Economic Committee for

Healthcare Products

Annual report 2000

April 2001

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In accordance with article D.162-2-5 of the Social Security Code, the Economic Committee for Healthcare Products submits once a year a report on its activity to the ministers responsible for Social Security, Healthcare, Economy and Industry.

This report thus describes the main activities of the Committee during 2000. It is set out using the same framework as the 1999 report, as follow:

The first part deals with drug cost-control[1]. It describes the actions undertaken to this end by the Committee during 2000 in application of the Social Security Code and the guidelines given by the ministers.

The second part relates to price negotiation. It starts by giving a statistical overview of the activity of the Committee with regards to drug price fixing (type of request, duration of treatments). It also describes principles and methods implemented by the Committee during 2000 for the negotiation of these prices.

The third part describes the structure and the workings of the Committee: both human and material resources set up as well as procedures for dossier processing.

1. The Regulation of the Drug Market

The Committee's mission consists in fixing the price of reimbursable drug to the greatest possible advantage of those insured through the Social Security system. It ensures that the methods used to fix prices contribute to the total cost of drug expenditure being compatible to the National Health Insurance Spending Objective (*objectif national des dépenses d'assurance maladie*, ONDAM) and allow for a satisfactory supply of the reimbursable drugs market, for both patients and Public Health purposes.

In 2000, Ministers confirmed, the directions they gave to the Committee in 1999 in particular their willingness to have the objectives assigned to the Committee being achieved as far as possible via the route of the Conventions. Furthermore, the Committee was specifically required to carry out, together with the pharmaceutical companies concerned, the consultation necessary for the implementation of the results for the re-evaluation process of reimbursable drugs.

The regulation activity of the Committee during 2000 took place in the context of a rapid increase in drug expenditure which should be borne in mind.

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[1] *The Social Security finance law for 2000 has extended the scope of the Committee to reimbursable health products other than drugs. However, as the application decrees of this law were not yet published in 2000, the present report only concerns drugs.*

A. Trends in drug expenditure

1. THE MONITORING OF DRUG EXPENDITURE ON; THE "PERIMETER" GROUP.

As planned in the *accord sectoriel*, the Committee undertook the monitoring of drug expenditure in consultation with the SNIP, in the context of the permanent joint working group, the so-called "Perimeter Group".

During 2000, the group continued to set its work on the objectives which were initially assigned to it.

The first of these objectives was to devise a permanent monitoring method which would explain the gap between the industry sales, as measured by the GERS, and the expenditure from reimbursed drugs, which result from the compulsory health insurance accounts. This consultation easily led to a consensus on the measurement of the consequence of moving certain drugs from a hospital distribution to an ambulatory distribution. . A specific sub-working group was set up to study more technical aspects, in particular, the comparison of the various sources of data. This sub-group also studied the results in terms of the movement of drug expenditure and the creation of the universal sickness cover. On this subject, the analysis will be pursued into the year 2001.

The second objective was to set up a system, recognised both by companies and the Committee, to determine the amount of non-reimbursed sales by drug. The creation and distribution by the CNAMTS, of detailed data on reimbursement has allowed for considerable progress to be made. Beyond the public release of the main findings, industry representatives were provided with the full statistics. The comparison of these data with the GERS sales can thus provide in the future, a more robust approach than before, of the use which is made of reimbursable drugs, drug by drug. This information should be consolidated in the future with that of other compulsory health insurance schemes.

Finally, the group was of course a place for regular confrontation about the analyses and the forecasts for the growth of the market undertaken both by the Industry and by the public service.

2. TRENDS IN DRUG EXPENDITURE

The following changes are largely due to the work undertaken the *Direction de la Securite Sociale* on behalf of the Committee, (department of financial studies and forecasts).

a) Growth in sales and growth in expenditure

The increase in the global reimbursable pharmaceutical industry turnover was at least 7.7 % in 2000, following a 6.7 % in 1999.

This increase represents the total sales of ambulatory drug spending in addition to the total amount of sales to the hospital sector. However, although the pace of growth in sales between the ambulatory sector and the hospital sector was very similar, 2000 was the exception; the

increase in hospital sales appears to have been significantly lower than in previous years, whilst ambulatory pharmacy sales increased by 8.9 % (source: GERS).

This is explained by the transfer of several drugs to the ambulatory sector (immunosuppressants as well as a drug for the treatment of hepatitis C), which, up to that point, were cross-charged to patients by hospital pharmacies. The result of this transfer is to reduce the growth of sales to hospitals by 5 points, whilst ambulatory spending increased by about one point.

It is also possible that added to these easily identifiable and measurable transfers is an effect resulting from the implementation of the Universal Sickness Cover, whereby some beneficiaries would have had access to drugs in the ambulatory sector which previously were available by alternative routes. This latter phenomenon is however very difficult to quantify and is unlikely to have markedly influenced the growth of ambulatory pharmacy sales.

Reimbursement expenditure on drugs by all the compulsory health insurance schemes will have increased by approximately 10.6 % in 2000.

The corresponding level is 11 % for the scheme managed only by the CNAMTS, whose expenditure regularly increases faster than that of other compulsory schemes. A large gap of approximately 1.7 points can thus be seen and needs to be explained between the rise in MSP (manufacturer selling price) sales in the ambulatory sector (8.9 %) and the increase of drug sales reimbursable by the compulsory health insurance (10.6 %).

The determining factors for the difference

At least four types of reasons can help explain why the growth of ambulatory expenditure and that of reimbursement are different.

Distribution margins

The distribution margin (wholesale margin + pharmacist margin) being on a sliding scale, reimbursements should grow a little less than manufacturers' turnover insofar as the growth of sales depends to a large extent on the increase in the average price of units sold (cf. b) below). However, all of the activities which accompanied the recent reform of the margin system, meant that this effect did not take place in 2000, the distribution margins thus remaining proportional to the manufacturers turnover.

The level of reimbursement

The growth in the real mean level of reimbursement results in a higher increase in expenditure of reimbursed drugs than that purchase of drugs presented for reimbursement. This growth in the mean level of reimbursement has several causes. The first factor to play a role, which is linked to the ageing of the population, is the increase in the proportion of patients who are fully covered, within the context of a long term disease (ALD – *Affection de Longue Duree*). In addition, the fact that sales of drugs that are reimbursed at 65 % or at 100 % grow more rapidly than for drugs reimbursed at 35 %, also plays a role. In 2000, the mean level of reimbursement therefore increased by 0.8 points to 73.8 %. This increase explains approximately 1.2 points of the difference between sales and reimbursement.

The hospital cross-charge effect

Drugs subject to cross-charging are dispensed at the hospital although they give rise to a specific reimbursement charged to ambulatory care spending. These drugs are therefore included in the CNAMTS expenditure although they are not part of the company turnover which tracks sales to ambulatory pharmacies. Drugs of hospital origin formed therefore part of the CNAMTS spending in 2000 although they did not appear previously in the GERS turnover. This situation, though far from explaining the difference between the growth in sales and that of reimbursement, increases by approximately 0.8 points the difference requiring explanation. It is also possible on the other hand that these cross-charges may have been increased. This potential effect could not be measured.

The gap between accounting dates

A possible explanation for the gap may be that drug sales are accounted for at the time of delivery to the ambulatory pharmacy whilst spending is recorded at the time of reimbursement. However, it is most unlikely that this effect plays a significant role since, if it were the case, this compensation would occur from one financial year to the next, which does not appear to be the case from the figures. The existence of CNAMTS data on drug expenditure by date of care should bring about an improvement in the understanding of these differences over the coming months.

We are therefore obliged to accept that the difference between sales growth and reimbursement remains in essence poorly explained.

b) Analysis of the growth of reimbursable sales in the ambulatory sector

The net pharmaceutical companies turnover was of 87.6 billion French francs in 2000, following-on from 80.4 billion in 1999 (i.e. an increase of 8.9 %) and 75.5 billion in 1998 (i.e. an increase of 6.6 %). The rise in turnover in 2000 is therefore almost 7.2 billion compared with 1999.

- The major part of this increase is attributable to the shift in consumption towards more expensive drugs.

The 8.9 % growth in turnover, including transfers, can be broken down into several parts:

The fall in the unit price of drug packs was **- 0.9 %** between 1999 and 2000. This fall in unit price mainly reflects the measures of price reductions occurring within the context of the Conventions signed between the Committee and pharmaceutical companies.

The increase in the number of packs sold between 1999 and 2000 was **+ 2.9 %.** This high level is perhaps explained in part by the implementation of the CMU, the aim of which was to enable its beneficiaries to have an easier access to healthcare, which therefore gave rise to an increase in volumes purchased in the ambulatory sector.

The outcome consequent to the rise in the mean pack price per constant unit pack price was put at **+ 6.8 %.** This effect is commonly **called a structure effect**; it corresponds to a distortion of the sales structure towards more expensive drugs or packs.

This structure effect has two components: a 'within class' component and a 'between class' component. The 'within class' component is the structural move, within a given therapeutic class[2], towards new innovative drugs marketed at prices higher than the old ones. **The 'within-class' structure effect was put at + 4.3 %** for 2000. The structural distortion, reduced by the advance of generic drugs, can also take place between different therapeutic classes, the most expensive classes developing at a more dynamic pace than other classes. This is the 'between class' effect. Between 1999 and 2000, **the 'between-class' effect was + 2.4 %.**

Table 1: The components of expenditure growth

	PRICE EFFECT	PACK EFFECT	WITHIN-CLASS EFFECT	BETWEEN-CLASS EFFECT
Year 2000	- 0.9 %	+ 2.9 %	+ 4.3 %	+ 2.4 %
Year 1999	- 0.7 %	+ 1.8 %	+ 3.0 %	+ 2.3 %

Compared to 1999, there was a more dynamic growth of 2.3 %. This pace was not related either to the price or to the 'between-class' structure effect. On the other hand, half of it is attributable to the quickening of the 'within-class' structure effect and half to increases in volume. The increase for 2000 is therefore due to an increase in volume sales as much as to a shift in prescriptions towards more expensive drugs.

- The major part of the increase in the turnover (T/O) in 2000 was limited to a small number of therapeutic classes.

When the increase in the turnover of 7.2 billion francs is broken down, it follows that three quarters of this increase is attributable to 18 out of the existing 320 therapeutic classes of drugs, which can be rearranged into 4 categories:

- **Major classes in terms of turnover which have shown a very marked growth;**

This group includes the statins, which increased from a turnover of 3.5 billion francs in 1999 to 4.4 billion in 2000 and proton pump inhibitors (PPIs) which had a turnover of 3.8 billion in 2000 compared with 3 billion in 1999.

These are the two most important classes in terms of turnover for 2000 and their high growth rate (25 % approximately) is not slowing down.

Non-narcotic antipyretic analgesics and antidepressants can also be added to this group (top 3 and 4 classes in terms of T/O), even if their growth has been somewhat less sustained (8 and 10 % respectively). These two established classes continue to grow at a high rate even though no new drugs have appeared.

All in all, these 4 classes contribute to almost a third of the total growth.

- **Small to medium classes which have undergone an extraordinary growth in 2000 due notably to the arrival of new drugs in the market;**

[2] *The classes used for this evaluation are the 4th grade ones in the EPHMRA classification*

The atypical antipsychotic group grew by 57 % in 2000 and the platelet anti-aggregant group also grew by over 50 %. In the treatment of arterial hypertension, the sartan class (CO9C + CO9D) is also highly dynamic; turnover increased by more than 32 % from 1.5 billion francs in 1999 to 2 billion in 2000.

