.9	111.6	119.2	121.7	127.5
Average margin	2.12 €	2.30 €	2.39 €	2.58 €	2.56 €	2.67 €
Margin rate	47.3 %	49.0 %	48.0 %	48.8 %	46.8 %	46.4 %

After relatively moderate growth in 2002, the consequence of reductions for drugs with an insufficient medical benefit (SMR) and targeted reductions in 2001, the average price per medicinal product pack rose again in 2003 despite the development of the generics market and despite the falls in most originator drugs of groups corresponding to the TFR rates and paracetamols. As a result of the degressivity, the reduction in the margin rate observed in

2003, as in 2002, and the scale of this reduction, resulted in shifts in prescriptions towards more expensive medicinal products, possibly towards new medicinal products sold at markedly higher prices.

2.5 TREND BY THERAPEUTIC CLASS

Table 9: Contribution by classes to the growth in sales

millions of €

Classes	Pre-tax Turnover 02	Pre-tax Turnover 03	Difference	Growth
Statins	812	947	135	16.5 %
Proton pump inhibitors	831	941	110	13.7 %
Anticancer drugs	278	379	101	73.4%
ACE inhibitors and sartans	927	1,021	94	10.1 %
Antiasthmatics	679	746	67	9.8%
HIV and hepatitis drugs	186	251	65	34.9%
Platelet aggregation inhibitors	280	345	65	23.1%
Osteoporosis drugs	109	157	49	44.9%
Vaccines	168	213	45	26.8%
Antidiabetic drugs	378	412	34	9.2%
Total	4,648	5,412	764	16.4%

This table groups the 10 classes or aggregates of classes[2] with the largest disparity in pre-tax turnover (CAHT) in 2003 compared with 2002. They appear in the table in descending order according to the scale of the disparity. The appearance in this table of cancer, hepatitis, HIV and diabetes drugs, as well as vaccines, is of note. These classes replace, in the top group, four central nervous system classes which appeared in the 2002 table: Anti-alzheimers treatments, antidepressants, anti-psychotics and analgesics.

The average growth in these classes, which account for almost one third of the overall market, is 16.4%.

Conversely, as in 2002 the biggest decline was in antibiotics whose volume of sales fell by 8.5% and turnover by 7.6%, along with all nootropes-vasodilatators whose turnover fell by 12.3%. Added to this are hormone replacement treatments. It is worth noting that for all antibiotics, the faster reduction in volumes than in turnover translates for this sharply declining class in a relative shift in sales towards more expensive products.

3. The growth in reimbursements

The reimbursement of costs relating to medicines reassigned by hospitals (*rétrocession*) is included in health insurance expenditure. It is advisable, therefore, in tracking compulsory health insurance reimbursements, to consider the sum of outpatient pharmacy sales corresponding to hospital *rétrocessions*.

[2] These aggregates are presented in Annex 3 in the Table of thresholds triggering discounts by aggregate.

3.1 LA *RÉTROCESSION HOSPITALIÈRE*

According to the estimates of the Public Accounts Office, medicine sales reassigned by hospitals (*rétrocession*) increased in 2003 by 11.8%. For 2002, the final figure recorded by the Healthcare and Hospitalisation Directorate with regard to *rétrocession* is €1.29 billion. The 11.8% increase is said to correspond to sales in 2003 of €1.44 billion (see following table). On these assumptions, total sales after tax of reimbursable medicines would be €24.64 billion in 2003, namely an increase of 5.8% compared with the previous year.

Table 11: Total sales after tax of reimbursable medicines

Millions of €

Year	Ambulatory sales (inc. tax)	*Rétrocession* (inc. tax)	Total turnover (inc. tax)
2002	22,002	1.287	23,289
2003	23,196	1.439	24,636
Rate of growth from 2002 to 2003	5.4 %	11.8 %	5.8 %

3.2 REIMBURSEMENTS UNDER THE GENERAL SCHEME

Compulsory health insurance reimburses, on the basis of their public price inclusive of tax, medicines sold in retail pharmacies and medicines reassigned by hospitals (*rétrocession*), where they have been prescribed by a qualified health professional and presented for reimbursement.

The average actual reimbursement rate calculated by the CNAMTS for the general scheme (*régime général*) is 74.9% in 2003 (74.8% in 2002[3]). The average actual rate of reimbursement is equal to the ratio between the reimbursements made under the general scheme and the value, inclusive of tax, of medicines presented for reimbursement. The calculation of this actual reimbursement rate incorporates reimbursements relating to hospital reassignments (*rétrocession*) which are considered to be 100% reimbursed.

According to CNAMTS figures displayed in table 12, *rétrocession* expenditure rose, on the reimbursement date, by 30.1% in 2003 compared with 2002. The considerable disparity between the growth in sales estimated by the Public Accounts Office (see 3.1 above) and that of reimbursements recorded by the CNAMTS is surprising; the time lag between sales and their invoicing by hospitals could however go some way to explaining the gap.

Reimbursements relating to retail pharmacy sales reportedly rose by 4.6% (compared with 5.4% growth in retail pharmacy sales inclusive of tax) and the total reimbursements rose by 6.4%.

[3] Monthly statistics. Results at end December 2002 and Results at end December 2003 – DSE - CNAMTS

Table 12: Reimbursements under the general scheme

Millions of €

Year	Ambulatory	*Rétrocession* [4]	Total[5]
2002	13,463 (73.5 %)	1,008 (100 %)	14,471 (74.8 %)
2003	14,083 (73.2 %)	1,311 (100 %)	15,394 (74.9%)
Rate of growth from 2002 to 2003	4.6 %	30.1 %	6.4 %

The sum of health insurance reimbursements is subject to the trend in tax-inclusive sales incorporating hospital *rétrocession*, the distribution of sales of medicinal products according to their reimbursement rate of 35%, 65% and 100%, and finally to the trend in sales without patient co-payment, especially in cases of protracted illness (*affections de longue durée*) for which prescribed medicines are fully reimbursed.

From 2002 to 2003, ambulatory sales increased by 5.4% at public prices and reimbursements under the general scheme by 4.6%. The 0.8% gap arises basically from the impact of the changes in the reimbursement rate which under the general scheme alone, according to CNAMTS[6], accounts for savings of €135 million. As regards ambulatory sales, this fall in reimbursement rates more than offsets the structural increase in the average rate of the reimbursement of medicines.

Overall, according to the statistics produced by the National Sickness Fund for Salaried Workers (CNAMTS), reimbursement of medicines under the general scheme rose in 2003 by 6.4%. For compulsory health insurance schemes as a whole, according to the finding whereby reimbursements under the general scheme normally increase more quickly than those under other schemes[7], the increase in reimbursements could well be of the order of 6.1% to 6.2%.

In 2003, on average, each inhabitant of metropolitan France purchased from retail pharmacies 46 packs of reimbursable medicines totalling €387, of which 5 packs were generic drugs at an average price after tax of €4.6 per pack and 41 packs were non-generics at an average price of €8.9. These medicinal products presented for reimbursement gave rise in over 95% of cases to reimbursement under compulsory health insurance scheme of €290. Moreover, on average, each inhabitant spent €25 on medicinal products in hospital pharmacies which were fully reimbursed from compulsory health insurance funds.

[4] point conjonturel n° 23 - March 2004 - DES - CNAMTS

[5] Monthly statistics Results at end December 2002 and Results at end December 2003 – DSE - CNAMTS

[6] point conjonturel n° 21 – January 2004 - DES - CNAMTS

[7] Chiefly on account of the proportionally more rapid increase in the number of persons taken on by the general scheme.

CHAPTER II – THE INSTITUTIONAL CONTEXT AND REGULATION

1. The institutional context

On the eve of the opening of a new conventions period, the Social Security Finance Law for 2003 of 20 December 2002 entailed several provisions concerning medicines, the implementation of which in accordance with the ministerial guidelines of 24 December 2002, influenced the activities of the Committee as well as the negotiations and content of the new framework agreement (*Accord Cadre*) reached with drug companies.

1.1 THE SOCIAL SECURITY FINANCE LAW FOR 2003

The Social Security Finance Law for 2003 contained a variety of measures relating to medicines. Alongside provisions with a directly financial effect such as the reform of the assessment basis and of the tax rates on promotion, the text amended the rules applicable in several important respects.

The new article L. 162-17-4 of the Social Security Code provides the possibility for an accord to specify the framework for conventions establishing relations between the Committee and each drug company, thereby giving a legislative foundation to collective agreements entered into between CEPS and representatives from the pharmaceutical industry.

In order to step up access by patients to the most innovative medicinal products, the law likewise provides a procedure for the fast-track pricing of these medicinal products according to rules to be specified in the framework agreement (*Accord Cadre*) or, failing that, by decree (new article L.162-17-6).

Two provisions relate to generic drugs. First of all, it is now possible to create generic groups for molecules for which no benchmark medicinal product exists. Above all, reimbursement reference prices (TFR) may be set, within the generic groups, limiting health insurance reimbursement to amounts which are possibly lower than the purchase price of the medicinal products belonging to these groups.

The law institutes a new system of sanctions, on the Committee's advice, in the event of a publicity ban or misrepresentations by the company when registering a product. This new system of sanctions was not applied in 2003 as no breach postdating the introduction of the law gave rise to a ban.

1.2 MINISTERIAL GUIDELINES

In their letter to the Committee dated 24 December 2002 (Annex 1), the ministers set forth the guidelines which they wish to see it follow in 2003 in respect of pricing, expenditure tracking and the financial regulation of the medicine market as well as the implementation of the provisions of the Social Security Finance Law for 2003.

Emphasising their attachment to the conventions procedure and the need for proper recognition of innovation, the ministers state in this letter specific objectives of the future framework agreement (*Accord Cadre*) and express in particular their wish to see, without

exception, the price of the most innovative medicinal products fixed and maintained for a period of five years at a level in line with the price charged in the major European countries.

As for savings to be made, the ministers' letter focuses on the vital development of generics and calls on the Committee to be increasingly vigilant towards the registration of medicinal products which could hinder such development. They also ask that the Committee propose principles for the initial implementation of reimbursement reference prices (TFR).

The letter ends by inviting the Committee to combine whenever necessary the registration of new medicinal products with studies which allow their use and effects in practice to be observed.

1.3 *ACCORD CADRE* 2003-2006

The negotiation of the future framework agreement (*Accord Cadre*) between drug companies and the Committee began in January 2003. At the end of 12 meetings held between January and May, the agreement was signed on 13 June 2003 (see Annex 2). Relating to the period 2003-2006, it borrows heavily in terms of architecture and form from the previous sector-based agreement (*Accord Sectoriel*) together with the annual financial regulation mechanisms whilst of course incorporating the consequences of the new provisions of the law and the ministerial guidelines.

1.3.1 Acceleration of registration procedures

The speeding up of registration procedures is one of the main advances of the 2003-2006 framework agreement (*Accord Cadre*) by comparison with the previous sector-based agreement (*Accord Sectoriel*). It relates primarily to medicinal products granted centralised marketing authorisation for which the preliminary examination of dossiers may be carried out at the company's request, to medicines benefiting from an improvement in medical benefit (ASMR) and to paediatric drugs which the Committee undertakes to propose or reject, giving reasons, no later than 75 days from the transmission of the Transparency Commission's opinion, and to the most innovative medicinal products for which the price notification procedure is envisaged.

Companies subscribing to the agreement may ask - for medicines awarded by the Transparency Commission an ASMR of level I, II and level III on the assumption of a projected turnover of less than €40 million in the 3rd year - to benefit from the price notification procedure, at the end of which, unless opposed by the Committee within 15 days following the company's application, the price it proposes is accepted. The proposal is non-negotiable. The company must therefore propose straightaway, in accordance with the framework agreement (*Accord Cadre*), a price coherent with the prices accepted throughout the major European markets. It must also commit itself to any studies that might be demanded of it as well as to sales volumes predicted in the first 4 years of commercialisation and to the consequences arising in the event that these volumes are exceeded.

The Committee's objection to the price notification must be reasoned. It may be based primarily on explicit public health considerations, on the excessiveness of the proposed price or on the obvious inadequacy of the company's commitments. In the event of an objection, pricing will be carried out subject to the conditions ordinarily applicable.

1.3.2 Follow-up studies

In the framework agreement (*Accord Cadre*), the parties agree to the importance attached to introducing studies on the use in real situations of the new medicines awarded a level I, II or III ASMR rating, since these medicines may be used by a wide population, or are likely to have a significant impact on the organisation of the health system, or might be used for other than the stated indications thereby exposing the treated population to an unassessed risk. The framework agreement (*Accord Cadre*) specifies, moreover, the conditions under which such studies are carried out, financed and used.

