STUDY OF CONTROL OF MEDICINES

REPORT BY : DR N J B EVANS CB
P . W CUNLIFFE CBE

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(EVANS CUNLIFFE)

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SUMMARY OF CONCLUSIONS AND RECOMMENDATIONS.

1. We have no doubt that it is still appropriate, in the public interest, to scrutinise the quality, safety and efficacy of medicines before they are put on sale, and to supervise their manufacture and promotion. Such arrangements for the control of medicines are best kept separate, as now, from considerations of price and prescribing practice. But the process of scrutiny should not be more burdensome than is necessary to protect the public: longer delays than are needed to evaluate the medicines thoroughly keep useful new medicines out of patients' hands, and damage the industry - partly because the effective patent life of new medicines is so short.

2 The Medicines Act 1968 has stood the test of time well, as has the general principle whereby a licensing office takes advice from independent expert bodies and reports to Ministers. The high reputation which the UK deservedly holds for medicines control depends upon the excellence of the professional judgements made by staff and those advisory bodies, on the balance of benefit and risk from medicines.

3 The workload from licence applications received by Medicines Division of DHSS has gone up steadily and is still rising. On the whole, the office has coped suprisingly well with this increase and without proportionate increase in staff, but it is now showing signs of overload. Licences for New Active Substances (ie, the important new drugs) are currently held up on average for as much as two years, compared with the European Community (EC) specified figure of 210 days, and many minor applications are held up almost as long, compared with the EC figure of 120 days; also, companies report growing numbers of minor errors in documentation. These delays are not attributable to extra thorough care in assessment (for which the EC recommended periods are sufficient), but to problems in the office which we describe below. Although these delays are smaller than those reported from several other countries, we consider they warrant urgent attention now, especially as we expect the total number of licence applications received to go on growing over the next 5 years, perhaps by 10% per year. It is quite likely that towards the end of that time developments in medicines control in the EC may begin to supplement or replace national licensing controls, but in our view it would be unwise to postpone action on that account.

4 Substantially the whole of Medicines Division, some 300 people, is engaged on the control of medicines, predominantly the processing of licence applications and the assessing of voluminous supporting data. Computing and information technology support is seriously deficient, and the database is almost unusable because erroneous and out of date. Consequently there is heavy reliance on labour intensive clerical operations and on traditional paper files, but without an effective system for keeping track of the files or of the transit of work through the office. The organisational structure of the Division reflects its historic origins as a headquarters policy division and is inappropriate for the present task; in particular the diffusion of managerial responsibility means that there is no effective

overall control of the flow of work, and it is frustratingly hard to bring about change.

5 The other principal area of difficulty relates to staff: because civil service salaries for pharmacists and doctors are uncompetitive and there is too little secretarial and other support, it is difficult to recruit experienced professional staff for this highly specialised work and - once trained and experienced - they leave for posts in industry. Other rigidities compound the problem, for example the control of staff numbers by arbitrary headcount, and the dilatory procedures for filling vacancies. The Association of the British Pharmaceutical Industry told us that their members would be prepared to pay higher fees if it led to the engagement of more senior and experienced professionals, because such staff would greatly expedite the assessment of applications.

6. The heart of our recommendations is our proposal to organise the staff, of all disciplines, into functional teams each related to an identifiable 'business' and each with a team leader managerially responsible for the quality and quantity of its work. For example, there will be one team for New Active Substance applications, another for Adverse Drug Reaction monitoring, and so on. Team leaders will be accountable to functional managers headed by the Director of Medicines Control, whose task will be to control the work and promote the identity of the Directorate, as we propose to call it. Managerial staff will be selected for their personal qualities regardless of the discipline from which they come, though it is probable the Director will be a doctor. We suggest the Director's post, and some of the other senior posts, should be advertised.

7. We considered carefully whether the Medicines Directorate should be transferred from the Department of Health and Social Security (DHSS), as has been suggested, into a Special Health Authority or other independent body, but we decided that the balance of advantage lies in keeping the Directorate within DHSS under special financial and managerial arrangements to promote a considerable degree of autonomy and flexibility, for example over pay for specialised posts. These arrangements (technically called "exemption from gross running cost controls") are permissable under Public Expenditure Survey rules providing certain conditions are met, notably that the full cost of gross expenditure is recouped from receipts. We think it reasonable, if exemption is granted from gross running cost control, to ask the industry to carry the full cost of the Directorate (which we propose should not include the British Pharmacopoeia) and suggest their representatives should join DHSS and H.M.Treasury representatives on a Budget Committee to ensure cost-efficient management.

8. Other recommendations provide for the urgent introduction of modern technology, simplification of office procedures and removal of unnecessary work, and flexible pay arrangements for specialised posts. None of our recommendations will require primary legislation. One recommendation, to provide for the appointment of temporary members to the Medicines Commission to facilitate the hearing of appeals, will require secondary

legislation by Statutory Order under the Medicines Act. The remainder can be achieved by political resolve and administrative action. We are confident that if they are put into effect wholeheartedly, they will improve the arrangements for the control of medicines and help to sustain the UK reputation in this field.