The corticoid class used as topical therapy for allergic rhinitis achieved a turnover of 470 million francs in 2000, an increase of 50 %. The growth of β interferons is also close to 50 % in 2000 even though it slowed a little compared to 1999 (a growth of virtually 90 % in 1999). The turnover achieved was therefore 620 million francs.

- **Small classes, for which the growth rate was very high in 2000 due to their removal from the hospital drug budget at the end of 1999 and the beginning of 2000;**

The drug classes in question are the non-HIV antivirals and immunosupressants.

- **Medium classes for which the growth rate is similar to that of the global market;**

β2 inhaled stimulants, which represented 1.3 billion francs T/O in 2000, have grown at a rate of 13 %; inhaled corticoids for which the growth rate is 12 % correspond to 1.9 billion T/O in 2000; Non-steroidal anti-inflammatories for which the T/O was 1.9 billion in 2000, are growing at a rate of 8 %. The arrival of Cox-2s in the market should lead to a high growth in this class in 2001.

- **Contrary to these classes, which have enjoyed a steep growth, only 7 classes saw their turnover fall in 2000 compared with 1999:**

- The vasodilators class fell by almost 8 % in 2000 and veinotonics by 2 %.

- The anti-H2 receptor antagonists fell by nearly 12 % (their T/O was 1.25 billion francs in 2000) although their fall is more than compensated by the important growth of PPIs. This fall in the anti-H2s turnover was largely due to the progress of generics in this class - even though the number of generic units sold slowed down in the past few months - and to a lesser extent to a global decrease in all units sold.

- The turnover of drugs which increase gastrointestinal motility fell by a little over 7 % in 2000.

- The ACE inhibitor and the fibrate classes fell by 2 and 4 % respectively, even though this fall is not comparable to the parallel growth in the sartans and statins.

- Finally, broad spectrum antibiotics are falling by close to 3 %. It is however very difficult to draw any conclusions from it as sales in this class depends heavily on the prevalence of epidemics, particularly influenza, in 1999 and in 2000.

B. CONTROLS FROM THE CONVENTIONS

The strong increase in sales and reimbursement of drugs in 2000, which allowed to predict from the first month of the year that the threshold of the contribution called “safeguard contribution” would be widely exceeded, led the Committee to implement the financial

regulation instruments made available to it by application of the law: Conventions' discounts and price reductions.

1. REGULATION BY DISCOUNTS

a) Priority to discounts by classes

Regarding the quantitative year-end discounts that, in accordance with the *Accord Sectoriel*, pharmaceutical companies which have agreed with the Committee an exemption from the contribution for several years, have agreed to pay back the compulsory health insurance, similarly to 1999, the Committee gave more importance to the discounts related to the global change in pharmaco-therapeutic classes sales than to those based directly on the turnover of each company.

A revised version of the class threshold table (attached in appendix 5) has been distributed to all companies, accompanied by an explanation of the principles used in the creation of this table.

The Committee felt it useful to repeat that the growth rates that are shown in this table are neither forecasts nor ceilings limiting the prescription or the sales of the drugs involved, but thresholds beyond which it believes that the community should pay proportionately less for these products through obtaining a quantitative year-end discount.

It also reiterates that the real significance of the levels only appears when they are compared to the natural changes in the trend of sales in the corresponding classes. A rate, even when negative, which is applied to one class for which the foreseeable trend is that of an even greater decrease, does not mean that the Committee wishes to reduce the net resources set aside for these drugs, but rather, that it wishes to limit the reduction. On the other hand, a positive level, even when high, which is applied to a class where the expected change in expenditure is greater, means that the Committee deems justified to moderate the growth of public resources allocated to drugs of this class.

Apart from the creation and running of the table, which can be found in the 1999 report as well as in the appended documents, its revision for 2000 merits a few comments. The Committee first decided to prolong the table into 2003 i.e. beyond the validity of the Conventions, believing that the conventions were meant to be renewed and that the visibility period of the table should be maintained. The 2000-2002 levels themselves were adjusted, either to make room for the arrival of new drugs, or to take into account the actual sales for 1999, particularly when these sales exceeded the 1999 thresholds, and this "rebasing" thus justified a reduction in the initially foreseen thresholds for subsequent years.

b) The new discount levels

The strong acceleration of ambulatory sales from 1999 justified an increase in the overall discount level applicable to going over the threshold, which was 25 % in 1999 and which rose to 35 %, so that the financial return of the Conventions' system of regulation might be compatible with the aims of the safeguard legislative system.

Moreover, the Committee wanted the distribution of the class discounts, which, in 1999, were based half on the turnover achieved by each company in the class and half on the individual

exceeding of thresholds, to be modified in order for the turnover to have a greater impact. It became clear that the 50-50 distribution was unjustly penalising products being launched, whether non-exempt innovations or drugs without an ASMR registered at an attractive price for the health insurance. Following discussion with the SNIP, and concerned to avoid a too sudden fall, the new distribution was set at 65 % - 35 % for 2000.

c) The exemption system

This system has been clarified and consolidated. The duration of exemption for ASMR 1 drugs has been extended to 3 years. ASMRs I and II given to existing drugs for new indications, give rise to exemptions proportional to the prescriptions, which take effect at the date at which the opinion of the Transparency commission become final.

Low price exemptions are applied in full right to generic drugs as well as, on a case-by-case basis, to drugs whose prices are comparable generics'. On the other hand, the Committee systematically refused to exempt drugs on the sole grounds that their daily treatment cost was inferior to the average cost of the class. This happened particularly in classes where fairly homogenous old groups of low price drugs co-existed with more recent and more expensive groups of drugs due to the ASMR they had been granted. The Committee did not accept to exempt drugs in the less expensive group, considering that their price was correct in this group, though this may lead to a segmentation of the classes involved when the table is next modified.

Publication by the CNAMTS of its drug reimbursement database has finally enabled to forecast in certain cases a partial exemption for drugs where a significant proportion of the sales does not imply reimbursement.

2. REGULATION THROUGH PRICE REDUCTION

The Committee carried out price reductions within the Conventions in three circumstances.

a) Price reductions due to Insufficient SMR (Service Medical Rendered)

In accordance with ministers' instructions and as a result of the initial consequences of the re-evaluation of reimbursable drugs, companies selling drugs whose SMR was declared by the Transparency Commission to be insufficient to justify their reimbursement by the health insurance, were asked to take initial[3] price reductions.

Companies were therefore submitted Conventions of reductions for more than 600 drugs (to which calcium-based products were added), in accordance to scales which essentially took into account the range of daily treatment costs in the various classes. These scales were also adjusted so that the impact of the reductions on companies was, in almost all cases, equal at most to 3 % of their turnover.

The Committee accepted to adjust these proposed reductions within the Conventions as long as the overall impact on the company remained constant and that would not have brought any serious distortion of competition between comparable drugs. The Committee also accepted, with the agreement of the regulatory authorities, that de-reimbursement be substituted to the

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[3] *For some drugs, a price reduction had already taken place in 1999, but on a different basis, which was that of a harmonization of the costs of daily treatment in the former classes of economically substitutable drugs.*

required price cuts when the risk of transferring prescriptions to reimbursed drugs was considered to be low.

In all, this operation resulted savings of 702 million francs, expressed as annual net turnover from manufacturers, and includes 550 million francs of price cuts and 152 million francs of de-reimbursements. This amount represents exactly 7 % of the total turnover involved in this operation.

b) Price reductions via the application of revision clauses in the Conventions

A number of price Conventions contain revision clauses indexed on sales volumes, dosages used, or finally, when the drug is available in several formulations or dosages, on the average daily treatment cost observed (see part B of the second section). In 2000, reductions undertaken on this basis represented 192 million francs (value for the full year).

c) Price reductions without clauses

The Committee also asked, outside any revision clauses, for a certain number of price cuts in the case of drugs which were estimated to have become abnormally expensive for the community, given their sales volumes. These price cuts requests were often– but not exclusively – asked at drug re-registration time, as the regulation clearly sets out. These were mostly drugs which had already enjoyed long and successful sales and for which prescribing was found to be significantly superior to what was foreseen at the time of registration, or re-registration drugs belonging to classes in which, since the initial pricing decision, less expensive competitors were marketed. In 2000, these reductions represented 322 million francs (value for the whole year).

3. 2000 EXEMPTIONS TO THE CONVENTION

The law states that "companies that have concluded (…) an agreement with the Health Products Economic Committee (…) still valid on the 31st December of the calendar year for which the contribution is due, are not liable for the contribution set out in article L 138-10".

At the end of May, the Committee therefore addressed to all companies a proposal of amendment to the Convention regarding the calculation methods for year-end quantitative reductions, the acceptance of which determined the exemption to the Convention for 2000, without detriment to the special clauses requiring negotiation between each company and the Committee.

In practice, negotiations took place rather late and occurred during the last weeks of the year for the majority of companies. Given below in report form are a description of the principles which guided the Committee in this negotiation as well as the National Health Convention figures.

a) Principles implemented during negotiations

The Committee applied strictly the clauses of the *Accord Sectoriel* as well as the rules which it had published on the calculation of discounts. Specifically, class discount exemptions were agreed as per entirely uniform principles. Numerous companies deducted that room for

individual negotiation was fairly limited, which was true. The Committee had in effect considered that equality of treatment between companies required that the results of collective negotiation with industry representatives be directly applicable to specific conventions.

With regards to discounts related to the global turnover of each company, the Committee very often asked for a revision with the aim of lowering the triggering thresholds of these discounts contracted for 2000 in the initial Conventions. The Committee restated at this time the terms of the Social Security Code, explicitly repeated in the specific conventions and which foresaw that the Committee should call for the revision of the conventions when, as was the case, changes in drug expenditure were clearly not compatible with the ONDAM. It was furthermore necessary, in accordance with an explicit request from industry representatives, to maintain a significant place for turnover discounts in the overall discount.

The negotiation of Convention amendments also took into consideration, for each company, the safeguard contribution that it would have had to pay in the absence of a convention. This reference to the safeguard system was realistically considered both by the Committee and by the companies in question as being a useful guide. However, in the essence of the *Accord Sectoriel*, these "indicators" were systematically adjusted for companies whose ambulatory market growth in 2000 was strongly influenced by the increase in their generic sales, or by the transfer of their drug from the hospital to the ambulatory sector.

The Committee maintained the simplified Conventions system, created in 1999, for the benefit of small companies and for whom the principle benefit, over and above the formal simplification of conventions, was a maximum discount of 1 % of their turnover. In 2000, these simplified conventions involved 79 companies for which, by way of illustration, the global amount of safeguard contributions which they would have had to pay in the absence of a convention, represented hardly any more than 1 % of what would have been the total contribution from the industry.