1.3.3 The recognition of innovation in the regulation

Besides orphan drugs, paediatric drugs and low-cost drugs including generic drugs benefiting from an exemption from rebates by pharmacotherapeutic aggregate, the 2003-2006 framework agreement (*Accord Cadre*) likewise provides that from now on, all medicinal products awarded an ASMR rating by the Transparency Commission will benefit from such an exemption. With effect from the date of their marketing, medicinal products awarded an ASMR I or II rating will benefit from a total exemption for 36 months or 24 months, respectively. For ASMR III and IV, the exemption will be 50% and 25%, respectively, for 24 months. It should be noted, in the event of an indication extension for which the medicine benefits from an ASMR, or an ASMR for part of the indications of a medicine, then these exemptions apply to the share of sales corresponding to those indications.

2. Regulation in 2003

2.1 THE INTRODUCTION OF REFERENCE PRICES (TFR)

Article 43 of the Social Security Finance Law for 2003, amending article L. 162-16 of the Social Security Code, establishes the possibility of reimbursement limited to a reference price drawn up by health and social security ministers, on the advice of CEPS, for the medicines featuring in the same generic group.

Prompted to put forward proposals for the initial application of this new enacting clause, the Committee set out to find the best possible compromise between immediate and certain savings resulting from the introduction of TFR and the need to maintain a strong generic offering, a precondition of the sustainability of the system in the long-term.

Indeed, it seemed to the Committee that the reference prices might only be socially accepted if they did not culminate, in practice, in payment of the excess by a significant proportion of patients and that, as a consequence, reference prices should only be introduced in those groups and at such a starting price as to ensure a sufficiently plentiful offering so that all patients who so wish are sure of obtaining the medicinal product at a price equal to the reference price. Account was thus taken of the reservation voiced on this matter by the Constitutional Council by not running the risk of creating unequal access to care which would depend on the behaviour of prescribers.

This led, marginally, to the abandonment of subjecting to reference prices some groups - of insignificant value - in which there are virtually no generics, due for example to the fact that the price of the originator drug is too low compared with drug manufacturing costs to allow the use of generics which are cheaper still.

The Committee believed above all that the growth of the French generics market continued to play a key regulating role in the medium to long term for the overall medicine market. There is indeed no doubt that the possibility of introducing reference prices which allow collective savings to be made following the lapse of patents without passing on the cost to patients rests on the existence of a credible alternative offering of generics and therefore on the existence of powerful generics suppliers.

Now, uncertainty surrounded the manner in which sales would be distributed, in groups where reference prices were introduced, between the generics and the originator drug in the event that the prices of the originator drugs were aligned with the reference price.

On the basis of the Committee's proposals and an analysis of the rates of penetration of generics in the different classes at the end of the first four months of 2003, the ministerial decree of 29 July 2003 drew up the list of 29 molecules, corresponding to 61 generic groups and 72 tariffs applicable to the different pharmaceutical specialities concerned. This list included the generic groups in which the penetration rate of generics ranged between 10 % and 45 %.

Reference prices were first introduced on 8 September 2003, with the fixing of new price labels, and became wholly effective from 23 October with the discontinuation of reimbursement of the old labelled packs.

In 70% of cases the companies manufacturing the originator molecules immediately aligned their prices with other containment flat rates. In one case, one of the manufacturers decided to increase the price of its originator drug..

For 2003, the impact on turnover after tax of the changes in price of the originator drugs of the TFR groups was €25 million (€15 million excluding tax) and that of the reduction in generics margins was €7 million, namely €32 million in total.

The rate of penetration, as a value inclusive of tax, of generics of the TFR groups which, over the first eight months of the year, stood at 25%, increased twofold to 49% over the last two months of the year. The price alignment of the originator drugs appears not to have led to an ebbing of generics but has without doubt curbed their growth, as might be expected, compared with the groups in which the originator drugs was not aligned.

Overall, the development of the generics market and the introduction of TFR are believed to have reduced by €145 million (€130 million and €15 million, respectively), i.e. by 0.9 points, the growth of pre-tax ambulatory sales of medicines.

2.2 DELISTINGS AND CHANGES IN REIMBURSEMENT RATES

Responsibility for these decisions does not lie with the Committee but with the Minister. Insofar however as such decisions have an impact on the operation of the companies concerned and on the trend in health insurance spending, it is worth recalling that:

- By decree of 24 September 2003, 82 of the 835 pharmaceutical specialities whose medical benefit (SMR) had been regarded as insufficient by the Transparency Commission at the time of their reassessment were struck off the reimbursement list.

In 2002, ex-manufacturer price pre-tax sales of these specialities stood at €39 million.

- Following the reassessment, the decree of 18 April 2003 drew up the list of 616 specialities with weak or moderate medical benefit (SMR) whose reimbursement rate fell from 65% to 35%. The annual turnover in 2003 at public sale price after tax of these products was €1.51 billion. In the absence of their substitution by better reimbursed medicinal products, the CNAMTS estimates the savings likely to result over a full year from this measure for all health insurance schemes to be €356 million.

2.3 CONVENTIONS

The framework agreement (*Accord Cadre*) of 13 June provides for the signing on an individual basis by companies of a multiannual convention. These incorporate, in an initial section, the list of reimbursable medicines marketed by the company and the clauses relating thereto, in a second section, the company's commitments towards promotion and finally, in a third section, the company's accession to the agreed mechanism exempting them from the " safeguard" clause. These conventions, amendable by codicil, are updated each year, prior to the end of the 1st half-year, to take into account changes in companies' portfolio likely to affect the first two sections and prior to 31 December as regards the third section.

In 2003, companies received the first and second sections of the convention, soon after the finalisation of the *Accord Cadre*, supplemented in October by the dispatch of the table of aggregates (see Annex 4) with, from November onwards, following negotiations and scrutiny in session by the Committee, the dispatch of the third section of the convention outlining the accession by the company to the agreed mechanism exempting it from the " safeguard" clause and setting the ceilings and thresholds applicable to the calculation of quantitative year-end rebates as well as the applicable exemptions and usable rebate credits.

2.3.1 Rebates by aggregate

Rebates by aggregate are linked to the overall trend of sales in aggregates. They are the key element of the year-end agreed mechanism.

The 2003 table of thresholds triggering rebates by aggregates, drawn up following consultations with companies, was annexed to the proposed codicil sent to each company at the start of the year-end agreement campaign.

At the request of companies, the 2003 table (see Annex 3), devised and balanced on the basis of the same principles as the previous table of classes, now shows only 65 aggregates as opposed to 147 classes previously.

The call-up rate of aggregate rebates was maintained as in the previous year at 28% of the overrun as was the division of the rebate between the section based on the turnover achieved in the aggregate (65%) and the section based on the growth in that turnover (35%).

2.3.1.1 Exemptions

Under the new rules of the framework agreement (*Accord Cadre*), all products which, at the time of their registration or extension of their indication, benefited from an ASMR, at whatever level, were exempted, wholly or in part according to ASMR level, from the

corresponding aggregate rebates. The same applied to orphan drugs and paediatric drugs, the latter being considered in the application of the new exemption rules as benefiting from an ASMR at a level immediately above the one awarded by the Transparency Commission.

The generic drugs as well as the low-price drugs mentioned in the codicils were exempted from any aggregate rebate, as was the share of sales not presented for reimbursement.

2.3.1.2 Reductions

The framework agreement (*Accord Cadre*) now specifies the mechanism whereby specific rebates paid under particular conventions applicable to certain medicines are deducted from the turnover serving to calculate aggregate rebates.

Besides the rules made explicit in the agreement (*Accord Cadre*), the Committee accepted a reduction in the rebate due for medicines launched in 2003 or late in 2002, for which the mechanism for calculating rebates led to an abnormal contribution by way of the growth recorded between the two years.

2.3.2 Rebates on turnover

As regards rebates on turnover, agreed codicils were negotiated as in previous years by taking into account, as an indicator, the estimation of the safeguard contribution which each company would have had to pay in the absence of a convention.

This indicator, pursuant to the framework agreement (*Accord Cadre*), was systematically adjusted for those companies whose growth on the ambulatory market in 2003 resulted from the rise in their sales of generic drugs, from the transition to ambulatory distribution of medicines hitherto sold in hospitals, from medicines not presented for reimbursement or from medicines subject to TFR. In 2003 however, as the very sharp increase in sales in December had not been anticipated, the Committee underestimated the value of the safeguard contribution indicator, leading to a limited yield from the rebate on turnover.

2.3.3 The rebate ceiling

In many cases, as in previous years, companies wanted rebate ceilings to be set by convention, either for total rebates or for rebates on turnover only. It was major firms who most wanted a ceiling on total rebates to be set in order to safeguard their provisions set aside when drafting their annual accounts. In most cases, the Committee accepted a ceiling slightly higher than the expected yield from rebates as assessable at the time of negotiations.

Turnover rebate ceilings could be set particularly in the case of a disagreement between the company and the Committee over sales estimates, where the Committee’s forecast was lower than that of the company. In such instances, the threshold was set at a level which allowed the expected yield to be achieved if the Committee’s low forecast proved right, and a rebate limited to the ceiling if the company's forecast was accurate or even exceeded.

2.3.4 Rebate credits

The 2003 – 2006 framework agreement (*Accord Cadre*) provides that rebate credits acquired by companies during the 1999 – 2002 agreement period and still unused at the end

of that period may be carried forward for those companies subscribing to conventions. The sum of credits carried forward from the previous year stood at €119 million, rising by €36 million in 2003 by taking into account, pursuant to the framework agreement (*Accord Cadre*), the impact of price reductions and dereimbursement, the financing of leaflets in Braille and in part the impact of price reductions for originator drugs included in the TFR groups. In 2003, €64 million were available for use by companies eligible for credits to offset their year-end quantitative rebates or their specific rebates. Following payment of their 2003 contribution, the balance of rebate credits still available to companies stands at €91 million.

2.3.5 Overview of the regulation

2.3.5.1 The signatory companies

172 of the 180 companies operating in the ambulatory market in 2003 signed up to the agreed convention exempting them from the "safeguard contribution". Accordingly, they were able to benefit from the provisions of article L.138-10 of the Social Security Code which provides that companies who have entered into a convention with the Economic Committee for Health Products valid as at 31 December of the year in which the contribution is due are not liable for payment of the contribution required in that selfsame article. The signatory companies were likewise able, within the framework of this agreed mechanism, to benefit from the measures set forth in the framework agreement (*Accord Cadre*) to offset the year-end quantitative rebates.

8 companies accounting for a total of 1/1000th of ambulatory sales of reimbursable medicines did not sign a convention. All but one were very small companies, most of whom were no longer producing reimbursable medicines by the end of 2003.

In 2003, the Committee maintained for 75 companies whose expected turnover was less than €10 million, the system whereby their year-end quantitative rebates were set at a ceiling of 1% of turnover.

2.3.5.2 Financial results

Total rebates paid to ACOSS by pharmaceutical companies for 2003 will have been €190 million. This sum, net of usable rebate credits available to the companies, encompasses year-end quantitative rebates and specific rebates per product, without the possibility of making a distinction between what pertains to one or the other in this overall amount. Indeed, the undifferentiated allocation of rebate credits to offset all or part of the year-end rebates or specific rebates, as indeed the impact of the deductions of specific rebates on the year-end quantitative rebates, prevent a coherent presentation of the itemised rebates.

For the record, the 2003 safeguard contribution would have been €153 million.

CHAPTER III – PRICING OF MEDICINES

The pricing of medicines is the primary task of the CEPS and its core activity. This activity will be related on the one hand, from a quantitative point of view, by a census of the features of the dossiers forwarded, scrutinised and processed by the Committee in 2003 and

their processing times, and on the other hand by presenting the pricing methods to which the Committee referred in its negotiations with companies, in the wake of the ministerial guidelines for 2003.

1. Activity of the medicines section in 2003

Faced with a slight rise in the influx of new applications, the heightened level of activity throughout 2003 resulted in a significant reduction in the backlog of pending cases. Moreover, the reprocessing of CEPS files led to the actual abandonment of a number of old applications which had not yet been formally closed. Overall, cases were processed more rapidly in 2003. The fact remains nonetheless that there were significant delays which in part account for the remedial measures taken in 2003.

Below is a review of the activities for 2003, an analysis of processing periods and finally an analysis of the backlog of pending dossiers at the close of the year.

1.1 REVIEW OF THE ACTIVITIES OF THE MEDICINES SECTION IN 2003

1.1.1 Applications submitted to the Committee in 2003

Recorded in terms of number of presentations, 1,209 applications were filed with the Committee between 1 January and 31 December 2003. This represents an increase of 4% over the previous year. These 1,209 presentations correspond to 537 dossiers per product, 294 of which, i.e. more than half, relate to generic drugs.

Table 13: Dossiers filed in 2003

Number of applications:	1st registration	Re-registration	Price change	Extension of indication	Total
Per presentation	631	2	482	94	1,209
Per dossier	375	2	118	42	537
of which are generics dossiers	242	1	50	1	294

There were virtually no re-registrations in 2003 following the transition from 3 to 5 years of the validity period of registrations in 1999. The other application categories all rose sharply compared with 2002, especially price change applications which increased threefold on the previous year due primarily to the introduction of the TFR.