9 Our detailed recommendations are, in summary, as follows (the numbers in brackets refer to the paragraphs in which the full text of the recommendations can be found):

Organisation

1 The control of medicines should remain a Ministerial responsibility (6.4.1)

2 Medicines Division should become the Medicines Directorate (5.25) within DHSS (6.7)

3 Its Director should be accountable to a Deputy Secretary for all the work of the Directorate (6.7)

4 The staff should be organised into multidisciplinary functional teams, each responsible to a leader (5.22)

5 The managerial structure above the teams and responsible to the Director should be functional not divided by professional discipline (5.24)

6 DHSS should consider transferring responsibility for the British Pharmacopoeia to the Pharmaceutical Society of Great Britain (PSGB) (7.3)

7 DHSS should study the costs and benefits of moving the Directorate out of London (4.18)

8 The Director should seek advice on the management of change (5.27).

9 Steps should be taken to improve public understanding of the Medicines Directorate and the licensing system (3.9)

New Technology

10 Completion of the file-tracking system should have high priority (5.2)

11 Modern information technology should be introduced urgently for processing of applications and adverse drug reaction data (5.3)

12 But computerisation of data input for assessment has low priority (5.4)

Staffing and Personnel

13 Job-satisfaction should be increased by 'whole-job' and team working (5.18)

14 Much more flexibility is required in personnel matters (4.7)

15 Action is needed to improve the numbers and calibre of professional staff (4.5)

16 Better clerical and secretarial support is required for professional staff (5.18)

17 There should be a modest increase in numbers of professional staff and some over-complementing (5.18)

18 Recruitment should be simplified and speeded up (5.18)

19 External assessors should be tried out to relieve bottlenecks (5.18)

20 There should be more use of individual or merit promotion (5.19)

21 The pay of pharmacists and doctors in the Directorate should be determined flexibly to allow recruitment of experienced staff at market rates (5.19 & 6.5)

22 Administrative and clerical staff should be moved around less often (5.18)

23 More flexibility is needed to take on temporary staff (5.18)

24 There should be more emphasis on training, including joint training with industry (5.18).

Improved Procedures

25 Companies should ensure, by supervision and training, that their applications are satisfactory (5.6)

26 DHSS should rewrite its guidance notes MAL 2 (5.5)

27 Newcomers to the UK control system should be encouraged to get consultancy advice (5.5)

28 The licensing authority should define the criteria for notification and variation respectively (5.8)

29 There should be triage of abridged applications and variations, in which a senior pharmacist deals with minor matters on receipt and in other cases determines their subsequent handling (5.9)

30 To facilitate triage, companies should submit a simple statement specifying what they are seeking and certifying the data is complete (5.10)

31 Seriously deficient applications should be sent back at before triage (5.7)

32 The licensing authority should publish Statements of

Acceptable Specification to simplify the approval process for well-established medicines (5.12)

33 Officially-certified copies of documents should be supplied where it would simplify the scrutiny of data (5.13)

34 DHSS and applicants should each nominate a contact point for enquiries (5.15)

35 Informal communication should be encouraged (5.14),

36 When a subcommittee of the Committee on Safety of Medicines (CSM) advises against acceptance of an application there should be an interval for discussion before the CSM meets (5.15)

37 Product licencing is not appropriate for the control of homeopathic and similar alternative medicines (7.5)

38 The management of the Directorate should review procedures periodically, in search of further simplification (5.16)

Adverse Drug Reaction Monitoring

39 Adverse drug reaction (ADR) monitoring should be developed, and should remain the responsibility of the Directorate even though many or all of the studies may be carried out by others (7.4)

40 Anonymised ADR data, including copies of yellow cards should be available to those with a bona fide interest (7.4)

41 The Directorate should pursue measures for the international collation and exchange of ADR data (7.4)

The expert advisory committees

42 Ministers should take powers to enable the appointment of temporary members of the Medicines Commission (4.12)

43 The Medicines Commission should help the Section 4 Committees to concentrate on essentials (4.11)

44 The Committee on the Review of Medicines should be wound up in 1990 (4.10)

Appeals

45 When appealing to the CSM or the Medicines Commission, companies should have the choice, whether or not to have the data reassessed (4.15)

46 The Committee on Safety of Medicines should decline to take account of new evidence without the opportunity to consider it beforehand (4.16)

47 If presented with new data relating to an appeal, the Medicines Commission should normally seek the views of the CSM before reaching a conclusion (4.16)

48 The Medicines Commission and the Committee on Safety of Medicines should revise the manner in which they hear appeal to encourage a less stilted discussion (4.17)

Finance

49 DHSS should apply for the Medicines Directorate to be exempted from gross running cost controls (6.8)

50 The full cost of the Medicines Directorate should be charg to the pharmaceutical industry (6.10)

51 The emphasis should shift somewhat from the levy on turnover towards fees, which should relate to the cost of carrying out that category of work. (6.11).

52 There should be fees for appeals, which should reflect t extra cost of reassessment when companies choose to have this done (4.15)

53 A Budget Committee should determine the funding of the Directorate and monitor the cost-effectiveness of its management (6.12)

54 The Directorate should monitor performance (3.14, 3.15) an use management yardsticks to cut out wasted time but preserve full and thorough scrutiny of medicines (6.13).