Finally, the Committee applied the following principles regarding the question of compensation between discounts and price reductions: in accordance with the *Accord Sectoriel*, the collective price cuts initiated by the Committee, particularly all cuts for reason of insufficient SMR, gave rise to discount credits to companies. On the other hand, the cuts which resulted from the application of price review clauses in the Conventions, cannot, by definition, be compensated for in the discounts. Other reductions were treated on a case by case basis: those put forward spontaneously by companies were deducted from the discounts as planned for in the *Accord Sectoriel*; certain reductions suggested by the Committee in the course of the final negotiation were also considered as deductible, when it was realised there was a means of anticipating the price revisions which normally would open the discussions in 2001.

b) Year 2000 figures for the Convention

Conventions or amendments of exemptions to the Conventions for the 2000 safeguard contribution were concluded with 165 companies or pharmaceutical groups. All in all, these companies represented 99.9 % of the reimbursable drugs ambulatory turnover for the industry. A dozen very small companies refused the proposed conventions put to them.

4. GLOBAL RESULTS OF REGULATION

Overall, the whole of the conventional measures taken in 2000, whether discount agreements or price cuts, will reduce the net reimbursable drug turnover of the pharmaceutical industry for 2001 by almost 3 billion francs. This sum is made up of a little less than 1.8 billion francs of discounts for payment in 2001 through the application of Conventions in force at the end of 2000, and close to 1.2 billion franc resulting from the impact in 2001 of the price cuts and de-reimbursement agreed in 2000

Expressed as an impact on the growth of the net sales of reimbursable drugs, and all other things being equals, these measures will reduce the increase in year 2001 sales compared to 2000 by 2.3 points, 1.3 point due to the price cuts and 1 point due to the positive difference between the discounts paid in 2001 and those which were paid in 2000 (913 million francs).

It happens that this overall amount is of the same order of size as the return of the safeguard contribution would have been the in the absence of conventions (2.9 billion francs). The two concepts are not however directly comparable since, in the absence of Conventions of exemptions, a significant proportion of the price reductions and the specific discounts per product would have been added to the safeguard clause.

C. THE OUTCOMES OF THE ADVERTISING BANS

Article L. 162-17-4 of the Social Security Code, as it results from the Social Security Financing Law (SSFL) for 1999, foresaw that "when a ban on advertising has been announced by the French health safety agency for healthcare products (…), the economic committee for healthcare products can ask the company concerned (…) to modify the prices of drugs which are subject to a ban on advertising, or to pay a discount".

2000 was the first year this arrangement was implemented. The Committee systematically examined the advertising bans announced by the French health safety agency for healthcare products (AFSSAPS).

a) Procedure

The Committee implemented a procedure closely inspired from the one used to fix drug prices within the Conventions, although leaving a specific place for the contradictory debate with the company.

As soon as it is informed of the ban, the Committee names a *rapporteur* who studies the dossier and then presents it at the meeting. The Committee rules its position and, apart from cases where it believes that the advertising ban alone is a sufficient consequence for the offence committed, it sends an explanatory Convention proposal to the company within a one-month period as per the law, inviting it, if it so wishes, to present its observations.

The company could then, as it chooses, be heard in session by the Committee or could meet up with the President of the Committee for an oral discussion. In all cases, companies make their position known in writing. The dossier is then again entered on the Committee's agenda, which rules its definitive position and informs the company of it.

In one case, the company did not accept the Committee's proposal of Convention and the price cut that the Committee had proposed was then decided by interministerial decree.

b) Principles

The Committee endeavoured above all to propose measures proportional to the severity of the breach brought to light by the bans. This severity was evaluated with regard to two main criteria:

- the risk to health which can result from the poor use of the drug encouraged or suggested by advertising;
- the economic risk related to the unjustified expenditure for the health insurance body or a threat to honest competition between companies which can result from the advertising.

The Committee naturally was deemed to be bound by the pronouncement of the banning decisions and in particular, refused to enter into any discussion with companies which questioned the substance or the terms of practices being the subject of the ban.

For the determination of the proposed price cut rates, the Committee took into account the effect of these reductions on the turnover of companies. Thus, for the same severity, it could ask for greater or lesser reductions depending on whether the drugs in question represented a greater or lesser proportion of the total sales of the company.

Apart from cases where the Committee had believed, as the law allows it to do so, that there was no cause to take measures of an economic nature beyond the ban itself, it systematically proposed price cuts, sometimes over a limited time span though, by considering that the payments of discounts set out in the law were more adapted, as a complement to the fall in price, when it could be established that the advertising ban had resulted in unjustified expenditure for the Social Security body, which thus merited compensation.

c) Statement

In this context, in 2000, the Committee gave a ruling on 15 pharmaceutical products, for which, for the majority, the representatives reported properties or indications invalidated by the corresponding marketing authorisation (AMM). Price cuts of between – 1 % to - 5 % were decreed in 12 cases with a duration of 1 year (7 cases) or unlimited (5 cases). In 3 cases, the Committee did not feel justified to propose a price cut.

D. THE GENERIC MARKET

The development of generics is playing a growing role in the regulation of drug costs. In this respect, the Committee tries to encourage and to accelerate the progression of dossiers of such formulations, as it was committed to do in the *Accord Sectoriel*. As a general rule, the registration of generic drugs is no longer subject to the approval of the Transparency Commission.

The control of drug costs in the Conventions has no bearing on generics; the turnover achieved by virtue of their sales, like for all those innovative drugs, reduces the quantitative year-end discount base. Likewise, no constraint regarding the growth rate of promotional expenditure was imposed on generics.

Regarding the price of generics, the Committee accepted the price proposals of the company providing it was at least 30 % lower than the net manufacturing price (NMP) of the reference

product. The NMP of the chosen reference product is the one in force since the 1st January 1996 for generics listed in the directory of August 1999, and the one in force at the date of the company's submission for products corresponding to generic groups created since the directory of January 2000.

In spite of the right of substitution which has been available to pharmacists since June 1999, with a view to encourage the development of generic sales and therefore lowering the average price of drugs in the groups in question, and even though the incentives were considerable (adjustment of margins to reference products, exemption of the tax on direct sales and greater commercial discounts for generics than for reference products), generic sales only increased moderately. The growth of direct sales of reference products perhaps explains part of this limitation.

Overall, in the last generic directory appearing in the Official Journal of the 13th January 2001, the Social Security assesses, for 2000, the proportion of generic drugs in the market to be of 2.7 % in terms of the value of reimbursable drugs (net turnover: NT/O). On the basis of this same directory, the value of generic groups (NT/O) was 13.1 billion francs, 2.4 billion of which were generic drugs. By way of comparison, in 1999, on the basis of the directory published on August 29th 1999, the field under discussion was 8.8 billion francs, 1.6 billion of which was for generic drugs (Source: GERS).

II. Drug price negotiation

The price fixing of drugs is the basic role of the CEPS and represents the main part of its activities.

This activity, during the 2000 twelve-month period will be looked at:

- on the one hand, from a quantitative standpoint, from the census and the analysis of dossiers forwarded and processed by the Committee;
- and on the other hand, by revealing the price calculation methods which the Committee used in its negotiations with companies.

A. CEPS ACTIVITY IN 2000

2000 was marked by a strong growth in the number of dossiers filed with the Committee and by the parallel increase in its activity measured by the number of dossiers processed. For all that, the number of dossiers not yet dealt with within the twelve-month period is at a high level. The overall delays in the processing of dossiers remain significant. Difficulties remain, generating additional delays in the processing of dossiers, which are not all under the control of the Committee alone (delays by the Transparency Commission, company response delays, delays in the signature of decrees).

We give in sequence, an assessment of the activity in 2000 (applications submitted[4] and processed), an analysis of processing delays, finally an analysis of the supply of on-going dossiers for the 2000 twelve-month period.

1.OVERALL ACTIVITY OF THE COMMITTEE IN 2000

a) Applications put to the Committee in 2000

1,649 applications were submitted to the Committee between January 1st and December 31st 2000[5]. Compared to the previous year, the number of applications submitted has increased by 21 %. In 1999, 1,364 applications were submitted, 1,076 in 1998.

The pace of submissions was found to be more uniform than in 1999, a year during which a peak in submissions in July was observed (20 % of applications for the year). Moreover, the growth of submissions previously seen at the end of the twelve month period was less marked.

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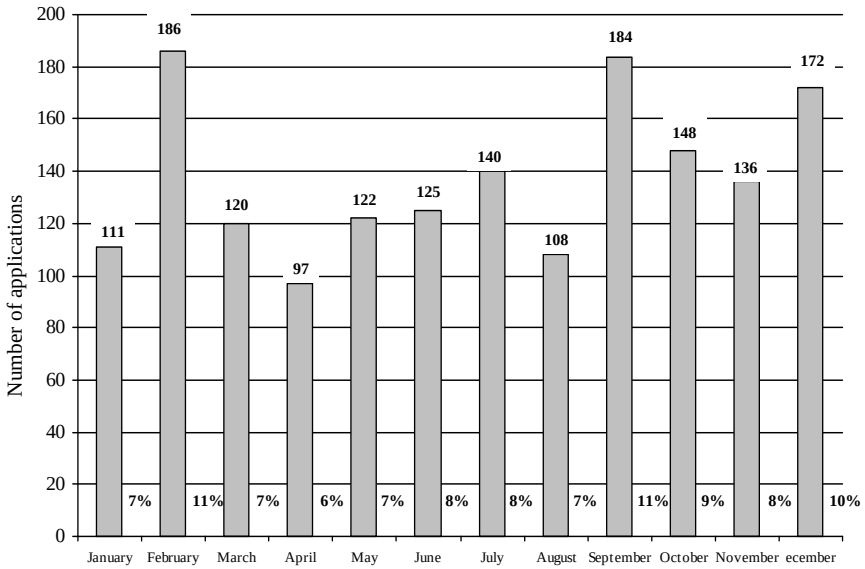
[4] *By price applications, we mean the applications which were made at the time of registration, of a renewal of registration, of a price modification or an extension of therapeutic indications, to an application corresponding to a presentation (or a CIP number); there are as many applications as presentations: for example, a drug packaged in 5 ml or 10 mls corresponds to two presentations and therefore two applications.*

[5] *This detailed account does not include strike-off applications.*

Figure 1: Rate of application of submissions to the CEPS during 2000



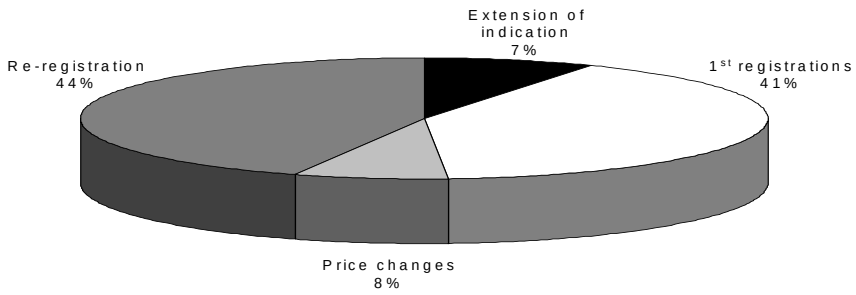
Among the applications submitted in 2000, 35 % correspond to generic drug presentations.

Table 2: Characteristics of the applications submitted in 2000.

	1ST REGISTRATION	RE-REGISTRATION	PRICE CHANGE	EXTENSION OF INDICATIONS	TOTAL
GENERICS	329	212	24	7	**572**
OTHERS	346	522	107	102	**1351**
ALL	**675**	**734**	**131**	**109**	**1649**

It can be seen that the important growth in applications forwarded to the Committee is mainly due to the large number of re-registrations and also the extension of indications. When confined to first registrations, the growth in applications is only 3% compared to 1999 and is therefore not significant.