Initial registration applications also increased on account of registrations of generics which accounted for two-thirds of such applications in 2003, double that of 2002.

1.1.2 Dossiers closed in 2003

In 2003, 624 dossiers corresponding to as many products and to 1,335 different presentations were successfully concluded either by an agreement reached between the company and the Committee giving rise to a publication in the Official Journal, or by a rejection or abandonment.

Table 14: Number of dossiers concluded in 2003
according to type of application and decision

	1st registration	Re-registration	Price change	Extension of indication	Total
Agreement	350	93	86	30	559
Abandonment*	16	-	6	4	26
Rejection	12	-	24	3	39
Total	378	93	116	37	624

* Abandonments are decided by the Committee either in the case of explicit withdrawal by a company of its application, or when it does not accept the Committee's proposal and persistently fails to act.

The 624 dossiers processed by the Committee in 2003 were filed by 135 different companies, namely 70% of the companies operating on the French market.

1.1.3 Applications pending

The "outgoing" flow made up of the number of applications conclusively dealt with in 2003 - which stands at 624 cases - should be brought more closely into line with the "incoming" flow of dossiers filed in the same year, namely 537 applications. The difference between these two figures, i.e. 87, gives rise to a decrease by the same amount in the number of dossiers pending, which stood at 229 at the close of 2003.

Among these 229 dossiers were 156 applications for initial registration, 73 of which had been scrutinised in session by the Committee prior to 31 December 2003. For 33 of the applications already scrutinised, a decision was taken on that date and publication of the price reports was in progress. On average, as at 31 December 2003 applications for initial registration had been on file for 120 days.

1.2 DOSSIER PROCESSING TIMES

Article R.163-7-I specifies that for the registration of a medicinal product "decisions (…) have to be taken and notified to the pharmaceutical company within a period of one hundred and eighty days following receipt of the application (…). The registration of the medicinal product on the list and its price shall be published in the *Journal Officiel* within this period.". As regards price change applications filed by companies, the Committee is required to reach a decision within a period of under 90 days.

The following account analyses, according to type of application and decision taken by the Committee, the processing periods for dossiers, from the time of their filing until the publication, where appropriate, of orders or notices in the *Journal Officiel* (abandonments or rejections do not give rise to publication in the JO). It therefore incorporates the processing times of cases by the Committee but also the periods relating to the perusal of these dossiers by the Transparency Commission.

The new price notification procedure arranged by the framework agreement (*Accord Cadre*) was used only once in 2003. In two instances, companies who could have benefited from it preferred the ordinary negotiation procedure.

1.2.1 Overall timescales

1.2.1.1 Overall timescale according to application type

The average period for the processing of the 624 applications conclusively dealt with in 2003 was 216 days, against 243[8] in the previous year, namely a 10% reduction in the overall average period.

The following table presents these times according to type of application submitted by companies.

Table 15: Average processing period according to categories of application

(number of days)

Type of application	Number of dossiers processed	Average period	Median period	Standard deviation	Maximum period
Initial registration	378	174	118	151	1,031
Re-registration [9]	93	532	481	208	1,200
Price change	116	94	73	77	416
Extension of indication	37	224	181	138	641
Overall	624	216	133	203	1,200

The shortest average and median processing periods are recorded for price change applications on which the Committee is required under the regulations to rule within 90 days. The total average period in fact covers applications and decisions of different kinds. Hence, where these applications culminated in a rejection, the observed decision-making period was 73 days whereas the average period observed for dossiers resulting in an agreement which incorporates additional periods for the collection of signatures and the publication of notices is 99 days. The latter encompass a number of dossiers corresponding to price reductions, opened at the behest of the Committee for which the 90-day period is of scant significance.

1.2.1.2 Overall timescales according to drug type

Table 16: Overall average period according to drug type and application

	Generics		Non-generics		Overall	
Type of application	Average period	Number of dossiers	Average period	Number of dossiers	Average period	Number of dossiers
Initial registration	99	235	298	143	174	378
Re-registration	607	13	520	80	532	93
Price change	86	48	102	68	94	116
Extension of indication	200	1	225	36	224	37
Overall	119	297	303	327	216	624

The generic drug dossiers successfully concluded in 2003 were processed in 119 days on average (135 days in 2002). The average processing period for non-generic drugs is 2.5

[8] In 2002 this period had been calculated on the basis of recording applications per presentation.

[9] This is a question of regularising re-registrations whose publication in the JO should have occurred prior to 2003. The lateness with which this regularisation occurred is the source of the significant delays recorded

times as long, averaging 303 days. The gap between the two drug categories is especially wide for the initial registrations.

1.2.2 Analysis of the initial registration timescales

Of the 378 initial registration dossiers concluded in 2003, 12 rejections were notified in an average period of 305 days after the application was filed, 16 abandonments were recorded in an average period of 362 days and 350 dossiers gave rise to publication or a price notice in the *Journal Officiel* in an average period of 161 days. The analysis of intermediate periods relates exclusively to those applications for initial registration culminating in publication in the *Journal Officiel*, singling out from all those applications the ones relating to generic drugs.

1.2.2.1 Initial registration timescales according to drug type

Among the 350 dossiers resulting in publication in the JO, 231 relate to generic drugs and 119 dossiers to non-generic drugs. On average, publication occurred 161 days after the application was filed (99 for generics and 282 days for non-generics). The median is 114 days. In 240 cases out of 350, publication in the J.O occurred less than 180 days following the dossier's filing.

Table 17: Initial registration application processing periods giving rise to publication in the JO

	Generics		Non-generics		Overall	
Period	no. days	no. dossiers	no. days	no. dossiers	no. days	no. dossiers
Average	99	231	282	119	160	350
Median	81		238		113	
Maximum	330		1031		1031	
Minimum	50		38		38	
Standard deviation	46		153		130	
< 180 days	214 / 231 i.e. (93 %)		26 / 119 i.e. (22%)		230 / 350 i.e. (69%)	

The average period for the processing of generic drug registrations is virtually identical to that of 2002. The average period for the processing of other drug dossiers was reduced by 13%, from 325 days to 282 days.

1.2.2.2 Intermediate timescales for initial registration according to drug type

The overall timescale for processing an initial registration dossier has been broken down into 5 stages: from filing of the dossier to the forwarding to the Committee of the report by the Transparency Commission (CT); from forwarding of the report to the first session of the Committee (Investigation); from the first to the last session of the Committee devoted to the same dossier (Negotiation), from the last session to the signing of the codicil (Agreement), from the signing by both parties of the codicil to publication in the *Journal Officiel* of the registration order and of the price notice (JO).

Table 18: Average intermediate timescales for the processing of initial registration applications according to drug type

Number of days

Medicine	CT	Investigation	Negotiation	Agreement	J.O.	TOTAL

Non-generics	125	46	38	32	41	**282**
Generics	(109*)	28***	7	24	40	**99**
Overall	**	**34**	**18**	**27**	**40**	**160**

* The average is calculated on the 10 generic drug dossiers scrutinised by the Transparency Commission on account of packaging which differs from that of the originator drug.
** Not significant, 221 generic drugs dossiers not examined by the CT.
*** For generic drugs, this consists in the average period between filing of the application and its first scrutiny in session by the Committee.

These intermediate periods are very close to those observed in 2003 apart from the time spent on the negotiation of non-generic drugs which fell sharply from 80 days in 2002 to 38 days in 2003.

1.2.2.3 Analysis of intermediate timescales for initial registrations

1.2.2.3.1 Stage one: Transparency Commission

Dossiers must be filed simultaneously with the Committee and with the Transparency Commission. This first stage entails scrutiny of the application by the Transparency Commission and issuance of the Commission's opinion to the Committee. Without exception, non-generic drugs alone are scrutinised. The Commission's final opinion is received by the Committee 125 days on average after the non-generic drug dossier is filed. By comparison with this average, the average duration of this initial phase was 156 days for products warranting an ASMR rating and 116 days for products with no ASMR.

10 generic drugs whose packaging differed from that of the originator drug were submitted for an opinion from the Transparency Commission which was forwarded to the Committee on average within 109 days subsequent to filing.

1.2.2.3.2 Stage two: Investigation by the rapporteurs

For non-generic drugs, this stage spans from the date on which the Transparency Commission's opinion is forwarded to the Committee until the time when the presentation is first examined by the Committee and includes the investigation of the dossier by the rapporteur in liaison with the company and the period relating to its inclusion on the Committee's Agenda (one clear week at least after the report has been forwarded to the Committee members). This stage lasted an average of 46 days

As regards generic drugs, bearing in mind the low number of dossiers submitted to the Transparency Commission, this stage was defined as corresponding to the period elapsing between filing of the dossier and its initial scrutiny in session by the Committee. In 2003, this period averaged 20 days for generic drugs.

1.2.2.3.3 Stage three: Negotiation

The period between the date of the Committee's first and last examination in session corresponds in part to the time necessary for the Committee to finalise its proposal, if none have been adopted in a single session, but serves equally as a negotiating stage between the Committee and the company. If the Committee's proposal is turned down by the company, its counter-proposals are then examined, following discussions with the rapporteur. The period

observed in 2003 averaged 7 days for generic drugs, 89 days for medicines benefiting from an ASMR rating and 21 days for the other non-generic drugs.

Table 19: Negotiating timescales

drug type	per dossier			Negotiating timescale
	no. dossiers	Average no. sessions	more than one session	
Generic	231	1.1 sessions	28 (12 %)	7 days
Non-generic	119	2.1 sessions	50 (42 %)	38 days
- without ASMR	93	1.7 sessions	36 (39 %)	21 days
- with ASMR	26	3.3 sessions	14 (54 %)	86 days
Overall	350	1.4 sessions	78 (34 %)	18 days

42 % of registration application dossiers concerning non-generic drugs gave rise to more than one examination in session.

This third stage of negotiations with the company is only formally dissociated from the following stage which also comprises final negotiations on the precise terms of the contractual codicil and its acceptance by the company.

1.2.2.3.4 Stage four: Agreement

This is the period between the last Committee session devoted to a dossier and the signing of the relevant codicil. It provides time for finalising the codicil, which may give rise to several exchanges between the Committee and company, and the logistical time-frame necessary for collecting the signatures of both parties. Moreover, the length of this stage may vary according to the urgency felt by the company in the marketing of its product and hence the time it will take to sign the codicil. The fourth stage does in fact include a negotiation deadline hard to distinguish from the logistical timescales. The period averaged 29 days.

1.2.2.3.5 Stage five: Signing and publication in the JO

This last stage includes the preparation and signing by the Committee of the price notices and reimbursement registration orders by the relevant departments of the Ministry of Health, along with their transmission to the General Secretariat of the Government for publication in the JO of the registration orders and price notices. This period was reduced to an average of 40 days in 2003 (against 46 days in 2002) and is much the same for all drugs.

2. Medicine pricing methods

The basic rules applicable to the pricing of reimbursable medicines are highly stable, based as they are on the straightforward and fully-established texts of the Social Security Code, clarified by equally permanent general principles. The Committee considers it expedient however to present them once again, in as operational a manner as possible, to incorporate the policy shifts or clarifications emerging from the ministerial guidelines and experience alike.

Article L.162-16-1 of the Social Security Code lays down the rules for the pricing of reimbursable medicinal products by the Social Security:

> "The sale price to the public of each of the medicines mentioned in subparagraph 1 of article L. 162-17 is set by agreement between the pharmaceutical company and the Economic Committee for Health Products in pursuance of article L. 162-17-4 or, failing that, by decree of the Ministers responsible for Social Security, Health and the Economy, following the Committee's report. Account is primarily taken, when setting the price, of the improvement in medical benefit of the medicine, the prices of medicines serving the same therapeutic purpose, forecast or recorded sales volumes and the foreseeable and actual conditions of use of the medicine".

Article R.163-5-I-2° specifies that "medicinal products which deliver no improvement in medical benefit, as assessed by the Commission mentioned in article R.163-15, or savings in the cost of drug treatment" may not be entered on the list provided in article L.162-17 of the Social Security Code.

In compliance with these texts, the Committee's task is to secure the most advantageous prices and conditions for the Health Insurance System mindful at one and the same time of the global market for medicinal products, ONDAM constraints, public health needs and the need to treat companies equally.

Acknowledgement of the global medicines market calls for clarification of all detailed discussions concerning the price of a medicine, over and above the bilateral framework of the negotiation, through an analysis of the economic consequences of that price on the market trend and the costs of health insurance: direct and immediate consequences on the price structures in the classes; indirect consequences on class-related trends; medium-term consequences when it comes to estimating the financial burden of the reimbursement on the ONDAM; and more remote consequences too, where it is possible to anticipate the subsequent arrival of medicines with the same indications.

The aim of meeting health needs means that by its action the Committee must allow access by patients to the necessary medicinal products, of which pricing is just one of the various means.

The principle of equal treatment of medicinal products is respected regardless of whichever company markets them. One of the consequences of this principle is that the Committee does not consider it justified, whatever interest it shows in research and innovation, to pre-finance research through the price of medicines which do not in themselves incorporate the successful outcome of such research, nor, *a fortiori*, where innovative medicines are concerned, to treat them differently according to the country of origin of the innovation.

2.1 MEDICINES WITH NO ASMR RATING

For the pricing of medicinal products with no ASMR rating, the application of the rule laid down in article R.163-5-I-2 assumes that the Committee answers two questions: savings compared with what? By how much?

2.1.1 Savings compared with what?

There are times when the method of comparison in relation to which savings are to be obtained is clear and beyond dispute in the light of the Transparency Commission's opinion. This however is far from being always the case.

It often happens when additional ranges are registered, that the Committee must ask itself whether the right comparator, when ascertaining the effect of the medicine's registration on social security expenditure, is the range in which the new product fits and which will in part be replaced by it or indeed equivalent products marketed at a potentially lower price by other companies. More often than not, the Committee opts for the comparison with cheaper rival medicines so as not to perpetuate unjustified price gaps between products providing the same service. It sometimes accepts, where an agreement cannot be finalised at that price, especially where the new presentation is called upon to replace en masse an existing presentation, a price midway between that of the replaced presentation and that of the cheaper comparison medicine.

An equally frequent difficulty lies in the choice of measurement tool: daily treatment cost, cost of treatment or cost of packaging. Although the daily treatment cost (CTJ) most often prevails, especially for the treatment of chronic diseases in solid or injectable forms, the solution is at times less clear for short-term treatments or when the dosage of the medicine is itself uncertain (local application forms, liquid forms, etc). Reasoning in terms of cost of treatment is however only permitted exceptionally by the Committee, aware that prescribing practices very often fail to conform with the protocols of clinical studies or the wording of the Summary of Product Characteristics. It happens therefore, where the CTJ is clearly unsuitable and the cost of treatment is far too uncertain, that the Committee will resign itself to a comparison of the packs or bottles on the assumption of analogous average prescriptions.

Finally the committee only very exceptionally agrees to take into account, in the cost comparisons, announced prospects of a reduction in co-prescriptions with other medicinal products, even if they appear to be well supported by the clinical studies. Experience has taught it that these prospects have almost systematically been disproved in practice.

2.1.2 By how much?

Generally speaking, the price advantage compared with the last one registered must be all the greater where the price of the comparator is high and the time has elapsed between the two registrations is longer.

The expected saving is not measured however as the difference in unit prices between the new medicinal product and already registered products with which it was compared by the Transparency Commission, but as a cost saving, which is the outcome of price differentials by volume. This general observation gives rise to two main consequences.

The first leads to a distinction between the classes in which the prescription volumes are rigid (reliable diagnosis, precise and limited indications) and those in which there is a risk of an unjustified growth in volumes. In the first classes, the arrival of a new contender may lead only to a shift in market share, hence the rival is welcome, even though the price advantage is relatively insignificant. Quite the reverse applies in the second classes where the relative price advantage linked to the arrival of a new player risks being offset, and overrun even, by the overall rise in volumes which results from the increased promotional pressure on prescribers. The Committee is more exacting in such cases.

A second consequence is that savings will only be really achieved if the new medicinal product secures a market share and that they will be commensurate with that market share. Now, given the fact that prescriptions still depend, without exception, more on the promotional efforts of laboratories that on price differentials, the inevitable conclusion is that on a parity of service provided, the more expensive medicinal products sell somewhat better than the cheaper ones. The Committee can therefore accept prices no lower than that of the last registered comparison drug, where it believes that a lower price would be such a competitive handicap to the producer of the medicinal product pending registration that it would sell only very few.

Finally, the Committee is careful, in cases of pharmaceutical innovations without an ASMR rating, to verify whether the effect of registering these new medicines might be, purposely perhaps where products whose patents are due to expire are concerned, to close the path either commercially or legally to the development of generics. In such an event the Committee only accepts registration at a price equal at most to that of the corresponding generics.

2.2 MEDICINES WITH AN ASMR RATING

The registration of these medicines is able to generate additional savings for the Social Security, but determining the acceptable additional expenditure is a difficult matter and there is no model on which to base a solution.

There is in fact no scale of acceptable price differentials relating to the ASMR scale. Discussion of the price of a medicinal product with an ASMR rating therefore takes the form of an open negotiation where the demands of the company are confronted by the greater or lesser necessity or urgency, in terms of meeting health needs, to register the medicine for reimbursement.

In two important respects, nonetheless, the ministerial guidelines specify the framework of negotiations. Firstly, they deal with medicinal products whose ASMR is equal to or superior than III for which, in accordance with the ministerial guidelines and under the terms laid down in the framework agreement, the Committee accepts, on registration, prices consistent with the main European Union States. This principle does not mean that all medicinal products benefiting from such an ASMR level are entitled to reimbursement at a European price level but that, if reimbursement is decided upon, it is at that price. It cannot be ruled out therefore, if the cost entailed in this price level appears disproportionate to the expected advantage to patients or public health, that the product will not be reimbursed.

Above all, discussion of the registration price of these medicinal products is more often than not accompanied by a discussion of contractual clauses, just as important as the price itself since their aim most frequently is to ensure the best possible adaptation of the use of the medicines to identified needs or to predict, depending on the size of the amounts in question, quantity rebates (see 2.3). Very often, the registration of these medicinal products is likewise subject to the conditions laid down in clause 6 of the framework agreement (*Accord Cadre*).

Conversely, where a medicinal product with an ASMR IV rating is intended to replace the prescription of a genericisable drug or passes as one, registration can only be made at such

a price - or price schedule - that the registration incurs no additional cost in the short or medium term for the health insurance system.

For the other ASMR IV medicinal products, the price discussion will have to take into account the characteristics of the target population. For example, where the medicine has the same target population as its comparator, the Committee willingly sees the increase in its market share as a sufficient benefit of the innovation for the company without the need to add a price advantage. It may be different where the ASMR results from a specific advantage for a narrower population.

2.3 PRICE REVIEW CLAUSES

Pricing is accompanied by review clauses in three main scenarios:

- Where the initial price is set in consideration of assumptions which can only be invalidated or confirmed by time or usage and where it is advisable to ensure that the real cost per disease of the use of a medicinal product remains consistently in line with what was agreed with the company at the time of the registration: this is basically the domain of the daily treatment cost (CTJ) clauses.
- Where assurances are needed that the quantities sold of a medicinal product remain consistent with the medically justified "target" of that medicinal product: this is the object of the volume clauses.
- Where the price level and probable sales volumes justify, especially for medicinal products benefiting from the registration of a European price owing to their ASMR, that this price is not maintained beyond the period guaranteed under the framework agreement. Unconditional price reduction clauses may therefore be concluded according to a timetable established in the agreement.

2.3.1 Daily treatment cost (CTJ) clauses

The CTJ clauses are divided into two categories: CTJ dosage range clauses and posology clauses. Many medicines, when a “dose effect” has been established in their use, come in several dosage presentations either when first marketed or subsequently with the registration of additional dosages. The Committee took the view in such cases that the best way of ensuring at one and the same time proper use of the medicine’s different dosages and equal treatment among rival companies in the category under consideration was that all dosages of the same medicine be sold at the same price per galenic unit. The uniform prices discourage companies from specifically promoting the sale of the highest and most costly dosages. Furthermore, they allow the cost of treatment to be maintained over time and achieve a balance in relative prices between rival laboratories, since the real costs of treatment are then independent of the distribution of sales among the different dosages.

Where it is impossible to fix uniform prices, especially for reasons of international price uniformity, a dosage range CTJ clause is introduced instead in order to achieve roughly equivalent effects. In such cases, what is agreed with the company upon registration is in reality a daily treatment cost, translated into different dosage prices on the assumption of the distribution of prescriptions. If it is established that the actual distribution differs, in practice, from the supposed distribution, the prices are reviewed to restore the agreed cost of treatment.

The aim and mechanism of the posology clauses are exactly the same as the dosage range CTJ clauses. The agreement is reached at the time of registration of a treatment cost

based on an average posology assumption (posology for which market authorisation is granted or posology attested by studies conducted prior to registration, including in countries where the medicinal product has already been marketed). If the posology established in practices varies from the one on the basis of which the sale price was set, then this price is reviewed to restore the agreed treatment cost.

2.3.2 Volume clauses

The Committee feels that volume clauses are unjustified where their main effect would be to divide up the markets among rival companies. Furthermore, they make, without exception, hardly any sense for the registration of products with no ASMR rating, sales of which lead to a saving for Social Security, the saving being all the greater because the sales achieved in replacement of more expensive products are themselves significant. The year-end quantitative rebate mechanism by therapeutic class therefore seems more suitable in the Committee's opinion.

These clauses are indispensable, on the contrary, in fairly frequent cases where the ASMR rating of an innovative drug relates to only part of its indications or to a limited patient population or where, independent of all financial considerations, public health reasons demand that a medicinal product be used only for restricted indications where it is strictly indispensable, as is often the case in particular of antibiotics.

The Committee has endeavoured not to enter any longer into agreements which include CTJ or volume clauses whose implementation would only be sanctioned by the payment of refunds. It frequently agrees, however, in order to prevent slight and possibly reversible overruns of the thresholds set by the clauses from resulting in marginal and subsequently management-costly price changes, to subjecting the actual application of price reductions to the crossing of a variation threshold, the price reductions not made then being offset by equivalent refunds. Above all, in accordance with the framework agreement, the price variation clauses entered into for medicinal products with an ASMR III rating or more generally provide for their conversion to rebates during the first five years of marketing.

2.4 PRICE CHANGES

Besides price reductions by the application of clauses, which call for no further comment, there are three scenarios where prices may be lowered on the initiative of the Committee.

The registration renewal is an opportunity to examine a medicine's actual place on the market, which may differ widely from what was foreseeable at the time of its registration. A notable case, even in the absence of misuse of a medicine, is when it has enjoyed, since its registration, considerable growth in prescribed volumes, especially in the wake of extended indications. The price reduction may also be justified by the marketing, in accordance with the Social Security Code, after the initial registration of the medicinal product, of rival proprietary products which are equally effective and cheaper.

Pursuant to article L. 162-17-4 of the Social Security Code, where the trend in spending on medicinal products is clearly incompatible with observance of the ONDAM and yet complies of course with the ministerial guidelines and commitments under the framework agreement.

Reductions may equally be justified by the outcome of studies relating to the use of the medicinal products in real situations conducted in accordance with article 6 of the framework agreement and, more generally speaking, in the event of a significant change in the scientific and epidemiological data taken into account for the purposes of reaching agreements.

Reductions may of course be proposed by the companies. These are by definition competitive price reductions, observed until now essentially for the originator drugs of generic groups placed under the containment flat rate. The Committee has not given up hope of extending the application of these reductions to patented drugs, as prescribers and patients grow more aware of prices and as companies will be forced to state in their promotional leaflets the lower cost of their medicines, at a parity of medical benefit provided.

The Committee accepts price rises for medicinal products which are vital to meeting health needs registered at a price which would no longer allow coverage of manufacturing and marketing costs. These are generally old products whose market has gradually declined, orphan drugs or medicinal products which, without strictly fitting the definition of orphan drug, may be treated as such economically.

Conversely, the Committee rejects proposals from companies to adjust prices to zero-earnings, which, even if their immediate result may be neutral or profitable for Social Security, prove more often than not to be costly in the long-run and always likely to cause relative price imbalances in the pharmacotherapeutic classes.

PART TWO –MEDICAL DEVICES

CHAPTER I – SPENDING ON MEDICAL DEVICES

Pursuant to articles L. 165-5 and R 165-17 of the Social Security Code, the manufacturers and distributors of products and services (LPP) mentioned in article L. 165-1 of the same code achieving a pre-tax turnover greater than €760,000 must send AFSSAPS and the Economic Committee for Health Products a declaration each year on their sales throughout the country in the previous year. Owing to the insufficient level of response and to the insufficiently accurate definition and framing of the information requested, the first application of this mechanism in 2002 did not allow a satisfactory statement of sales achieved in the year to be drawn up. The overhaul of this mechanism for 2003 should improve knowledge of the sector and companies concerned.

While awaiting the operating results in the 2003 returns, the only sound information available to date from which to assess the trend in sales relates to compulsory sickness insurance reimbursements which point to growth of 8.7% in 2003, giving rise to reimbursements of €3.2 billion, corresponding to reimbursable expenditure of €4 billion.

The existence or otherwise according to LPP parts or chapters of upper-limit sale prices and, where existing, the widely varying discrepancies between the prices charged and the tariffs adopted - leading on average to reimbursements of between 7% and 8% of total sales in the field of optics and up to the whole amount where implantable medical devices are concerned - allow only an estimation of matching sales.