Figure 2: Type of application submitted to CEPS (all submissions)

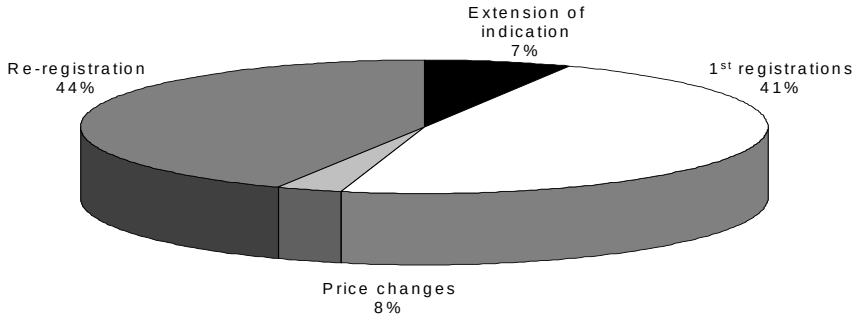


Finally, these figures do not include dossiers open at the initiative of the Committee, and in particular, not all price cuts agreed for drugs with an insufficient SMR.

b) Dossiers closed in 2000

In 2000, 1,398 dossiers were brought to a conclusion, whether by means of an agreement between the company and the Committee having given rise to a public decree in the Official Journal, or a rejection or withdrawal. This number of dossiers is growing by 21 % compared to 1999, a year during which 1,156 dossiers were concluded.

Figure 3: Distribution of dossiers processed in 2000 according to the nature of the request



The 1,398 applications processed by the Committee in 2000 correspond to 142 different companies, i.e. close to 10 applications on average per company and a maximum of 60 applications for one in particular.

It can be seen that in 1999, the number of applications having been concluded was less than the applications forwarded to the Committee during the twelve-month period. This difference, which amounts to 251 applications, therefore gives rise to a growth of the same level in the amount of on-going dossiers at the end of the twelve-month period (cf. 3 below).

This situation, which is clearly unsatisfactory, calls however for two comments:

- The first is that, on the one hand, the difference observed can be explained by the work of the Transparency Commission being interrupted during the summer of 2000 which, for several weeks, up to the nomination of the new commission, affected the activity of the Committee;

- The second comment is that more than four fifths of the growth in dossiers involved re-registrations and the extension of indications. On the other hand, in the most sensitive field, i.e. market access for new formulations, the Committee concluded a number of new registrations which were almost equivalent to that of the applications submitted to it (659 versus 675).

2. DOSSIER PROCESSING DELAYS

Article R.163-7-1 specifies that for the registration of a drug "decisions (…) must be taken and notified to the company selling the drug, within 180 days from the day of reception of the application (…). Registration of the drug on the list and the setting of its price are published in the Official Journal within this time limit". Regarding the requests for price changes, the dossiers submitted must be dealt with within at least 3 months.

The following presentation analyses, according to the type of application and the decisions taken by the Committee, the delay in processing dossiers, since their submission to the Committee, up to, when appropriate, the publication of decrees in the Official Journal (withdrawals or rejections are not published in the OJ). They integrate therefore the processing delays of applications by the Committee and also those relative to the examination of these dossiers by the Transparency Commission, or the negotiation between the Committee and the company.

a) The total delay

For the whole of 2000 dossiers, having caused the publication of a decree in the Official Journal, the mean delay between the submission of the application to the Committee and its conclusion was, as in 1999, **196 days**.

This delay was only slightly influenced by the interruption in the running of the Transparency Commission, since a large proportion of applications for which the processing had suffered from this interruption, were not yet concluded by December 31st and were not therefore accounted for in this 12 month-period.

The mean applications processing delays differed significantly according to the nature of the request and the type of decision taken by the Committee, but also according to the category of drug, generic drugs and other drugs being the subject of the application.

The total delay according to the nature of the application

Initial registration, re-registration, price changes and indication extensions are treated separately:

- **The initial registrations,** having brought about the publication of decrees in the Official Journal, were processed with a mean delay of **177 days**. (Median delay: 132 days). 68 % of dossiers were processed in under 6 months.

- **Re-registrations** were processed with a mean delay of **233 days**, a delay 30 % greater than that seen for initial registrations. This mean delay for renewing registration, paradoxically longer than that of the initial registrations, may be explained particularly by the procedure followed, leading companies to submit their dossier, sometimes more than 6 months prior to the planned date of re-registration. The applications thus submitted are not immediately examined which further lengthen the delays between the actual submission and examination in session of these applications. Indeed, the fact should also be taken into account that among these re-registration dossiers, the proportion of dossiers relating to generic drugs is of little importance.

- **The indication extension application** was concluded with a mean delay of **257 days**.

- **Price change applications** were concluded with a mean delay of **77 days**, which corresponds to 83 days for applications having brought about a publication in the Official Journal and to 68 days for rejected applications.

The total delay according to the type of drug

Generic drugs

The mean delay in the processing of dossiers corresponding to generic drugs was 140 days, which corresponds to 109 days on average for initial registration requests, 222 days for re-registration applications and to 69 days for price modifications. This mean processing delay hides a marked acceleration in the processing of these dossiers by the Committee during 2000. Though the mean delay observed was 184 days for dossiers submitted during the first quarter, it was only 145 days for those submitted during the second quarter and 103 days for those submitted during the thirdarter.

Other drugs

The mean processing delay for applications for other drugs was 233 days, which corresponds to 259 days for initial registrations, 234 days for re-registrations and to 87 days for price modification requests.

Compared with the processing delays for generic drugs, the delays for other drugs were two thirds longer. In the main, the difference is the result of the fact that the generic drug dossiers were no longer required to be examined by the Transparency Commission, even though a tiny fraction of them (5 %) were still looked at during 2000.

b) Intermediate delays

Analysis of the intermediate delays only involved applications for an initial registration having ended with a publication in the Official Journal.

The total processing delay for an initial registration dossier has been broken down into 4 stages, from the submission of the dossier to the CEPS, the passing on of the opinion of the Transparency Commission (CT) to the Committee, the passing on to the first session of the Committee (Instruction), from the first to the last session of the Committee given over to one dossier (Examination) and from this last session to the publication of the corresponding decree in the Official Journal (OJ).

In the following table, the delays are allocated according to these 4 stages.

Table 3: Processing delays for application for an initial registration (number of days)

TYPE OF DRUG	CT	INSTRUCTION	EXAMINATION	OJ	TOTAL
NON-GENERIC	96	55	53	55	259
GENERIC	1*	53	4	51	109
TOTAL	NS	54	26	53	177

** Residual delay, 4 % of generic dossiers having been concluded in 2000 were subject to examination by the CT.*

Overall, the initial registration dossiers were processed with a delay of **177 days** between the date of their submission and the date of their publication in the Official Journal.

The mean difference in the delay between generic drugs and other drugs is considerable, 109 days for generics, 259 days for other drugs. Apart from the wish of the Committee to accelerate the processing of applications corresponding to generic drugs, this difference results mainly from the future absence of the need for examination by the Transparency Commission. It is also due to the fact that a very small proportion of the initial registration dossiers for generic drugs are subject to several sessionary examinations by the Committee (8 %), whilst this was the case for close to 50 % of non-generic, initial registration drug dossiers.

First stage: Transparency Commission

Dossiers must be simultaneously submitted to the Committee and to the Transparency Commission. This first stage corresponds to the examination of the application by the Transparency Commission and the passing on of the opinion of the Commission to the Committee. With regard to the initial registration of non-generic drugs, the opinion of the CT was given with a mean delay of **72 days** after submission of the dossier[6]. This delay was greater by 21 days to the delay observed in 1999, which was 51 days.

The delay seen in this stage with regard to generic drugs is very short, of the order of 1 day, only 4 % of generic drug dossiers having been subject to such an examination.

To this examination delay by the CT can be added that relating to the forwarding of the opinion to the Committee. On average, during 2000, notifications were passed on to the Committee **24 days** after their definitive adoption[7].

In all, the mean duration of this initial stage was **96 days** for the initial registrations of non-generic drugs.

Second stage: Instructions by rapporteurs

This stage, which extends from the date at which the opinion of the CT is passed on to the Committee where the presentation is examined for the first time in session by the Committee, includes, among others, the naming of a rapporteur, the studying of the dossier by the rapporteur in liaison with the company and the delay linked to the entry on the Committee's agenda (one week after communication of the report to the members of the Committee).

Between the forwarding of the opinion to the Commission and examination in session of the corresponding application by the Committee, an average of **55 days** goes by in the case of non-generic drugs, this delay being more or less identical in the case of generic drugs. This latter delay, which is clearly abnormal, can be explained by the implementation, at the end of 1999 and the beginning of 2000, of a new generic examination scheme and the determination of cases in which drugs could be exempted from Transparency Commission approval.

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[6] *The opinions of the Transparency Commission **given during 2000** were on average 89 days after submission of dossiers, all applications included. This mean delay, which was 73 days before the renewal of the Commission increased to 109 days after the 3 months interruption.*

[7] *This delay includes the time granted to companies to compile their observations on the opinion of the CT.*

Third stage: Examination by the Committee

The delay between the date of the first and that of the last examination in session by the Committee corresponds to a negotiation stage between the Committee and the company. The counter propositions of the company are examined and discussions are undertaken by the *rapporteur* to achieve an agreement which satisfies both parties. This delay is an average of 53 days in the case of non-generic drugs, but only 4 days for generics. 90 % of initial registration applications for generic drugs are examined at one single session, whilst this is not the case for 50 % of initial registrations involving other drugs.

Fourth stage: Signature and publication in the OJ

This stage corresponds to:

- On the one hand, examination by the company of the Committee's proposition, if this differs from its application and, following agreement, the signing of the convention between the Committee and the company. This stage can be more or less long depending on the urgency felt by the company for the marketing of the presentation;

- On the other hand, the signing of the decrees by management of the Ministry of Employment and Solidarity and finally the publication delay in the OJ.

In the case of non-generic drugs, the mean delay observed in 2000 was **55 days**. It was 51 days in the case of generics. In 95 % of cases, the publication took place less than 3 months after the last session of the Committee given over to the application.

3. ON-GOING APPLICATIONS

The spate of "outflows0", made up from the number of dossiers concluded during 2000 twelve month period, which rose to 1,398 dossiers, parallels the spate of "inflows" during the same year, i.e. 1,649 dossiers. The difference between these two figures, i.e. 251 has led to a proportional inflation in the number of on-going dossiers which reached 1,042 dossiers at the end of 2000 (the number of on-going dossiers on the 31st December 1999 was 791).

In the case of 136 on-going applications on the 31st December, the decision was ruled and the propositions of the Committee at the time of signature or the decrees corresponding to the signature or in the OJ publication …[8] 250 other applications were the subject of at least an initial examination by the Committee before the end of 2000.

At December 31st 2000, 367 first registration applications were on-going, 70 of which corresponded to generic drugs and 297 to non-generic drugs among which, 164 were not subject to an opinion by the Transparency Commission. Overall, 40 % of first registration on-going applications were already subject to at least an initial examination by the Committee. The mean duration of applications, not having been subject to such an examination by the end of 2000, was 116 days.

[8] Translator's note: This sentence makes no sense in French – something is missing.