The Directorate of Research, Studies, Assessment and Statistics (DREES) estimated in the National Health Accounts for 2002[10], that with growth of 9.3% over the previous year[11] LPP-related sales reached €8.1 billion, €2.3 billion of which for Category I, €3.8 billion[12] for optics, €2.65 billion of which within the scope of LPP (Chapter 2 of Category II) and €2.0 billion for prostheses, ortheses and vehicles for the physically disabled (VHP). The extrapolation for 2003 of these figures in proportion to the growth recorded in compulsory health insurance reimbursements places sales estimates for 2003 in the region of €7.3 billion, €2.6 billion of which for Category I, €2.6 billion for optics and €2.1 billion for prostheses, ortheses and VHP combined (Category II apart from Chapter 2, Category III and IV of the LPP).

[10] National Health Accounts– DREES – Ministry of Health, the Family and the Disabled

[11] Namely a growth of 40% less than that of corresponding reimbursements under the general scheme which rose by 15.4% in 2002.

[12] Only 70% of which, namely €2.65 billion, reportedly fall within the LPP according to other sources.

1. Trend in reimbursements under the general scheme

According to CNAMTS, reimbursements under the general scheme of medical devices increased by 8.7% in 2003, i.e. a sharp decline compared with 2002 and 2001 during which growth had stood at 15%.

Table 20: Trend in reimbursement under the general scheme in 2003

Millions of €

Item	Chap	2002	2003	Trend %	Relative share*
HOMECARE RESPIRATORY SUPPORT EQUIPMENT	1	288	334	16 %	20 %
OTHER HOME TREATMENT EQUIPMENT	1,2	380	419	10 %	25 %
COMPRESSION MATERIALS AND EQUIPMENT	3	27	25	-9 %	2 %
MISCELLANEOUS HEALTHCARE MATERIALS AND EQUIPMENT	1	508	579	14 %	35 %
DRESSINGS	3	261	291	11 %	18 %
GLUTEN-FREE FOODS		1	1	22 %	-- %
TOTAL CATEGORY I		**1,465**	**1,648**	**13 %**	**57 %**
ORTHESES	1	171	178	4 %	33 %
OPTICS	2	142	142	--	26 %
ELECTRONIC HEARING AIDS	3	48	55	15 %	10 %
NON-ORTHOPAEDIC EXTERNAL PROSTHESES	4	4	5	--	1 %
OCULAR AND FACIAL PROSTHESES	5	11	10	--	2 %
FOOT ORTHESES	6	46	50	9 %	9 %
ORTHOPROSTHESES	7	88	100	13 %	18 %
PROSTHESES & ORTHOPEDICS ACCESSORIES - FITTING CENTRES		12	4	--	1 %
TOTAL CATEGORY II		**524**	**544**	**4 %**	**19 %**
INERT INTERNAL PROSTHESES	1,2,3	550	571	4 %	87 %
ACTIVE INTERNAL PROSTHESES	4	81	84	4 %	13 %
TOTAL CATEGORY III		**631**	**655**	**4 %**	**23 %**
CATEGORY IV VEHICLES FOR THE PHYSICALLY DISABLED		**55**	**60**	**8 %**	**2 %**
TOTAL CATEGORY I, II, III, IV		**2,674**	**2,907**	**8.7 %**	**100%**

*Relative share in 2003 : for the Chapters, in relation to the category; for the categories, in relation to total reimbursements

2. Evaluation of reimbursable expenses (CNAMTS, CANAM, MSA)

With regard to the tariffs adopted for medical devices, the average reimbursement rate under the general scheme has fluctuated slightly for several years at around 90%. It can be taken into account to assess the scale of total expenditures submitted for reimbursement by the general scheme. In this case € 2.9 billion in reimbursements corresponds to €3.24 billion in expenditures submitted for reimbursement, which corresponds to an average reimbursement rate of 89.8%. It transpires from this average reimbursement rate that 70% of sales of LPP products and services are exempt from the patient co-payment. The extrapolation to the 3 main schemes for which the overall reimbursement rate is closely similar leads to an estimation of €3.85 billion as the expenditure submitted to them for reimbursement and, besides, approximately €4 billion as the expenditure submitted for

reimbursement by all the compulsory health insurance schemes for the products and services appearing in the list mentioned in article L. 165-1 of the Social Security Code.

Table 21 : Evaluation of reimbursable expenditures

Billions €

Title	2003 reimbursements under the general scheme	Average reimbursement rate under the general scheme	Reimbursable expenditure submitted for reimbursement under the general scheme	Reimbursable expenditure submitted for reimbursement under the 3 schemes
HOMECARE RESPIRATORY SUPPORT EQUIPMENT	334	90.9 %	367	
OTHER HOME TREATMENT EQUIPMENT	419	93.3 %	450	
COMPRESSION MATERIALS AND EQUIPMENT	25	78.2 %	32	
MISCELLANEOUS HEALTHCARE MATERIALS AND EQUIPMENT	579	94.3 %	614	
DRESSINGS	291	83.4 %	349	
GLUTEN-FREE FOODS	1	75.8 %	1	**2,160**
TOTAL CATEGORY I	**1,648**	**91.0 %**	**1,812**	
ORTHESES	178	73.5 %	242	
OPTICS	142	66.0 %	215	
ELECTRONIC HEARING AIDS	55	71.0 %	77	
NON-ORTHOPAEDIC EXTERNAL PROSTHESES	5	95.3 %	5	
OCULAR AND FACIAL PROSTHESES	10	98.7 %	10	
FOOT ORTHESES	50	91.4 %	55	
ORTHOPROSTHESES	99	100 %	99	
PROSTHESES ORTHOPROSTHESES ACCESSORIES	4	100 %	4	**840**
TOTAL CATEGORY II	**544**	**76.9 %**	**707**	
INERT INTERNAL PROSTHESES	571	99.9 %	571	
ACTIVE INTERNAL PROSTHESES	84	99.9 %	84	
TOTAL CATEGORY III	**655**	**99.9 %**	**655**	**780**
TOTAL CATEGORY IV : VEHICLES FOR THE DISABLED	**60**	**100 %**	**60**	**70**
TOTAL CATEGORY I, II, III, IV	**2,907**	**89.8 %**	**3,235**	**3,850**

3. Trend in sales and spending by category

LPP products and services were newly codified in 2003 whereby, apart from Category 1, Chapter 1 and Category II Chapter 7, the old alphanumeric codification was replaced by a 7-digit numerical codification, the first digit corresponding to the Category, the second to the Chapter, the last constituting a key and the other digits being sequential numbers allowing each of the products or services registered under their brand name, together with each of the generic lines, to be isolated. This new codification should refine the use of LPP-related data and therefore facilitate tracking of the trend in LPP-related sales and expenditures.

3.1 CATEGORY I: HOMECARE TREATMENT AND LIFE ENHANCEMENT APPLIANCES, DIETARY FOODS AND DRESSINGS

Category I encompasses devices, products and services designed for the domiciliary care of the elderly, the disabled, patients requiring postoperative care who would have

hitherto been kept longer in hospital, and chronic diseases. It continues to increase in relation most notably to the ageing population and accounts primarily, in keeping with the pattern of recent years, for the overall growth in the LPP products market. The 13% increase recorded in 2003 is however not as rapid as the increase of just under 20% which prevailed in the 3 previous years.

Mindful of these trends, Category I now accounts for 57% of reimbursements under the general scheme against less than 50% 3 years ago. On average, three quarters of expenditures under this heading relate to patients exempted from co-payment and the tariffs, which in the main correspond to the sale price, are therefore wholly reimbursed. Nevertheless, in several sectors, the example that of compression equipment or foods, differentials between tariffs and prices still exist.

On the basis of DREES estimates and the reimbursement trend, sales in 2003 under this Chapter could be of the order of €2.6 billion.

3.2 CATEGORY II : EXTERNAL ORTHESES AND PROSTHESES

Category II, which now accounts for less than 1/5th of spending under the general scheme, grew by only 4% in 2003, at least insofar as reimbursements are concerned, against 11% in 2002. The item which experienced the strongest growth remains, as in the previous year, Chapter 3: electronic hearing aids, up by 15% (20% in 2002). The latest effects over the year as a whole of the measures to reimburse the cost of stereophony may account for the continued buoyancy of this item. With an overall reimbursement rate of 77%, it is estimated that only 1/3rd of patients are exempted under this heading from co-payment. Under certain Chapters of Category II, the gap between the tariffs constituting the reimbursable base and the prices charged, whether it be the upper-limit sale price or otherwise, is very wide, especially with regard to ortheses (30% to 45 % of balance due), hearing aids for adults (from 75% to 88% of balance due by class of device according to the survey by DAFSA commissioned by the DSS) and especially under Chapter 2 : Optics, in respect of which reimbursements under the general scheme, €142 million in 2003 as in 2002, account for only 7% to 8% of corresponding total sales.

It is hardly possible therefore, mindful of the uncertainties surrounding these differentials, solely from the figures on compulsory health insurance reimbursements and their trend, to arrive at a fully substantiated estimate of the trend or, *a fortiori*, of the corresponding level of turnover as a retail price inclusive of tax. The most that might be assumed, on the basis of the weak growth in reimbursements under this heading (4%) and the shifting trend in reimbursements in the optics sector recorded since 2000, is a virtual stagnation of sales in optics and the limited increase in the other Chapters, yielding a total turnover of just under €3.8 billion, €2.6 billion of which for optics.

3.3 CATEGORY III: IMPLANTABLE MEDICAL DEVICES, HUMAN-DERIVED OR CONSTITUENT IMPLANTS AND HUMAN-DERIVED TISSUE GRAFTS.

The reimbursements made under Category III which now account for less than one quarter of the total grew by less than 4% in 2003. The arrival on the market, at the end of the third quarter, of coated stents had only limited impact on reimbursements for the year. On account of a reimbursement rate of nearly 100% and of tariffs equivalent to the upper-limit

sale prices, total reimbursements under this heading are expected to closely match corresponding sales, which for 2003 can be estimated at €0.9 billion.

3.4 CATEGORY IV: VEHICLES FOR THE PYSICALLY DISABLED (VHP), FOR PURCHASE

Reimbursements under Category IV relating to the purchase and maintenance of vehicles for the physically disabled rose by 8% in 2003. This too is a sector where reimbursement stands at 100% of the tariffs, with for standard manual wheelchairs (50% of the market in terms of volume) a price to the public approximating that of the LPP tariff. For other chairs and vehicles, there can at times be very wide gaps between tariffs and prices: a ratio of 1 to 2 for external electric chairs, of 1 to 4 for active manual wheelchairs, electrical vertical type wheelchairs …

Overall, the market is estimated to total €120 million (purchases only).

CHAPTER II – REIMBURSEMENT UNDERTAKING FOR MEDICAL DEVICES

1. The opinions of the Committee

Registration applications must be processed within a period of 180 days after the application is filed. Pursuant to article 21 of the law of 12 April 2000, the absence of a decision once this deadline has elapsed signifies a rejection which, at the request of the manufacturer or distributor, must be reasoned.

For price or tariff changes, the deadline is 90 days ; in the absence of a decision within this deadline, the tariff or price requested is tacitly granted.

However, if the data required for evaluation supplied by the manufacturer prove insufficient, the Ministers, Commission or Committee will notify the applicant that additional information is required. In this case the deadlines are suspended from the notification date until such time as the relevant information is received.

As regards registration renewal applications, these have to be sent at least 180 days prior to the target re-registration date. If at the end of this deadline no decision has been notified, the renewal is granted tacitly and the tariff and possibly the previously valid price are extended and published in the JO.

1.1 DOSSIERS FILED WITH THE COMMITTEE

During the course of 2003, 131 applications were filed by companies with the Committee, 90 of which were registration applications, 31 registration renewal applications, 8 upgrade applications and 9 product or company name changes. 7 of these applications were dual purpose.

1.2 THE PROCESSING OF DOSSIERS

In 13 cases registration applications were turned down by the administrative bodies responsible for registrations on account of an insufficient service rendered. In 4 cases the upgrade of prices/tariffs was refused pending the opinion of CEPP on the possibility of an improvement in the service rendered. There were 2 instances where the proposed prices/tariffs were rejected by companies. Moreover, in 4 cases the refusal related to two products regarded as outside the scope of the LPP (equipment used during an operation for example).

44 LPP-related orders were published in 2003, including 14 orders relating to the setting of upper-limit sale prices and 3 orders concerning tariff upgrades.