B. THE COMMITTEE'S PRICE NEGOTIATION METHODS FOR 2000[9]

Article L.162-16-1 of the Social Security Code determines the regulations for the price fixing of drugs reimbursable by Social Security:

"The sale price to the general public of each of the drugs mentioned in the first paragraph of article L.162-17 is fixed by Convention between the company marketing the drug and the drug's Economic Committee in accordance with article L. 162-17-4 or by default, by a Health and Economy Social Security ministerial decree after receiving the opinion of the Committee. The fixing of this price mainly takes into account the improvement in the medical service made possible by the drug, the prices of drugs with the same therapeutic aim, the sales volumes foreseen or observed as well as the foreseeable or actual conditions of use of the drug".

The law is clarified by registration reimbursement regulations (Art. R.163-5-1-2°) which state that "drugs which provide either no improvement in medical service as assessed by the Commission mentioned in article R.163-15, nor economic in terms of the cost of drug treatment" cannot be registered in the list as set out in article L.162-17 of the Social Security Code.

These public order regulations form the basis of the action of the Committee. It is however useful to recall the methods used by the Committee in its relationship with companies by distinguishing the general principles and those applied during the initial price negotiation and at the time of its upwards or downwards adjustment.

1. THE GENERAL NEGOTIATION FRAMEWORK

The mission of the Committee is to obtain the most advantageous economic conditions and price for the health insurance body by taking into account both the global drug market and the limitations of the ONDAM, the needs of Public Health and the requirement to treat companies equally fairly.

The principle of taking into account the global drug market requires that all specific drug price discussions be clarified over and above the bilateral framework of the negotiation, by an analysis of the economic consequences of this price on the effect on the market and health insurance expenditure: direct and immediate consequences on the class price structures, indirect consequences on the relative class effect, mid-term consequences when the financial impact of reimbursement on the ONDAM are estimated and also long term consequences when it is possible to anticipate the subsequent arrival of drugs with the same indications.

The priority principle of meeting the needs of healthcare signifies that, by its action, the Committee must allow for the provision of the market of reimbursable drugs, for which price fixing only represents one means.

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[9] *The details which follow are, with a few points of information, almost entirely resumed in the 1999 report, the Committee having deemed it useful to provide the readers of its report and especially company negotiators, with a complete account of the principals of price fixing which it applied.*

The principle of equality of behaviour between companies is rather a principle of equality of behaviour between drugs irrespective of the companies marketing them. On specific consequence among others of this principle is that the Committee does not consider itself justified, irrespective of the interest it has in research and in innovation, in pre-financing research through the price of drugs which in themselves do not incorporate the sought after results of this research, or, all the more so, with respect to innovative drugs, to treat them differently according to the area in which the innovation plays a role.

2. REGISTRATION COSTS

For the initial price determination, at the time of an initial registration, the rule set out by the decree on reimbursement leads to two situations being distinguished and two alone:

- either the candidate drug for reimbursement has no ASMR and its registration must lead to economies for the Social Security body;

- or it has one and its registration can cause additional costs.

The Committee has not discussed the ASMR level set by the Transparency Commission. The useful negotiating path is therefore clear as soon as it has given its opinion, it being recalled that the text in no way prevents the Committee from demanding a saving for Social Security – or at least cost neutrality – even when the drug has an ASMR, and in particular, a minor ASMR.

Price fixation must be matched to review clauses each time that the initial price is agreed by consideration of the hypotheses that only time and usage will permit invalidation or confirmation.

a) Price fixing

Drugs without an ASMR

The Committee must obtain the negotiated price which results in a saving for the Social Security body. Application of this rule calls for four main comments:

- The first is that savings are not necessarily measured by unit price differences between new drugs and those already registered, to which they are compared by the Transparency Commission, but to spending savings, which is the product of volume price deviations. One result is that the Committee can accept prices which are not lower than those of the previously registered comparison drug when it is shown that a lower price would constitute, for the company marketing the drug requiring registration, a competitive handicap in making this drug known to prescribers and that very little would be sold. The Committee has considered a similar case that might be beneficial for the health insurance body when the new competitor has the means of taking a significant part of the market, once this would be at a price lower than that of the most sold class of drugs. For the same reasons, the Committee accepted in one case, on an experimental basis, a significantly higher price than that of less expensive comparator drugs, but much lower than those of the most sold drugs in the group. The corresponding convention deals with the consequences which need to be drawn if the foreseen savings were not realised;

- The second comment rests on the distinction between classes of drugs in which prescription volumes are rigid (reliable diagnostics, precise and limited indications) and those in which there is an unjustified volume growth risk. In the former, the arrival of a new competitor can only have the effect of displacing parts of the market; this competitor is therefore welcome, even with a relatively slight price advantage. This is not the case in the latter where the relative price advantage related to the arrival of a new player risks being compensated, even overtaken, by the overall growth in volumes which result from the increase in promotional pressure on prescribers. The Committee is then more wary;

- The third, more specific comment, deals with the question of additions to the (product) range. Generally speaking, these new presentations do not benefit from any ASMR and the question which the Committee has to answer, is to know if a good comparator, for assessing the effect of registration of the drug on Social Security expenditure, is the product range in which the new product is inserted and which it will substitute in part, or if it is marketed equivalents sold at a possibly lower price by other companies. In 2000, the Committee most often accepted the comparison with less expensive competitor drugs;

- Final comment: the Committee was particularly careful, in cases of pharmaceutically novel compounds with no ASMR, to check that the registration of these new drugs could not have the effect, if not the aim for products for which patent expiry is imminent, of commercially or legally closing the development route for generics. In this situation, the Committee was able to subordinate the registration to obtaining a saving in relation to that which the corresponding generic would produce.

Drugs with an ASMR

The registration of drugs could cause additional costs for the Social Security. The determination of the acceptable additional cost was a difficult question for the Committee, the solution to which cannot be fitted to a model. It restricted itself therefore to stating a few principles which defined, from the Committee's point of view, the context of the negotiation.

It should first of all be recalled that any ASMR does not necessarily justify a price difference compared to already registered comparator drugs. In many cases, particularly for minor or modest ASMRs, the Committee determined that a sufficient "benefit" for the company consisted of the growth of its parts of the market, without there being a place for adding a price advantage.

Secondly, there are no acceptable price difference scales available which combine the ASMR scale, even though it is true that a minor ASMR cannot justify a major price difference. The price discussion of a markedly innovative drug constitutes therefore an open negotiation where the requirements of the company and the greater or lesser needs or urgency, in terms of satisfying healthcare needs for the drug to be registered for reimbursement are confronted. In this negotiation, the "European" price of the drug was considered realistically by the Committee as being a legitimate constraint for the company, but which was only opposable by the administration insofar as it estimated that registration was justified at this price. In other words, the Committee generally understood that a company did not accept a too reduced price compared with those which it had in other large markets of the European market, but there is a risk that the drug, if the innovation it brings is judged to be insufficient with regards to healthcare benefits and needs, is not registered at all. The Committee has, moreover, frequently brought to attention the fact that France is part of the European Union, that the

French drug market represents an important part of the European market and that as a result, no company can put forward a truly European price whilst the French reimbursement price has not been set.

Adding to the fact that in addition, the registration of truly innovative drugs frequently lends itself to the conclusion of volume clauses, particularly in the more numerous cases where a strong ASMR is accepted for the drug than in the case of limited indications.

In one case, the Committee concluded a convention with a company fixing, besides the initial registration price of the drug, the date and the amount of a programmed reduction of this price. This new mechanism was wanted by the Committee as it enabled a compromise to be reached between the limitations of International launching of the drug for the company and the need, as regards a drug inaugurating a named class in France, no doubt with the aim of producing heavy prescribing, to foresee from the onset the rapid return to supportable daily treatment costs for the collective resources.

b) The price review clauses

There are two types of price review clauses: daily treatment cost clauses (DTC) and volume clauses. The object of the first is to guarantee that the actual cost, per patient, of the use of a drug remains unchanged in accordance with that agreed with the company at the time of registration. The object of the second is to guarantee that the overall expenditure devoted to a drug remains in keeping with the medically justified "target" for this drug. The principle model-type clauses are given in appendix 6.

Daily treatment cost clauses (DTC)

The DTC clauses are divided into two categories: the dosage range DTC clauses and the dosage clauses.

The dosage range DTC clauses

Many drugs, for which a "dose-effect" has been established in their use, are made available in several dosages, either from the time of marketing, or subsequently with the registration of additional dosages. The Committee took the view in such a case that the best means of guaranteeing both the satisfactory use of different dosages of drugs and the equality of treatment between competitor companies in the category under consideration, was that all dosages of the same drug should be sold at the same price by pharmaceutical unit. The uniform price prevents companies from having an interest in specifically promoting the sale of the highest and the most expensive dosages. They further permit the maintenance over time of the cost of treatment as well as the balancing of relative prices between competitor companies, as the actual price of treatment is then independent of the distribution of sales between different dosages.

When uniform price fixing is not possible, particularly when due to price reasons of International uniformity, a dosage range DTC clause is substituted in order to obtain more or less equivalent results. In such cases, what is agreed with the company at the time of

registration is in reality a daily cost of treatment, translated into up-front prices of the various dosages in accordance with a prescription distribution hypothesis. If it is seen that the actual distribution use differs from the supposed distribution, the up-front prices are revised in order to re-establish the conventional treatment cost.

Dosage clauses

The aim and the mechanism of these clauses are exactly the same as for the dosage range DTC clauses. It is agreed at the time of registration of a treatment cost based on a mean dosage hypothesis (AMM dosage or dosage demonstrated by studies formerly carried out at registration, including in countries where the drug has already been marketed). If the dosage noted on use, differs from that on the basis of which the sales price was established, this price is revised to re-establish the agreed cost of treatment.

Volume clauses

The Committee was of the opinion that the volume clauses were not justified when their main effect was to divide up markets between competing companies. They have moreover, without exception, no meaning at all for the registration of products without an ASMR, the sales of which give rise to a saving for the Social Security body, this saving being all the greater, as the sales achieved by substitution of more expensive products are themselves significant. The end-of-year quantitative discount mechanism per therapeutic class seems therefore to be the most appropriate. In fact, a very large number of volume clauses were suspended in 1999, at the time of the conclusion of the company conventions.

The Committee on the other hand, negotiated price-volume clauses in the cases where the ASMR of an innovative drug was applicable to one part only of its indications, or for a quantifiable and limited population of patients, but where there is the risk nevertheless that the drug is prescribed for all its indications, by replacing less expensive drugs and with no advantage to patients.

These clauses also have their place, independent of any financial consideration, when Public Health reasons demand that a drug is only used in limited indications where it is strictly essential, as is very often the case for antibiotics.

The volume clauses have finally sometimes been used during registration of truly innovative drugs, when a great deal of uncertainty existed in the new product market, in order to limit the financial risk to Social Security. It has been the case when the innovation was the result of two or several companies in competition, that these companies were then jointly committed in a common volume clause.

Price reductions or discounts

The Committee no longer endeavoured to conclude conventions including DTC or volume clauses the implementation of which would only be approved by the payment of discounts. It has however frequently accepted, in order to avoid minor and possibly reversible excesses, thresholds set out by clauses not giving rise to marginal and successive price changes which are expensive to manage, to subordinate the effective application of price reductions to a

crossing of a variation threshold, the non-realised price reduction then being compensated for by equivalent discounts.

3. PRICE REDUCTIONS

Price reductions can result from the application of a pre-existing price review clause, on the initiative of the Committee or the initiative of the company.

a) Price reductions linked to the application of clauses

The price reductions are then automatic, insofar as the review clauses are themselves accurate. The Committee endeavoured in this respect, no longer to conclude, or as little as possible – conventions including simple rendezvous clauses of the "if such an event arises, the prices will be re-examined" type.

b) Price reductions on the initiative of the Committee

Even in the absence of any price review clause, the Committee believed itself to be justified in proposing price reductions by application of texts which govern its activity (cf. notably article L.162-17-4 2nd and 3rd paragraphs and articles R. 163-9 and R. 163-10 of the Social Security Code). This was often done, sometimes at the time of registration renewal, but not exclusively.

Registration renewal is in effect the time to examine the market position of a drug, which differs, possibly markedly from that which could be foreseen at the time of registration. This is particularly the case, even in the absence of a poor use of the drug, when this has been the subject, since the time of its registration, of a major growth in volume prescriptions, particularly following indication extensions. The price reduction can also be justified by the launch, subsequent to the initial registration, of equally effective and less expensive competitor drugs.

The price reductions on the initiative of the Committee can involve a single drug, a group of drugs belonging to the same class or all the drugs within a class.

c) Price reductions on the initiative of companies

These are by definition, competitive price reductions, seen up to now in the generic field, but for which the Committee does not give up hope of seeing the practice extended to patented drugs, as the price awareness of prescribers and patients increases and that, for an equal medical benefit, companies will be required to justify the lowest cost of their drugs in their promotional literature.

4. PRICE INCREASES

The Committee envisages with caution the propositions of companies for price variations which produce a nil effect, which, even if their immediate result is neutral or beneficial to the Social Security body, can prove expensive in the long term. Furthermore, these arrangements have a tendency to create an imbalance in the relative prices of pharmaco-therapeutic classes.

The Committee has, on the other hand, accepted price rises for essential drugs meeting healthcare needs registered at a price which no longer enables their manufacturing and marketing costs to be covered. These are usually old products the market share of which has progressively reduced, orphan drugs or drugs which, without strictly corresponding to the definition of an orphan drug, can be included with them on economic grounds.

Finally then, in one experimental case, the Committee concluded with a company a price increase Convention, the object of which was to enable this company to increase, through an increased promotional effort, its share of the drug market in question, in a class where sales gave rapidly way to the benefit of much more expensive drugs. It is expected from this convention that the immediate additional cost arising from the rise in price will be rapidly compensated and in the long term, through the observed substitution savings. The convention also sets out the repercussions which will take place if this expectation should prove disappointing.

III. The organisation and functioning of CEPS

The organisation and functioning of the Committee have only undergone, with regards to drugs, a few changes compared with 1999. Therefore, given below, by way of a reminder, is a brief description of the Committee's method of functioning and some information on the state of advancement of the renovation project for its information system.

The year has however been a time of major reform with the publication of the Social Security finance law for 2000, which confers upon the Committee, now called the Economic Committee for Healthcare Products, the responsibility of proposing the reimbursement tariffs to ministers, and, if required, the price limit of healthcare products and associated benefits and adaptations given in article L165-1 of the Social Security Code and particularly for reimbursable medical devices.

The results to be drawn on the organisation and the functioning of the Committee for the undertaking of this new mission will only be given in the next activity report, as the necessary decrees for the effective implementation of this reform have not been able to be published before the end of 2000. As of now however, it can indicate that, without waiting for the publication of texts, meetings have been organised, with the support and participation of the President of the Healthcare Benefits Consultative Commission and of the person responsible for the Interministerial Healthcare Benefits Tariff (IHBT), in order to define a working programme and procedures and to set out a plan for the transition from the old system to the new one. This period has also been used profitably, with regard to permanent Committee colleagues, in order to prepare for the link up between the drug team and the officials in charge of IHBT, who were up until then attached to hospital management and healthcare tenders. The organigramme given as an appendix integrates all of these numbers.

A. REMINDER ON THE FUNCTIONING OF THE COMMITTEE

This function is controlled by internal regulation, the text for which is given in appendix 4. Three aspects of this functioning, which more directly involve the relationship of companies with the Committee, are worth clarifying.

1. PROCEDURES FOR THE PRICE FIXING OF DRUGS

The price fixing procedure consists of three main stages:

- The putting together of the price application dossier
- The preparation of the *rapporteur*'s report
- The exchanges between the company and the Committee during the negotiation phase.

a) The price application dossier

At the time of the registration application (or renewal of registration etc.), the company simultaneously submits a dossier to both the Committee and Transparency Commission. This dossier includes a form explaining the price proposals and an economic appendix, for the purpose of providing a case for the proposed price. Strictly speaking, no model type of economic dossier exists, rather a standard which can enable a *rapporteur* to easily compile the necessary data for the putting together of his/her report and for the decision of the Committee.

The price request must be set out at the same time as the registration application, and therefore simultaneously with the submission of the dossier to the Transparency Commission.

Following verification that the dossier is complete[10], a copy of it is forwarded to each member of the Committee. This dossier is then added to, if needs be, by suggestions from the Transparency Commission, after receipt of this by the Committee and of the report prepared by the *rapporteur* designed to investigate the dossier. These documents are forwarded at least 7 days inclusive prior to session examination by the Committee.

At any time the dossier be can be supplemented with other sections, deemed useful or necessary for its understanding, such as correspondence exchanges between the Committee and the company, additional facts forwarded by the company, by the CT or the opinion of experts who are working for the Committee etc.

b) The content of the *rapporteur*'s report

For each price dossier studied by the Committee, an economic report is prepared in which the Committee's action is entered. This report is prepared by a *rapporteur* designated on receipt of the opinion of the Transparency Commission. It is the case that in accordance with the *Accord Sectoriel*, when a company requests it, the *rapporteur* should be designated even before referral to the Transparency Commission in order to "do the spadework" on the economic aspects of the dossier. It is however self-evident that no price convention can be concluded before transfer to Transparency.

The investigation of a dossier includes the critical analysis of the parts of the dossier. These must allow the *rapporteur* to put together price proposals which he/she will present to the Committee in session as well as those of the company and the arguments expanded by the latter in support of its propositions. This assumes, accept in the case of very simple dossiers, that the *rapporteur* personally made contact with the company.

The report is prepared using a predefined outline. This report must mainly show the financial consequences for the health insurance scheme of each of the price hypotheses presented.

When a dossier has already been examined at least once, it is supplemented, for each new examination, by a summary sheet prepared by the *rapporteur* recalling the history of the discussions.

c) Exchanges between the company and the Committee

The Committee decides its position on the requests of companies at the time of its weekly meetings in accordance with internal functioning regulations fixed by texts and its internal control.

After each deliberation, a letter is forwarded as soon as possible to the company clarifying the position of the Committee and its motives. This written procedure enables the criteria used

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[10] The company must verify the accuracy of the parts it forwards or to explain possible changes occurring during the procedure, such as the modification of the CIP Code for example. Indeed, the publication of the price of a presentation which no longer has the same CIP number gives rise to price label and/or reimbursement problems on the one hand and, on the other hand, requires the Committee to again review the dossier and to make any changes necessary to regulate the situation.

and the arguments put forward by the Committee to be clarified and is a proof of transparency for companies.

2. THE COMPANY HEARING

In accordance with article D. 162-2-4 of the Social Security Code and in particular in the framework of the propositions from the Convention, the Committee gave hearings to pharmaceutical companies usually at their request, but sometimes on its own initiative.

Generally speaking, the Committee deemed it to be more opportune to hold collective discussions with a company than to see individual contacts between companies and members of the Committee multiply.

There are two types of company hearing:

- either, the aim of the hearing is to explain or to clarify parts of a specific dossier, in order to reduce the stages to the bare essentials or to smooth out negotiation difficulties;
- or the hearing aims to improve reciprocal understanding between companies and the Committee.

Under no circumstances do these hearing constitute a preliminary stage necessary for the taking of a decision by the Committee.

Finally, the Committee accepts that companies can, if they wish, be accompanied by an expert who is not an executive employee. However, the Committee considers that this expert speaks in the name and on the account of the company.

3. THE USE OF ECONOMIC STUDIES

Companies sometimes produce, when putting forward their price proposals, economic studies mainly aimed at establishing the cost-efficacy assessment of the registration to the reimbursement of a drug or more simply, particularly in the case of products lacking an ASMR, the saving which will result for Social Security from this registration.

The use of these studies, if they are to enlighten *vis a vis* the Committee's decisions, requires that the validity of the data, the methods of analysis and the economic reasoning applied should first be assessed. The technical skills required for this assessment has led the Committee in liaison with the AFSSAPS to designate a group of economic healthcare experts, independent of the pharmaceutical industry. This group works at the request of the Committee and supplies technical advice on studies, opinions generally forwarded to the company having produced the study. This opinion does not bind the Committee and does not include moreover the assessment on the price level to accept, but simply provides information on the points to be aware of if the studies were conducted or otherwise in accordance with the state of the art.

B. COMMITTEE FUNCTIONING METHODS

Committee numbers were unchanged during 2000, except insofar as has already been indicated with regard to drug devices.

Work has been actively on-going in 2000 with regard to the implementation of the future database system. Among the aims assigned to this system, referred to in its preceding report,

the Committee has, after an initial general study of its needs, decided to prioritise the question of the automation of its procedures and of the production of conventions. A contractors help bureau was agreed after tendering and resulted, after a detailed analytical phase, in the compilation of specifications for the production of a data processing system for the management of procedures and documents. A new appeal for European competitor tenders was launched on this basis using the performance tendering method. The offers received are currently being examined.

Another appeal to European competitors was launched for the supply of International data on sales and the prescription of drugs. At the end of 2000, the handing over of this market was in its final phase.

Appendices

1. THE MEMBERS OF THE COMMITTEE
2. THE COMMITTEE'S RAPPORTEURS
3. ORGANIGRAM OF THE COMMITTEE

4. THE INTERNAL CONTROL OF CEPS

In view of the Social Security Code and particularly articles L. 172-17-3, L.162-16-1, L. 162-17-4 and L. 138-10, R. 162-20 to R. 162-20-3 and R. 163-6 to R. 163-10, D. 162-2-3 to D. 162-2-7.

Whereas the present interior regulation exclusively concerns the activities of CEPS in relation to drugs and that it will therefore be revised to take into account the new missions conferred by law on the Committee in the field of medical devices…

1 – ORGANISATION OF THE SERVICES OF THE COMMITTEE

a) **Secretary General and Committee services**

The Secretary General is responsible for the satisfactory functioning of the services of the Committee. He is particularly vigilant regarding the legal standing of the acts of the Committee, in the conduct of procedures and in adhering to deadlines. He negotiates with companies on these issues. He prepares the decisions of the President relative to the naming of *rapporteurs* and the compilation of the session agenda. He organises the work of the services of the Committee, with the exception of that of the general *rapporteur*. He prepares in liaison with the competent administrative authorities, decisions relative to the management of credits opened in the name of the Committee.

b) **General reporter**

The general reporter is responsible for the preparation of the Committee's annual report and, more generally, reports and information forwarded by the Committee to relevant ministers. He is vigilant with regard to formalization and adherence to the Committee's policy and proposes the means of ensuring its distribution to companies.

c) **President and Vice-President**

The agendas of the President and Vice-President are made available to other members, *rapporteurs* and agents with Committee functions by the Secretariat such that they might be informed, particularly of planned meetings with company staff and asked if they would like to be involved.