Table 22 : Published orders

Subject of orders	Category 1	Category 2	Category 3	Category 4	Total
Registration	6		8		14
Re-registration			1		1
Upgrade		3			3
Upper-limit sale price to public	2	2	10		14
Amendment (including reimbursement, generic lines)	8	4	10	1	22
Removal from register	1		1		2
Reimbursement end-dates	5	1	9		15
Total by Category	22	10	39	1	72

* Some orders may relate to more than one Category or concern more than one subject

In addition, 3 notices announcing the intention of the minister to change the nomenclature were published in the *journal officiel* :

- notice of 13 July relating to Category II, Chapter 7, concerning the draft amendment of the conditions for reimbursement of the cost of polyethylene and polyurethane orthoprostheses (known as Neofrakt) and the registration of 2 new generic lines for orthoprostheses of the trunk in Neofrakt ;
- notice of 26 December 2003 relating to Category III, Chapter 1, concerning the draft amendment of the procedure for the registration of annular digestive implants for gastroplasty designed to replace the registration by a generic line and registration under a brand name or commercial name ;
- notice of 3 September 2003 relating to Category III Chapter 1, concerning the plan to replace the heading “macroplastic implants” with “implants for the treatment of vesicorenal reflux”, the amendment of the reimbursement of these implants, their registration and the setting of upper-limit sale prices, inclusive of tax, of these implants at the same level as the tariffs.

For each of these notices, the manufacturers and distributors had a period of 30 days to submit their written observations or request a hearing by CEPP and forward their observations to CEPS on the prices and tariffs.

The notice of 21 January 2003 relating to Category III Chapter 4 announces for a number of pacemakers the renewal of their registration or the end of their reimbursement in the absence of an application for the renewal of their registration. .

1.3 PROCESSING TIMES

On average, for all orders published in the JO in 2003 following an application filed by a manufacturer or distributor, the period between the initial filing of the application and that of its publication was 409 days. This period was significantly worse than the previous year for reasons ascribable to CEPP and the Committee alike. This extension beyond the average period is due in part to the nature of the dossiers scrutinised but needs to be rectified in order that reasonable timescales can be restored.

2. The fixing of tariffs and prices

With regard to the methods for setting tariffs and pricing, the Committee deems it expedient to reproduce virtually unchanged the account devoted to this matter in its 2002 report, which remains relevant..

2.1 GENERAL PRINCIPLES

Three rules apply to the setting of tariffs and pricing of medical devices.

Two rules relate to tariffs:

Article R 165-4 of the Social Security Code provides that " products or services cannot be entered on the list (…) which bring neither improvement to the service rendered nor savings in the cost of treatment or which are likely to give rise to unjustified expenses for the health insurance scheme "

Article R. 165-14, provides that "the setting of tariffs takes into account principally the service rendered, its possible improvement, the tariffs and prices of comparable products or services entered on the list, forecast sales volumes and foreseeable and actual conditions of use ".

For their part, prices have to be set in compliance with the very broad provisions of article L. 162-38 of the same code, according to which the possible fixing by decree of prices or margins for products or services whose costs are reimbursed by the compulsory social security systems "shall take into account the trend in charges, income and volume of activity of the practitioners or enterprises concerned ".

In practice, these rules often have to be combined by the Committee and in particular automatically where a tariff and an upper-limit sale price are set at the same amount. Needless to say that this shared sum must comply at one and the same time with the rules relating to tariffs and those relating to prices.

The application of these rules - identical as regards tariffs to those in force for the price of medicinal products - to medical devices poses several problems however to do with the arrangements specific to registration for the reimbursement of medical devices, with the forms that the innovation most often takes and with the highly diverse nature and consistency of the products and services concerned. The following account provides an overview of the solutions adopted by the Committee.

2.2 TARIFF SYSTEM BY CATEGORY

The registration of products or services which bring no improvement to the service provided must, under the terms of article R 165-4, be accompanied by a saving in the cost of treatment. This simple and important rule however is seldom applied in practice in the medical devices sector. The code in fact is subject to the rule (article R. 165-3) that registration for reimbursement is carried out in principle by the generic description of the product or service, registration in the form of brand or commercial name being the exception. It ensues that the vast majority of products or services eligible for reimbursement achieve it as part of an existing nomenclature line, and hence at an equivalent tariff, although devoid of ASR [Improvement in Service Provided] status, to that of equivalent products or services already reimbursed.

By extension, the Committee treated similarly certain categories of devices registered under a brand name pursuant to the second scenario giving rise to an exception to generic registration provided by article R. 165-3 , " where the impact on health insurance expenditures, public health imperatives or the control of the minimum technical specifications necessitate special tracking of the product". The same goes for categories of devices which, prior to the reform, were placed under the approval numbers system and which, provisionally sometimes, were the subject of registrations by brand. The Committee took the view in such instances that it would be appropriate to treat the products concerned as though they belonged to generic lines, and the newly registered products are awarded a tariff and, if need be, an upper-limit sale price identical to those of products already registered in that category.

An initial consequence of the situation is that the rule requiring savings in the cost of treatment only applies in effect to new devices without ASR status not matching an existing generic definition, whether the expected service provided is obtained, for comparable devices already registered, by a different mode of action and technology, or the comparison is made with treatment methods outside the scope of the list: surgery, drug treatment, etc.

The second consequence is that the decline over time in the average price of the category of products, occurring naturally for medicinal products by the subsequent registration of medicinal products, each cheaper than its predecessor, can only be secured for medical devices, where justified, by the periodic downward revision of the tariff of generic lines.

2.3 THE VALUATION OF INNOVATIONS

For products with ASR status, the criteria explicitly laid down by the texts, although they provide a framework and guideline for tariff setting, are not of themselves sufficient to determine them. The rule of article R. 165-4 permits in such a case an additional cost, but makes no mention of its scale. The most that can be deduced from this is that in general, an ASR with a low rating does not allow acceptance of a large tariff differential with the comparator, assuming one exists, which is not always the case in the domain of medical devices. What is more, the recognition of an ASR is a necessary but insufficient condition for justifying an additional cost and the regulations do not therefore prohibit the registration of a new product with ASR status at a tariff lower than that of already registered comparators.

In practice, the Committee is therefore compelled to draw a rough distinction between the three main scenarios for setting the charging of innovative devices.

In the simplest cases, it is possible to show that the price proposed or accepted by the company, and therefore regarded by it as a reasonable valuation of its discovery, results in costs for health insurance that are lower, or at worst equivalent, to the savings produced by its use (account is only taken in such cases of direct costs incurred by health insurance, whatever their character). Registration thus poses no problems. But it shows how important reliable and compelling medicoeconomic studies are in such cases.

Secondly, it is current practice in the medical devices sector that progress in terms of service provided is achieved in the form of what are known as " incremental " innovations, possessing the dual characteristic of being both modest and fairly frequent. Where it appears that the prospect of the increased market share of the new product does not constitute a sufficient valuation of the innovation, and a price advantage is additionally necessary, the Committee may propose tariffs that are transitionally higher than those of comparable products already registered. In the event of a time lag in the registration of another equally innovative device, the committee accepts that the new device may be granted the same price/tariff advantage as its predecessor for the remainder of the period of the advantage awarded to it. The remuneration of the innovation is thus secured for a generally short term, at the end of which the innovation can be expected to be technologically outmoded. This practice, put in place by the Committee for the charging of pacemakers, allows ASR status devices to be valued whilst at the same time avoiding a tariff escalation.

This leaves the most difficult cases, those of innovations which are both critical and costly, for which the additional expenditure - at times considerable - brought to bear by them on the general taxpaying public has only compensations not financially measurable in terms of improvement in patient care. Cost effectiveness studies may help the decision-making process but are generally a delicate balancing act. In these situations, discussion of the price level, highly constrained by the existence of international markets, is largely supplanted by the issue of limiting quantities to the patient population for whom the expected advantage of the innovation is well established. This supposes that a solution is to be found to both the question of the identification and screening of the target populations and that of the resources, of all kinds, to be implemented so that those populations, and those alone, benefit from the innovation. Registration is accompanied systematically in such cases by contractual provisions concerning the limitation of volumes and the compensation due by companies in the event of an overrun as well as the introduction of follow-up studies.

2.4 DISPARITIES BETWEEN PRICES AND TARIFFS

The system in place for the reimbursement of medical devices, unlike that in place for medicinal products prior to the establishment of the reference prices (TFR), generally allows differences to be established between the tariff, the basis for reimbursement of compulsory health insurance, and the price.

When it is deemed necessary, from the viewpoint of equal access to care or to the compensation of a disability, that no such difference be created, the only way open since the new texts were introduced is to set an upper-limit sale price (see Committee report for 2001). The Committee has frequently proposed the use of this means. The setting of an upper-limit sale price supposes however, where appropriate, a solution to the issue of additional charges invoiced in return for services or accessories exceeding the definition given by the product list or reimbursable service. Such is often the case in the external prostheses and ortheses sectors,

where patients may request, and professionals offer, supplements of an aesthetic or technical character

Where such supplements are clearly separable from the reimbursable product or service, there is nothing stopping these professionals from invoicing separately, in observance of the upper-price limit for the main item, the supplements requested by the patient. This practice, adopted in some cases, calls for no special precautions in the Committee's opinion. It is a different matter when the supplements, especially those of an aesthetic nature, are not separable from the reimbursable device. It is advisable in such cases to avoid exemptions which over time could result in a major risk of the disappearance of all satisfactory offers at the reimbursement tariff and hence difficulty of access by less well-off patients. The Council of State however ruled in 2003, with regard to orthopaedic shoes, that an absolute prohibition on exemptions was unlawful. The Committee has therefore, in this particular case, replaced the prohibition, following the advice of the National Consumer Council, with rigorous arrangements whereby contributors are fully informed in advance.

2.5 TARIFF REVIEWS BY PROFESSION

The medical devices sector involves a number of professions, chiefly comprising small or very small companies whose operating conditions are more akin to those of providers of services to individuals or of artisans than those of industrial research and manufacturing companies. The tariffs and upper-limit sale prices applicable to the reimbursable services supplied by these professions cover, often to a large extent, wage costs.

The issue of tariffs is therefore raised in fairly different terms from those of other areas of medical devices. In particular, the criteria set forth in article L. 162-38 for pricing (charges, income, volume of trade) naturally occupy prime place.

The Committee regards itself as responsible for ensuring, in the proposals it puts forward for setting and above all periodically reviewing these tariffs, compliance with two objectives:

- the level of tariffs – and prices – must be sufficient to ensure that a sufficiently plentiful offer evenly distributed throughout the country is maintained, with a level of quality compatible with the expected service provided and justifying reimbursement ;
- this level must not however be such that it unduly favours the continuation of unproductive operating structures, leading as a result to a windfall effect for the most competitive companies.

The Committee felt that these objectives were more easily achieved by regular tariff reviews and has therefore proposed, in several instances, flat annual review mechanisms according to medium-term cost trends. This procedure goes hand-in-hand with a periodical observation of the real level of costs and margins in order that, if need be, the flat rates adopted can be corrected on the initiative of the Committee or of the professional organisations concerned.

- ANNEXES -

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ANNEX 1: MINISTERS' GUIDELINE LETTER

The Minister for the Economy, Finance and Industry

The Minister for Heath, the Family and the Disabled

The Secretary of State for Industry

Paris, 24 December 2002

Dear Chairman,

The Government has undertaken, especially in tabling the Social Security Finance Bill, a policy of regulating medicinal products, the general purpose of which is to improve the rationality and efficacy of the considerable amounts devoted by the general taxpaying public to spending on medication. The success of this policy relies to a large extent on the mobilisation of health professionals and increased patient responsibility. Progress is now being made in this direction. The policy likewise calls for decisive action on the part of the Economic Committee for Health Products within the scope of its powers: pricing, the monitoring of expenditures and the financial regulation of the market.

Implementation of this action must be achieved by treaty. The law now explicitly provides that an agreement should specify the framework in which conventions are reached which define the relations between companies trading in reimbursable medicinal products and the CEPS. We therefore ask the Committee to embark without delay on negotiations with representatives from the pharmaceutical industry with a view to concluding such an agreement at the earliest opportunity, in accordance with the following guidelines.

As regards pricing, improvement in the rationality and efficiency of spending supposes at one and the same time that the pharmaceutical innovation is even better recognised and valued and that, in all circumstances where the same medical service can be obtained at less cost, this saving is achieved.

Better recognition of innovation calls for progress in three areas.

First and foremost, it is important that the registration of the most innovative medicinal products is, in accordance with the latest provisions of the law, significantly speeded up. To that end, the new agreement will therefore have to define the price notification procedure. This procedure will be applicable as of right to medicinal products with an ASMR I and II rating. We ask the Committee to examine as a factor in the negotiations, whether special conditions exist which would warrant its application to certain medicinal products having been awarded an ASMR III rating and for which the economic repercussions for health insurance are moderate.

Particular emphasis will have to be placed on:

- the timescales, as brief as is reasonably possible, on expiry of which the prices and conditions proposed by the companies will be regarded, in the absence of the reasoned objection of the Committee, as tacitly accepted.
- the criteria for raising any objections.
- the commitments to which the companies will have to subscribe in order to be able to benefit from this new procedure.

An initial review of the implementation of this new procedure will be carried out 18 months after its application..

In order to take therapeutic innovation into greater account, it is desirable to register medicinal products presenting a marked improvement in the medical service provided at an initial price level consistent with the prices charged in the European Union Member States. In this context we believe it necessary, barring exceptions justified by a pharmaceutical speciality on the French market, that it be contractually guaranteed for medicinal products with an ASMR rating equal to or greater than III, over a period of five years with effect from their registration for reimbursement, that the price level will not be lower than for the lowest price recorded on the main comparable European markets (Germany, Spain, Italy, United Kingdom). This objective will be achieved in tandem with the introduction of rebates in all circumstances where it appears that the context of the French market (especially prospects of sales volumes, volumes recorded, costs of comparable medicinal products) justifies, pursuant to the Social Security Code, that the real prices paid by health insurance are, including from the time of registration, lower than the prices recorded elsewhere in Europe. The price floor will be realigned to the lowest European price as that price evolves over time.

For medicinal products already registered for reimbursement, we ask the Committee to make appropriate contractual arrangements so that, according to a suitable calendar, the price of medicines which have been registered for less than five years and which were awarded at the time an ASMR equal to or greater than III are not, where such is not already the case, lower than the level envisaged above. Needless to say that these price rises will have to be fully offset by rebates.

There is good cause to improve the recognition of products awarded an ASMR in the financial regulation mechanisms applicable to companies who are contractually exempted from the so-called safeguard contribution. It is possible to consider as part of the negotiations that the advantages hitherto awarded, with regard to agreed rebates, to recent medicinal products with an ASMR I and II rating be extended to those with an ASMR III and IV rating, in differentiated fashion of course according to ASMR levels.

In return, it is essential that savings are made wherever they can be without impairing the quality of care.

This supposes primarily that the fastening pace at which generics have gained a foothold, as recorded since the agreement reached in June with medical practitioners, is confirmed. The Committee will have to ensure that no obstacle stemming from the offer of medicinal products can thwart this progress. We ask the Committee specifically to be especially attentive, where companies apply for the registration of medicinal products designed to replace the pharmaceutical specialities which they market and which are

genericised or pass as such, to ensure that prices are not accepted which would result in an unjustified additional cost in health insurance spending, any such additional cost having to be assessed over time. This guideline is expected to lead, for new presentations with no ASMR but protected under a new patent, to acceptance of their registration only at a price equal at most to that of the generics of the replaced presentation.

Where such medicinal products benefit from a lower ASMR rating, their registration can only take place at a price - or price schedule - such that the registration does not entail, in the short or medium-term, any additional cost to health insurance.

The law now makes it possible to introduce reimbursement reference prices. The Committee will put all suitable proposals to us by 1 February next on the principles for applying the new law, to determine both those groups which will be subject to the scheme as a matter of priority and the reference price amounts. Decisions regarding the introduction of reference prices and the setting of their level are a ministerial prerogative, not dependent therefore on an agreement between the Committee and the companies concerned. It is our wish however that companies be consulted in advance of these decisions and we ask the Committee to engage promptly in this consultation procedure.

As regards the tracking of consumption of medicinal products, and spending on them, we attach the utmost importance to ensuring that the marketing in France of innovative medicinal products goes hand-in-hand with close observation of their use and effects in practice. Account will be taken of the results of these studies in the price changes or the terms and conditions for registration of the medicinal product. The agreement will therefore have to specify the circumstances in which the registration of new medicinal products will give rise to such an observation, especially those likely to be used by a wide population or for which non-compliance with the reimbursable indications might lead to unjustified expenditures for health insurance. In particular, the expected content of these studies will have to be set out at the time of registration.

The Committee will have to ensure that the regulatory resources, especially financial, entrusted to it by law are implemented both efficiently in terms of expected performance and are respectful of the guidelines set in qualitative terms: supporting innovation, encouraging the marketing of orphan drugs and of paediatric drug forms which are lacking, supporting generics, etc. the new agreement will be able to reproduce those of the provisions of the former agreement whose efficacy has been proven: corporate agreement mechanism, principles of differentiated rebates according to pharmacotherapeutic class, etc..

Finally, you will be able to propose any improvements which would be considered worthwhile making to the various existing levies.

As for medical devices, the Committee will have to endeavour to analyse the situation and trend in the main products, in addition to the price invoiced to contributors and the reimbursement tariff.

Likewise, the Committee will have to foster the use of innovative techniques with particular focus on:

- The setting of a medically and economically justified price for a provisional period corresponding to the natural cycle of the innovation;

- The restriction of the reimbursement of these innovations only to patients for whom the medical indication ensures that they will derive the most benefit from it in respect of outlay.

During the period elapsing between the end of agreements expiring on 31 December 2002 and the agreements to be signed in pursuance of the future framework agreement, we ask that you continue to use the existing agreed framework.

You can rely on the firm support of the services placed under our authority and which comprise the Committee over which you preside.

Yours sincerely.

The Minister for the Economy, Finance and Industry
Francis MER

The Minister for Health, the Family, and the Disabled
Jean-François MATTEI

The Secretary of State for Industry
Nicole FONTAINE

ANNEX 2: THE *ACCORD CADRE*

FRAMEWORK AGREEMENT
BETWEEN THE ECONOMIC COMMITTEE FOR HEALTH PRODUCTS
AND PHARMACEUTICAL COMPANIES
FOR THE PERIOD 2003-2006

Considering Community Law, the Social Security Code and the Ministerial Guidelines as set forth most notably in the tabling of the Social Security Finance Act for 2003 and the letter addressed to the Committee on 24 December 2002 ;

Considering that article L. 162-17-4 of the Social Security Code provides the possibility for an accord to specify the framework of conventions establishing relations between the Committee and each pharmaceutical company ;

Considering that there is a need to establish the proper place of medicinal products in prevention and healthcare and that this presupposes at one and the same time rapid access by patients to innovative drugs, improved efficiency and rationality in drugs expenditures and a sustained effort to avoid all abuse in consumption and to promote proper use;

Considering that medicines can be, at the same time, a source of improvement in the quality of care and a source of savings for the general taxpaying public where they are correctly used solely for medically justified needs, in a competitive area leaving room for generic drugs and self-medication;

Considering that account must be taken of therapeutic advances, demographics, epidemiological data and government public health action plans to assess the growth in the consumption of medicines;

Considering the importance attached, as has been reaffirmed in the work of the G10, to maintaining and developing a strong and competitive pharmaceutical industry and to respecting intellectual property, trademarks and the protection of registration data throughout the territory of the European Union ;

Considering that drug expenditures are primarily financed by the general taxpaying public from resources which are by nature limited and it is therefore expedient to introduce regulations, in accordance with the law and with the ministerial guidelines, on both equitable and transparent terms, commensurate with the contribution made by the medicinal product;

Considering that attempts must be made as a matter of priority to achieve the foregoing objectives by furthering co-operation between the public authorities and the pharmaceutical companies;

The Economic Committee for Health Products and the pharmaceutical companies agree to pursue their relations within the contractual framework defined by this agreement.

CHAPTER I: EXCHANGE OF INFORMATION AND MONITORING OF REIMBURSED EXPENSES

Clause 1: Exchange of information

In a desire for transparency on both sides, the two parties agree on the necessity of improving and sharing the information they have on the consumption and prescription of reimbursable medicines and the actual reimbursement of medicines.

The representatives of the pharmaceutical companies will assist access by members of the Committee to professional information available to companies, especially in computerised forms.

They will undertake communication, on paper and in computer form, of reports of professional information which the profession is responsible for managing, in particular statistics produced under the aegis of the Groupement d'Etudes et de Recherches Statistiques (GERS).

The pharmaceutical companies will communicate to the Committee, when requested, statistics concerning their monthly sales and information which they have on the actual conditions of use of products in the various indications noted in the marketing authorisation.

The Companies agree in addition to the Committee having access to information relating to prices charged in other countries of the European Union, reimbursement conditions and volumes of sales registered there.

b) The Committee and the compulsory health insurance bodies will make available for inspection by the pharmaceutical companies not only the data detailed in *MEDIC' Assurance Maladie* (medical statistics journal) but also the studies produced by them on the prescribing and consumption of medicinal products, subject to the same conditions as those for professional health organisations.

c) Each year the Committee will inform the pharmaceutical companies of its forecasts on the trend in sales of reimbursable medicinal products and its forecasts with regard to the application of the regulating mechanism stipulated in clauses 13 and 14.

d) The Committee and the pharmaceutical companies agree to set up a joint monitoring group responsible for examining together the application of this framework agreement.

Clause 2: Monitoring of reimbursed expenses

a) *Four-monthly monitoring*

The parties agree to regular consultation meetings with regard to the monitoring of drug expenses, mindful in particular of the statements in article L.162-17-3, paragraph II, of the

Social Security Code. This dialogue is organised in the framework of the joint monitoring group established in clause 1.

b) *Analysis of the trend in reimbursable turnover*
The joint monitoring group will likewise proceed to analyse variations within the scope of reimbursable and subsequently reimbursed turnovers under the statistics item "reimbursement of medicinal products in general pharmacy" resulting from changes of definition of the drug or ambulatory reimbursement area, as well as changes in prescribing, dispensing or reimbursement including hospital reassignments (*retrocession*).

CHAPTER II: ACCELERATION OF PROCEDURES

Clause 3: General measures in favour of new medicines

a) *Preliminary investigation for centralised marketing authorisation of medicines*

Without prejudice to any subsequent decision of the Commission of the European Union, a company with a registration dossier for a pharmaceutical speciality that has received approval from the Committee for Proprietary Medicinal Products of the European Agency may, without delay, submit a pre-dossier to the Committee and to the Transparency Commission as well as to the ministers in charge of registration to enable them to anticipate the analysis of the considerations involved in registering the new speciality for reimbursement and to speed up registration times. This step does not exempt the company from making an official application for admission for reimbursement or from fixing the price of this speciality in accordance with the procedures laid down in article R 163-8 of the Social Security Code. As soon as the official application has been filed, the Committee appoints a rapporteur tasked with opening the investigation of the dossier on the basis of evidence not necessitating the opinion of the Transparency Commission.

b) *Specific investigative timescales for medicinal products awarded an ASMR*
The parties agree on the importance of speeding up the procedure for admission to reimbursement of medicinal products constituting a therapeutic advance to less than the 180-day period laid down in the regulations.

For all medicinal products with an ASMR rating of at least IV but which nevertheless would not fall within the scope of clause 4 hereafter, the Committee undertakes within 75 days following the date on which the opinion of the Transparency Commission became final to offer in writing to the company a draft agreement or, failing that, to forward to it, likewise in writing, the reasons why it has not yet been possible for it to make a proposal.

This same procedure will be implemented for those paediatric drugs featuring on the list of paediatric requirements communicated to LEEM by the Committee.

c) Regulatory time-limits

For all pharmaceutical specialities, the Committee will ensure that the regulatory time-limit of 180 days is respected and will likewise monitor the publication times of the commitments it undertakes.

d) *Review*

The procedure and the commitment referred to above will be assessed jointly each year by the pharmaceutical companies and the Committee.

Clause 4: Accelerating the registration of innovative medicines: price notification

The fast-track registration procedure envisaged in article L.162-17-6 of the Social Security Code in favour of certain medicinal products which have been recognised as innovative is applicable subject to the following terms and conditions:

a) *Description of the procedure*

The companies referred to at b) below, one day at the earliest and one month at the latest after the company is notified of the final opinion of the Transparency Commission, may ask to benefit from a fast-track procedure for pricing of the pharmaceutical specialities at c). This request is submitted in accordance with the model shown in annex 1 and necessarily includes the commitments stipulated that d). If, at the end of two clear weeks following the week in which the Committee received the company's application, the Committee has not informed the company of its objection to the application under the terms laid down at e), the application is deemed to be accepted. The agreement is then signed within 48 hours and the order and price notice are published in the *Journal Officiel* (JO) without delay. The application submitted by the company is not open to negotiation. In the event of an objection, pricing will be carried out subject to the conditions ordinarily applicable.

In calculating timescales, the first 15 working days of the month of August and the last 7 days of the year are excluded. In addition, no pricing application can be made during these periods.

b) *Companies concerned*

This procedure is open to all companies who have concluded a multiannual convention with the CEPS in accordance with the provisions of Article L. 162-17-4.

c) *Medicines concerned*

Specialities awarded a level I or II ASMR rating by the Transparency Commission, on condition that these ASMR levels are applicable to the principal indications recorded in the marketing authorisations for these specialities;

Specialities awarded a level III ASMR rating by the Transparency Commission, on the same condition as for the level I or II ASMR rating, apart from pharmaceutical specialities whose projected turnover is estimated by the company to be greater than €40 million in the third year of their marketing at its proposed price. This exception does not apply to orphan drugs or to paediatric medicines featuring on the list of paediatric requirements communicated by the Committee.

d) *Commitments to be undertaken by the companies*

- As regards the price: the company undertakes to ensure that the pricing application is consistent with prices accepted in the following countries: Germany, Spain, Italy, United Kingdom; it likewise agrees, in the event that it subsequently emerges that the prices ruling in one or several of these countries compromise this consistency, to adjust it by accepting a contractual amendment of the price applied for.