II. RAPPORTEURS

Candidates for the function of *rapporteur*, who are not permanent state employees, a Public Body, or an obligatory health insurance body, must give their agreement to the Committee not to seek or to obtain employment in the Pharmaceutical Industry during the exercise of these functions or during the two-year period following cessation of these functions.

III. SESSION PREPARATION

a) **Dossier registration**

All dossiers forwarded to the Committee are subject to registration and an acknowledgement of receipt. The Secretary General of the Committee continuously keeps up-to-date non-finalized dossiers submitted by companies, with information for each of them of the deadline of the prescribed regulation, depending on the type of dossier and the texts in force. It ensures furthermore that re-registration dossiers have been submitted by companies at the date set out by the regulations.

b) **Allocation of dossiers to *rapporteurs* and the preparation of reports**

The *rapporteur* is designated from the time of submission of the dossier by the company or on the initiative of the company, following the discussions of the Committee. However, for dossiers that require an approval from the Transparency Commission, the *rapporteur* is only in contact with the company concerned after forwarding of the approval to the Committee.

Reports are compiled in accordance with one of the examples of the plans given in the appendix to the present regulation. The Secretary General fixes the deadline for the delivery of the reports and checks on the status of dossiers entered on the agenda.

When a dossier has already been entered on at least one occasion on the Committee's agenda, and is subject to further examination, the *rapporteur* puts together a summary sheet recapitulating in particular the preceding proceedings of the Committee and their motives as well as, if needs be, the subsequent suggestions of the company.

c) **The distribution of information between members of the Committee**

Dossiers submitted by companies are forwarded to members of the Committee at the time of their deposition. The agenda, the reports and the documents required for the examination of the points entered on the agenda are forwarded to the members of the Committee at least seven days before the session. If this time period is not adhered to, any member of the Committee can obtain the report of the corresponding debate at the following session.

d) Relations with companies

For the investigation of specific dossiers relating to a drug or to a company convention, contacts with the company are prioritised by the *rapporteur* and then by the President or the Vice-President. If the other members of the Committee have a bilateral contact with companies on subjects entrusted to a *rapporteur*, he/she will immediately be informed of it.

IV - SESSIONS

a) Session dates

Committee sessions take place every Thursday and commence at 9 am. It is not subject to a written notification. The day or the time of the session can be modified or a supplementary session added on the decision of the President after consultation with the Committee.

b) Agenda

The agenda consists of three parts:

- Part A is given over to all questions other than the examination of dossiers relating to a drug to a company;

- Part B is given over to the examination of specific drug dossiers or to a company other than those examined in Part C;

- Part C is given over to the examination of specific drug dossiers treated in accordance with the simplified procedure described in d) below.

All members of the Committee can put a point on the agenda within a minimum time period compatible with the information or the preliminary consideration of other members on the point proposed.

c) Attendance at Committee sessions

Those permitted to attend the Committee's sessions:

- Members with voting rights. These can be accompanied by anyone of their choice under their authority;

- With consultative powers, if need be, persons designated in article D. 162-2-3-II of the Social Security Code;

- The Secretary General and the general *rapporteur* of the Committee as well as, on the agreement of the President, any agent in the service of the Committee the presence of whom is necessary for the satisfactory progress of the session.

The *rapporteurs*, in the case of the dossiers for which they are responsible, as well as, at their request and with the agreement of the President, in respect of the other points in Part B of the agenda for which their assistance in the discussions of the Committee is useful to the exercise of their functions.

d) Report and discussion

- The points given in Part B of the agenda are added verbally by the *rapporteur*. The session President then gives permission to those members who wish to speak. The *rapporteur* assists in the discussion and answers questions from members of the

Committee. The session President can consult with the Secretary General, the General *Rapporteur* as well as any agent in the service of the Committee taking part in the session, particularly on questions of Committee law, procedure or doctrine.

- Entered in Part C of the agenda are dossiers which the President believes can be processed by means of a single written report of the *rapporteur*, without a preliminary verbal presentation. These are mainly certain re-registration dossiers as well as registration dossiers or relating to generic drug price changes or basically drugs similar to a drug which is already registered. The *rapporteur* is not allowed to participate in the session. Insofar as is possible, it is taken directly to a vote.

e) Hearings

The hearings set out in article 162-2-4 of the Social Security Code are determined by the Committee. Company hearings are determined by the President, on his/her initiative or at the request of the company in question. When a company with an agreed hearing decides to bring with it an expert who is not an executive employee, the latter is nevertheless considered to speak in the name and on behalf of the company.

f) Vote

This constitutes a decision within the meaning of the present interior regulation resulting from a deliberation of the Committee in a matter in which the law and its regulation grant it competence, whether an actual decision, a ministerial opinion, a convention proposition or amendment, the acceptance or the refusal of a convention proposition or an amendment drawn up by a company or the decision to postpone a decision.
For the points entered in Parts B and C of the agenda, a vote is only taken on decision projects justified and drawn up in session.

For the application of article D. 162-2-6 of the Social Security Code, voting is expressed by yes, no, abstention or objection. The objection must be clearly justified.

g) Minutes

The minutes relating to each decision taken in Part B or C of the agenda are prepared and approved forthwith at the same time as a vote is taken on this decision.

The minutes of each session are given to members at the time of the following session and formally submitted for the approval of the Committee one week later.

Furthermore, a register is kept of the questions entered in Part A of the agenda. An outcome given during the proceedings of the Committee on these questions is forwarded to it at least once a month.

h) Debate and voting confidentiality

The members of the Committee, the *rapporteurs*, agents in the service of the Committee and all other persons assisting in the session are subject to professional secrecy regarding the conduct of the debates, the meanings of the decisions of the Committee, the votes given by each member as well as, generally speaking, any other document or information of which they

are aware, as a result of their participation in the session. This secrecy is not an impediment to informing other senior authority members, these then being subject to the same requirement.

Information on the decisions of the Committee is normally ensured by regulatory publications or through letters addressed to companies. The Committee can however mandate the *rapporteur*, President or Vice-President to ensure an immediate and verbal supply of information to the companies concerned. In this case it up to the representative to ensure the accuracy of the contents of the information passed on.

V – IMPLEMENTATIONS OF THE PROCEEDINGS OF THE COMMITTEE

a) Company information

Within one week following Committee proceedings on a point entered in Parts B and C of the agenda, a letter is forwarded to the company in question to inform it of the result and the reasons for the proceedings. This letter is accompanied, if applicable, with the corresponding convention project or amendment, in duplicate.

b) Signatures and publications

The Secretary General of the Committee arranges the signature of the conventions and amendments, looks after, if applicable, the preparation of decrees or decisions submitted for signature to the competent ministers as well as the regulatory publications.

c) Disagreement reports

When the Committee, taking note of the absence of an agreement with a company, particularly on expiry of a set time, fixed, if applicable, by regulation, has to propose to competent ministers the signing of a decree or the notification of a registration or re-registration refusal, it first informs the company of this proposal.

d) Update of conventions

The Secretary General of the Committee looks after, in liaison with the companies concerned, the regular update of conventions lasting several years and concluded through the application of article L 162-17-4 of the Social Security Code and particularly appendices to these conventions in relation to the list of reimbursable drugs and to the directory of clauses applicable to these drugs.

5. DISCOUNT TRIGGERING THRESHOLD TABLE PER PHARMACOTHERAPEUTIC CLASS

1 – **CONSTRUCTION OF THE TABLE BY CLASS**

The table is made-up according to a process consisting of three distinct stages:

- Class segmentation;
- The establishment of classes in which the probable growth in sales should entail the payment of discounts;
- The general balancing of the table.

a) **Class segmentation**

The aim of class segmentation is to divide up all reimbursable drugs into groups of drugs each constituting a market in which companies are in direct competition. The segmentation criterion is therefore that of an adequate substitutability, in the economic meaning of the term, between drugs belonging to a same group.

It is a question of ensuring, particularly for classes for which quantitative discounts are due, that the joint and several liability of the fact, as established between companies, is fully justified by the competitive environment in which they find themselves for the sale of their products belonging to these classes, and therefore, inversely, no company is subjugated to discounts on its own products due to the growth in sales of non-competitor drugs.

By way of exception, and with a concern for simplification, certain non-uniform classes have been left in the table, but these are composed of drugs for which the level of growth is the same order of scale. These regroupings do not therefore by their nature give rise to abnormalities in terms of discounts.

Compared with the table published in 1999, the changes made to the new table, on the whole marginal, are all justified through the application of this segmentation criterion. Thus, class A11H3 has been regrouped with C10B0 in order to regroup vitamin E generics with their original compounds. Class A3 has been removed from a part of the sub-class A3F, this naturally being closer to class A4A9, etc. An important change on the other hand, consisted of breaking up into five groupings the very heterogeneous locomotor system class.

b) **Class determination prior to giving rise to quantitative discounts**

This determination rests on an analysis consisting of two successive stages. Initially, the Committee evaluated the normal growth prospects for sales in each of the classes. Then it identified those of these classes in which discounts appeared to it to be justified as well as the relative proportions in which these discounts were justified.

1) Assessment of the normal sales growth prospects

This assessment of the normal sales growth prospects in classes includes forecasting elements but strictly speaking does not constitute a prediction, as it assumes that the growth of sales within classes conforms to the growth of medically justified need. This evaluation of additional cost, rests on the growth of sales and does not prejudge the normal nature – or otherwise – of the levels of consumption actually observed.

This assessment is based on four criteria:

- **The growth in the prevalence of the illness requiring treatment**, irrespective of the reasons for this growth: advances in detection (e.g. diabetes), ageing of the population (e.g. osteoporosis), changes in the environment (e.g. asthma) or dietary habits, is assimilated with a positive growth in the prevalence of the movement to town (pharmacies) of patients previously treated exclusively in the hospital (e.g. hepatitis C);

- **On-going establishment or possible innovations** in the market for reimbursable drugs;

- **The penetration of generics**, which by its nature in the negative sense, reduces sales in classes where these drugs are present;

- **Recognised Public Health priorities**, whether their aim be to increase the use of certain drugs (e.g. vaccines, drugs for the treatment of pain) or to reduce them (e.g. antibiotics).

2) Identification of classes prior to giving rise to a greater or lesser degree of discount

The main purpose of quantitative discounts being, at a given registration price, to reduce the actual cost of drugs to the heath insurance fund, the determination of classes prior to giving rise to discounts requires the Committee to identify classes in which it believes that, at the current level of observed sales, prices are at least relatively too high, given the overall limitations on expenditure voted for by Parliament. Discounts therefore constitute a provisional alternative to the price reductions that this market situation calls for, the duration of this arrangement depending itself on factors of a diverse nature.

This estimation is itself based on four criteria:

- **The medical service rendered, as assessed by the Transparency Commission**. It particularly seemed natural to the Committee for the discount mechanisms to lead, for the health insurance fund, to a reduction in costs due to drugs for which the medical service rendered was deemed insufficient to justify their registration on the list of reimbursable drugs;

- **The age of marketed drugs**. The Committee also regarded it as normal that, for older groups of drugs, even if these drugs are still protected by patents, and even if the medical service rendered is considerable, the cost to health insurance should fall to enable, in respect of overall constraints, the financing of innovations;

- **The excessive sales of certain classes of drug with regard to medically justified needs**. This is particularly the case of drugs for which the medical service rendered is unquestionable but for which the use is widely expanded as a first-line therapy to the detriment of equally effective but less expensive products, whilst the price of the drugs concerned is only justified by the specific advantage that it brings to more restricted

populations of patients, or as second-line therapy (e.g. CIEs, and angiotensin II inhibitors in hypertension, inhaled corticoids particularly indicated in severe asthma but used in all forms of asthma, new generations of antibiotics etc);

- **The intrinsic importance of sales volumes**. These are classes for which the SMR is not disputed, and for which nothing suggests that the volumes are not justified, but for which the burden for heath insurance expenditure and in their growth is considerable (e.g. statins, proton pump inhibitors). Planned discounts in such a case are purely and simply volume discounts, justified only by the French health insurance system wholesale client class. The assessment of this criterion, as for former criteria, can take into account the differences observed in 1999 between the rates accepted by the Committee and the actual rates, this enabling it to be explained why certain rates were reduced compared with those initially foreseen for 2000 and subsequent years.

These criteria, like those of 1) above can sometimes correct themselves. They can also mutually reinforce themselves. It is of course the responsibility of the Committee to define, case by case, their weighting in order to infer a result.

c) **General balancing of the table**

This balancing must enable three constraints to be reconciled insofar as is possible.

- **The differences between the rates retained and the outlook for normal growth within the classes, as established according to the criteria of 1) must be consistent with the analysis of 2).** In other words, and by way of example, a class in which the criteria of 2) converge to lead the Committee to assess that discounts must be proportionally significant, will give rise to a rate, positive or negative, which is more or less lower than that of the normal growth of its sales. Conversely, a class for which none of the criteria of 2) justify discounts will give rise to a rate, also positive or negative, of at least equal to that of the normal growth of its sales.

- **The system retained must give rise to results acceptable to companies.** This is a realistic constraint which prohibits accepting even very justified rates, by application of the preceding criteria and principles, but which end in requiring from a government regulated company or from a group of government regulated companies, discounts representing an excessive proportion of their turnover.

- **The weighted sum of the rates accepted must be equal to the triggering threshold of the safeguard contribution.** This is the same principle as for the construction of the table and its reason for existence. It follows that the rates accepted are not indisputable as absolute figures, but that the Committee on the other hand tries to be able to justify, through the application of the stated criteria and in a relative between class approach, the meaning and the importance of the differences between accepted rates and the normal prospects for the growth of sales in these classes.

The device instituted gives rise for each class of drug to a growth rate expressed as a difference vis a vis an ONDAM rate, such that the change in the basis of each of these rates in each drug group gives rise to a global result equal to the ONDAM forecast. The reasoning for

the different rates is the adjustment, without up-front price changes of drugs, of the actual prices (discounts deducted) paid by the community for the various groups of drugs at their marginal use. This mechanism enables, coupled with the foreseen exemptions in favour, notably for the generics, or drugs with a significant innovation, to ensure consistency between the methods of financial regulation and the fundamental positioning of governmental drug policies: appropriate drug use and elimination of waste, development of the generic market and support for innovation. Secondly, this type of regulation can constitute an incentive, marginal but real, to companies to focus their promotion efforts on drug groups for which the threshold for the triggering of discounts is greater than the spontaneous sales trend and which would not therefore give rise to discounts.

II – **METHODS FOR THE CALCULATION OF DISCOUNTS**

a) **Mechanism**

1) The total discount

The total discount due for a class in which the sales growth was greater than the level given in the Committee's table is distributed between companies marketing products in this class as follows:

- 65 % of the total discount is distributed pro rata from sales achieved during the year;

- 35 % of the total discount is distributed between single companies the sales growth of which exceeded the level given in the Committee's table and pro rata the proportion of sales achieved above this level.

The aim is not to penalise the marketing of new products, including those with no ASMR and which give rise to a saving for the Social Security fund.

2) Exemption of innovative products

- Drugs with an ASMR are exempted from discounts during the 3 years which follow their marketing, those with an ASMR II are exempted for 2 years.

- In the case of drugs having obtained an ASMR for a particular indication or for an extension to an indication, the exemptions apply pro rata, conventionally determined from the turnover achieved in these indications.

- The duration of exemption is counted from the time of marketing, or for ASMRs obtained for an indication extension, from the time of the approval of the Transparency Commission. When this time period ends during a calendar year, the exemption is calculated pro rata for sales achieved during the period of exemption.

3) Exemption of low price products

This exemption concerns generics, those similar in price to the generics and original compounds with a generic price. It is notably not applicable to drugs for which it can simply be said that their cost is less than the mean cost of treatment of the class to which they belong.

b) **The discount levels**

The discount level is fixed at 35 % of the excess observed compared with the levels shown in the Committee's table. It remains accepted, in accordance with the Accord Sectoriel, that the net total (all government regulated companies included) discounts actually discharged as discount per class and as discounts on the turnover will not be greater than the total contributions which the same companies will have paid in application of article L. 138-10 of the Social Security Code. In order to ensure adherence to this limit, the level of 35 % will, if necessary, be uniformly reduced for all classes giving rise to a payment of discounts.

6. THE STANDARD CLAUSES

1. STANDARD DTC RANGE CLAUSE

ARTICLE 1:

The costs of first registration (or price changes…) shown in the table below are applicable from the time of publication in the Official Journal (or… will take effect from dd/mm/yy).

PRESENTATIONS (1)	EPHMRA CODE	NMP	PPTTC
FIRST REGISTRATION – CIP CODE PRESENTATION AAA	…….	___.___ F	___.___ F
FIRST REGISTRATION – CIP CODE PRESENTATION BBB	……..	___.___ F	___.___ F
PRICE CHANGE – CIP CODE PRESENTATION CCC	…….	___.___ F	___.___ F

ARTICLE 2:

2.1. The fixed prices in article 1 are given on condition that the daily cost of treatment of the recorded range (CTJGc) calculated from a range made up of aaa, bbb, ccc, …., is at most equal to ___,___ francs: daily reference range treatment cost (CTJGr).

2.2. The CTJGc is studied every year, and for the first time for the 12 month period preceding dd/mm/yy. It is calculated on the basis of the doses of each of the presentations given in 2.1 shown in the latest DOREMA published before the dd/mm/yyy and on the 12 month sales given in the latest GERS published before that date.

The CTJGc is calculated by dividing the turnover of the whole range (CAHTG) noted in the GERS, by the number of treatment days for the range (NJTG),

let: CTJGc = CAHTG/NJTG

NJTG is equal to the sum of the number of days treatment of each of the presentations in the range,

let: NJTG = $\sum$ NJTi

For a given presentation, the number of days treatment, NJTi is equal to the number of tablets (doses, units) sold for each presentation i of the range divided by the corresponding dosage (Pi) recorded in the DOREMA, i.e.

NJTi = (number of units per carton x number of cartons I / Pi.

If the CTJGc is greater than the CTJGr, the NMP of at least one of the presentations of the range given in 2.1 is reduced such that the CTJG is equal to the CTJGr.

If (CTJGc – CTJGr) / CTJGr is less than x %, the presentation NMPs are not changed.

2.3. If the CTJGc is greater than the CTJGr, i.e. if the application of 2.2. warrants a price reduction, whether or not made by application of the last paragraph of 2.2., the company is liable to a rebate (R) calculated according to the formula:

R = (CTJGc – CTJGr) x NJTG

2.4. The amount of the rebate due will be notified to the company by the Healthcare Products Economic Committee. Payment of the rebate will be made to the benefit of ACOSS by the company one month after CEPS notification. The company will inform CEPS by letter of the date and the amount of the payment made.

The sum of this rebate will, if applicable, by deducted from the quantitative discount base of the class as set out in the convention between the Healthcare Products Economic Committee and the company.

2. **STANDARD DOSAGE CLAUSE**

Article 1:

The prices shown in the table below are applicable from the time of their publication in the Official Journal (or….. take effect on dd/mm/yy).

PRESENTATIONS (1)	EPHMRA CODE	NMP	PPTTC
– CIP CODE PRESENTATION AAA	…….	___.___ F	___.___ F

Article 2:

2.1. The fixed price in article 1 (net reference manufacturers price: NMPr) is given on condition that the observed dosage (Pc) is at most equal to …….. (reference dosage: Pr).

2.2. The (Pc) dosage is examined every year and for the first time, on dd/mm/yy on the basis of the last DOREMA published before this date.

If the dosage observed (Pc) is greater than the reference dosage (Pr), the NMP fixed in article 1 is modified (NMPm) such that:

$$NMPm = \frac{Pr}{Pc} \times NMPr$$

If (Pc – Pr) / Pr is less than x %, the NMPr is not modified.

2.3. If the dosage observed (Pc) is greater than the reference dosage (Pr), i.e. if the application of 2.2. warrants a price reduction, whether or not made by application of the last paragraph of 2.2., the company is liable to a rebate (R) calculated according to the formula:

R = CAHTc – (NMPm x Vc)

where:

- CAHTc is the turnover noted in the GERS for the 12 month period preceding the date given in 2.2.;

- Vc is the sales volume of the presentation noted in the GERS over the same period.

2.4. The amount of rebate due will be notified to the company by the Healthcare Products Economic Committee. Payment of the rebate will be made to the benefit of ACOSS by the company one month after CEPS notification. The company will inform CEPS by letter of the date and the amount of the payment made.

The sum of this rebate will, if applicable, be by deduction from the quantitative discount base of the class as set out in the convention between the Healthcare Products Economic Committee and the company.

3. **STANDARD UNIT VOLUME CLAUSE**

Article 1:

The prices shown in the table below are applicable from the time of their publication in the Official Journal (or….. take effect on dd/mm/yy).

PRESENTATIONS (1)	EPHMRA CODE	NMP	PPTTC
– CIP CODE PRESENTATION AAA	…….	___.___ F	___.___ F

Article 2:

2.1. The (NMP) price given in article 1, (net reference manufacturers price: NMPr) requires that the annual volume of sales (Vc) be less than or equal to x units (reference sales volume Vr).

2.2. The sales volume Vc is examined every year and for the first time, on dd/mm/yy on the basis of the last GERS published before this date.

If the annual sales volume observed (Vc) is greater than the reference volume (Vr), the NMP is modified (NMPm) such that:

$$NMPm = NMPr \times \left(1 - \frac{N}{100} \times \frac{Vc - Vr}{Vc}\right)$$

The NMPm cannot however be less than ……. francs or greater than the NMPr which constitutes its lower limit and its upper limit respectively.

If (Vc – Vr) / Vr is less than x %, the NMP is not modified.

2.3. If Vc is greater than Vr i.e. if the application of 2.2. warrants a price reduction, whether or not made by application of the last paragraph of 2.2., the company is owed a rebate (R) calculated according to the formula:

$$R = Vc\ (NMPr - NMPm)$$

If the NMPm is less than the lower limit, it takes by default the lower limit for the calculation of the rebate.

2.4. The amount of the rebate due will be notified to the company by the Healthcare Products Economic Committee. Payment of the rebate will be made to the benefit of ACOSS by the company one month after CEPS notification. The company will inform CEPS by letter of the date and the amount of the payment made.

The sum of this rebate will, if applicable, be by deduction from the quantitative discount base of the class as set out in the convention between the Healthcare Products Economic Committee and the company.

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