As regards sale volumes: the company undertakes, if sales exceed the forecasts compulsorily supplied in the pricing application file for the first four years of marketing, to financially offset by agreed rebates the additional costs to health insurance which would not be justified by public health decisions taken at a later date by the public authorities.

As to carrying out any studies that might be requested of it pursuant to clause 6.

The company agrees, without prejudice to general or special disclosure obligations binding on pharmaceutical companies, to notify the Committee and the Transparency Commission of any new scientific data knowledge of which is likely to adversely affect the benefit/risk ratio insofar as could be ascertained at the time of evaluation by the Transparency Commission. If the company learns of such data prior to the end of the time-limit for lodging by the Committee of its objection, it shall waive the benefit of this procedure.

Over and above the foregoing commitments, which are binding, the company may commit itself to any clause (dosage, daily treatment cost, meetings, etc.) it considers might facilitate acceptance of its proposal by the Committee, bearing in mind the characteristics of the pharmaceutical specialities concerned

Prior to fulfilment of its contractual commitments, the company will be able to argue its case before the Committee.

e) *Conditions for the exercise by the Committee of its right of opposition*
Opposition by the Committee must be presented in a written form with reasons. It may be founded on:

- explicit public health considerations
- the excessiveness of the price proposed in respect of the prices charged in the 4 European Union States mentioned above
- the incompatibility of the sales forecasts with the target population taken into account by the Transparency Commission
- the obvious inadequacy of the commitments undertaken by the company
- non-compliance by the company of a commitment undertaken at the time of filing a previous application.

f) *Review*
An initial review of the implementation of this procedure will be carried out 18 months after its application.

CHAPTER III: IMPROVEMENT IN THE EFFICIENCY OF DRUG EXPENDITURES

Section I: Innovative drugs, orphan drugs, paediatric drugs

Clause 5: Specific advantages for innovative drugs, orphan drugs and paediatric drugs

Innovative drugs, orphan drugs and paediatric drugs will benefit, within the contractual framework, from the provisions set forth in clause 14 and in particular from the temporary, total or partial exemption from class rebates.

The parties wish to promote the marketing of orphan drugs in keeping with the incentives policy of the European Union expressed in EC regulation n°141/2000 of the European Parliament and of the Council of 16 December 1999.

They wish likewise to promote the marketing of paediatric drugs, thus anticipating the institution of European regulations in the course of preparation.

The Committee will inform LEEM of the list of paediatric needs established by AFSSAPS (French Agency for the Safety of Health Products) : new paediatric forms or validation of paediatric indications for existing presentations.

For the registration of paediatric specialities related to this list of priorities, the Committee undertakes to fix their price as though their ASMR rating were one level higher than that awarded to them by the Transparency Commission.

Clause 6: monitoring of new medicinal products in actual medical practice – public health perspectives

The parties agree on the importance attached to having data available on the effects of the use of new medicinal products in real situations.

Consequently, studies might be requested on medicinal products with an ASMR I, II or III rating belonging to the following categories:

- medicines which can be used by a wide population group;
- medicines which are highly likely to be used other than as indicated which would expose the population thus treated to an unassessed risk ;
- medicines likely to have a significant impact on the organisation of the health system.

Without exception, the studies are based at least in part on the data held by the CNAMTS (employee state sickness insurance organisation), especially for identifying samples of people to be studied and the measurement of certain types of exposure. The recommendations of the Association of French-speaking Epidemiologists (ADELF) and Good Clinical Practice will be applied to the conditions for collecting data and auditing the study. The public authorities will be able to carry out checks to ensure compliance with these rules.

The subject and the specifications of these studies as well as the timescales in which they are to be undertaken are defined by agreement, mindful of any observations or requests made by the Transparency Commission. The agreements will specify also whether validation of the study protocol is provided by the national observatory for prescriptions or whether a special scientific committee has to be set up. They require the compulsory publication of the studies, notwithstanding the property rights attached to them.

Where the establishment of a special scientific committee is envisaged, its composition, accompanied by declarations of conflicts of interests from the prospective members, is brought to the attention of the Minister of Health, who may comment on it. The scientific committee is responsible, apart from cases where the specifications already carry a statement to that effect, for defining the type of study best able to reply to the questions asked and to

propose and/or validate the study protocol. As far as possible, studies concerning the same speciality conducted in other European countries should be borne in mind.

The results of the studies are submitted to the Economic Committee for Health Products and to the Transparency Commission. The conclusions of the studies are examined by the Transparency Commission and are taken on board, particularly at the time of renewal of registration of the medicines concerned. The consequences to be drawn within the Committee's terms of reference from any new evaluation thus made will be subject to discussion.

The Committee will keep a watch on the reasonable cost of these studies in view of normal professional practice (number of cases, complexity), and on maintaining a reasonable proportion between the overall cost to the company that the expense relating to the study of a pharmaceutical speciality used in a real situation represents and the pre-tax turnover expected from the marketing of that speciality. In the event that the cost is disproportionate or that a study, for public health reasons, extends beyond the use alone of the speciality under study, the additional costs incurred may be offset by reductions in the contractual rebates.

These provisions do not rule out other studies submitted on the company's own initiative from being taken into account.

Section II: Sources of savings

Clause 7: Development of generics and reference prices

The joint monitoring group will examine the development of the generic drugs market and will produce a critical analysis of its workings and of the economic conditions prevailing for the companies affected by the development of this market.

The signatory parties agree on the critical contribution made by the development of the generic drug market to financing therapeutic progress.

Before giving the Minister its opinion concerning the creation of a tariff, the Committee will consult the companies concerned. The prices proposed to the Committee in the generic groups subject to a tariff will be published without delay. The Committee agrees to respect free competition in the groups. The Committee will bear in mind the logistical constraints borne by the companies when possible modifications of the flat-rate levels are contemplated. When companies ask the Minister to create a reference price rate, they can ask the Committee to give its opinion on the matter.

Clause 8: Development of self-medication not eligible for reimbursement

The signatory parties agree that responsible self-medication must be able to develop in France, thereby contributing to the correct use of medication without affecting reimbursements under the compulsory health insurance scheme.

Section III: Correct use of medication

Clause 9: Information for prescribers, promotion and publicity

a) *Information for prescribers and the promotion of medicinal products*

The parties mutually agree that the promotion of medicines, whilst playing an essential role in informing and training prescribers, may, to variable extents according to medicinal product categories, exert a decisive influence on prescribing behaviour.

They equally share the view that in cases where the principal object of the promotion is to secure a market share for competitive ends without any proven risk of it leading to the prescription of excessive overall volumes or the misuse of the medicine, control of the corresponding promotional expenses is not a priority concern of the contractual arrangements between the Committee and the Companies.

They do agree, however, that in all cases where there is a risk that medicinal products might be prescribed in quantities or in a manner that are unjustified, the promotional tools should be explicitly and positively implemented to encourage correct use of these medicines.

To that end, the Committee may request, for medicinal products specifically indicated among those referred to in the previous paragraph, that the companies concerned be bound by special agreements to adapt their advertising, along with training given at the time to medical representatives and the materials supplied to them, to promoting the correct use of these medicinal products and to respecting the target populations. At the Committee's behest, companies will have to provide a report demonstrating their abidance by these commitments.

Pharmaceutical companies undertake to produce and promote a quality charter for the medical visit in which the training requirements and the role of the representatives are refined and the quality of their materials and communication aids enhanced.

Advertising bans

Pursuant to paragraphs 8 and 9 of article L. 162-17-4 of the Social Security Code concerning advertising bans imposed by the AFSSAPS and the financial penalties that might arise therefrom, the parties agree that the following procedure will be instituted for drafting opinions to ministers.

For advertising bans which the Committee considers could give rise to financial penalties or if an opinion is expressly requested from it by ministers:

- the Committee will appoint a rapporteur who will examine the case and present it in session;
- the Committee will draft a duly substantiated opinion;
- the Committee will forward the draft opinion to the company inviting it to submit its comments in writing;
- the company may ask to be heard by the Committee; it may be assisted by experts or legal counsel;
- the Committee will deliberate again and inform the company of the opinion to be forwarded by it to ministers.

Clause 10: concerted action fostering the proper use of medicines

The pharmaceutical companies undertake to liaise with the social security bodies to actively pursue the actions initiated to further the proper use of medicines.

CHAPTER IV: CONVENTIONS WITH THE PHARMACEUTICAL COMPANIES

Clause 11: The contractual framework

All pharmaceutical companies producing medicinal products which are reimbursable under the compulsory health insurance scheme are urged to enter into a multiannual convention with the Economic Committee for Health Products in accordance with article L. 162-17-4 and L. 138-10 of the Social Security Code, which would exempt them from the contribution stipulated in that article.

The agreements cover the period 2003-2006.

The agreements are drawn up in such a manner as to ensure the application of the present agreement, adapted to the particular situation of each company and to its development prospects, and in compliance with the rules laid down by the Social Security Code and with the guidelines sent each year by the ministers to the Committee.

Within this framework and barring exceptions justified by a specific aspect of the French market, the agreements guarantee for medicinal products with an ASMR rating equal to or greater than III, over a period of 5 years with effect from their registration for reimbursement, that the price level will not be less than the lowest price among those charged in the 4 main comparable European markets mentioned in clause 4.

Companies who decide not to accede to the financial regulation mechanism envisaged in clauses 13 and 14, or where the mechanism is denounced by the company itself or by the Committee, may nevertheless enter into or maintain with the Committee an agreement pursuant to article L.162-17-4, but not exempting them from the contribution required under article L.138-10.

Clause 12: Form and content of multiannual company conventions

The agreements must comply with the model shown in annex 2. They comprise three sections:

The first section summarises the prices of the medicinal products produced by the company and registered on the list of reimbursable medicines as well as the special clauses attached to them, if need be, in the form of a price schedule and a directory of clauses. Pursuant to article R 5142-11 of the Public Health Code, the retail price of an imported pharmaceutical speciality, other than generic groups subject to TFR, is identical to that of the pharmaceutical speciality granted marketing authorisation in France

In compliance with article L. 162-17-4 of the Social Security Code, the second section contains the company's commitments aimed at controlling its promotional policy and at ensuring proper use of the medicine as well as all clauses whose purpose is to establish the

company's contribution to the fulfilment of the objectives set forth in chapter III of this agreement and to the implementation of ministerial guidelines.

The third part confirms the company's accession to the provisions of the present agreement, and specifically, if need be, to those set forth in clauses 13 and 14 hereafter. It also contains special clauses relating to the rules for the application of these clauses to the company or to the pharmaceutical specialities which it produces.

The agreements may be amended by codicil. The first and second sections are updated each year during the first six months of the calendar year. The third section is updated before 31st December of each year.

Clause 13: Annual financial regulation: principles

Any company wishing to be exempted from the contribution referred to in article L.138-10 of the Social Security Code undertakes contractually to pay ACOSS (central social security contributions collection agency) annual rebates known as year-end quantitative rebates.

However, whatever the commitments made, no year-end rebate is due if the growth in ambulatory sales of reimbursable medicinal products, all companies combined, does not exceed the K rate set annually by the Social Security Financing Act for the application of article L. 138-10. In addition, the Committee undertakes to ensure that the sum of the year-end rebates paid by all companies shall be less than the sum of the contributions that those companies would have had to pay in the absence of the agreement.

Were it to appear that, for a given financial year, the scale of sales of medicinal products transferred from the hospital circuit to the pharmacy circuit has substantially altered the expected sales growth reported by GERS, the parties would meet to examine whether this circumstance warrants a modification of the overall rebate ceiling set in the previous paragraph.

The contractual rebates are paid to ACOSS before 30th April of the following year, based on a statement issued by the Committee after discussions with the company, who may on that occasion rgue its case for the revision of the calculated rebates.

The year-end quantitative rebates are composed of rebates by pharmacotherapeutic aggregate and rebates related to turnover.

a) *Rebates by pharmacotherapeutic aggregate*
Each year, the Committee draws up a distribution schedule of these medicinal products into aggregates for the entire reimbursable drugs market. These aggregates are made up of groups of pharmacotherapeutic classes according to the EPHMRA nomenclature. To simplify matters, and in order to improve the ability of companies to forecast the rebates for which they may be liable, the number of aggregates selected is as limited as possible, provided that the same aggregate does not feature medicinal products or groups of medicinal products which not only would not rival one another but in addition would have such different growth profiles that certain companies would end up being made to pay, to an abnormal extent, rebates imputable to sales recorded in classes in which they are not present. Each aggregate is pegged by the Committee to a trend rate worked out in such a way that the weighted average