10 Finally, we add our thanks to all those who have helped us conduct this review, but especially to the present and past members of the Medicines Commission and the expert advisory committees on whose diligence and judgement the quality, safety and efficacy of our medicines depends.

Chapter 1 INTRODUCTION

In the Spring of 1987, the Medicines Act 1968 was almost twenty years old, and the Medicines Division of DHSS (which is the government department charged with implementation of licensing of medicines under the Act) was showing signs of overload. We were asked by Ministers to study the arrangements for the control of medicines, with the following terms of reference :

> "To examine the issues for DHSS arising from the continued increases in licence applications and other work under the Medicines Act and to recommend ways of dealing expeditiously with this work, while maintaining adequate standards for the safety, efficacy and quality of human medicines in the United Kingdom."

We have had considerable help from a number of individuals and from professional and other bodies with knowledge of and interest in the control of medicines. We have also examined the working of Medicines Division in some detail and have heard the views of many of its staff. At Annex 1 we reprint the letter sent out to solicit views from interested parties and given wider circulation through the trade press, while Annex 2 lists those who gave us their views orally or in writing.

In this report, we concentrate our attention - as our terms of reference require - on those issues bearing directly on the workload of Medicines Division of DHSS.

We are greatly indebted to all those who have helped us, but especially to Julian Oliver of DHSS who throughout has been an admirable Secretary to the study despite having a multitude of other responsibilities.

Chapter 2 BACKGROUND

2.1 The control of medicines is achieved primarily through the system of licensing specified in the Medicines Act 1968, by wh licences to market medicinal products are granted by Ministers (called "the Licensing Authority" in the Act) when they are satisfied by evidence supplied by the applicant company about th quality, safety and efficacy of the product. There are controls too on clinical trials; on the claims which may be made in advertising and other promotion; on wholesaling; and on manufacturers' premises. Annex 3 which is taken from the out-of-print DHSS publication MAL 99 itemises these and other controls in more detail.

2.2 In all these activities, the greater part of the work in assessing applications and in issuing licences on behalf of Ministers is done in Medicines Division of DHSS, assisted by the Medicines Commission and a number of expert statutory committees ("the Section 4 Committees") of which the Committee on Safety Medicines is probably the best known. Medicines Division comprises some 300 civil servants including 165 administrators, 97 pharmaceutical staff (mainly pharmacists) and 24 doctors, the most senior being two Grade 3 officers namely a Senior Principal Medical Officer and the administrative Under-Secretary. Not all of these staff work on licensing as such: a small proportion is engaged on other matters related to control (on enforcement, for example), to the study of adverse drug reactions, and to the British Pharmacopoeia. Most of the Division is located in Marke Towers, Vauxhall, but there are small offices of the Medicines Inspectorate in several regions, laboratories of the British Pharmacopoeia at Cannons Park and the main computer and its staf are in premises in Reading.

2.3 The costs of the Division (some £9.2 million per year excluding the British Pharmacopoeia) are met from the DHSS administration vote but in effect about 62% of this expenditure is recouped from the pharmaceutical industry in licence fees, which include an item proportional to companies' turnover. Technically the receipts from the industry are classed as negative public expenditure, and they are not netted against the gross cost. Table 1 sets out the figures for the latest availabl year.

2.4 There has been a progressive increase in the number of applications. Analysis is complicated by several factors, viz:

i) different kinds of application impose quite different burdens upon the Division. The assessment of a novel kind c medicine (a "New Active Substance") usually requires much more work than does that of the simpler ("Abridged") application for a medicine based on a familiar active ingredient; Clinical Trials Certificates and Exemption Certificates, Variations and Notifications are different again.

ii) when licensing began, some 39,000 products already on the market were given Licences of Right. Progressively, these have been and are being reviewed by the Division and the

Committee on the Review of Medicines. Some products have been withdrawn from the market by the manufacturers, some have had licences refused on review, and others satisfying the assessors have been given ordinary product licences. The tempo of work on the review has varied considerably in different years.

iii) even within one category - say, Abridged applications - there are marked differences in the complexity of the professional work needed in the Division. Such differences are hard to quantify, but the industry and DHSS staff agree that both New Active Substance and major Abridged applications are steadily becoming more complex. For example, medicines produced by recombinant DNA techniques present the assessors with quite new kinds of problem to solve.

Table 2 shows DHSS figures for the numbers of applications received each year from 1976 to 1987, without attempting any correction for this increase in complexity. The growth overall approximates to 5% per year. Table 3 shows how the Division's staff has increased over the same period, with a commendable increase in efficiency.

2.5 The growing workload has brought problems. In particular, the time taken to deal with an application, measured from its receipt to the grant of licence, has grown to embarrassing dimensions (Table 4). These times currently considerably exceed the periods stipulated in EC directives yet they are not necessary for the careful scrutiny of the data submitted nor do they contribute to its rigorous assessment; indeed, the public is the loser because new medicines take so long to get into patients' hands. The delays are also commercially detrimental to the applicant companies; when it is remembered that a fairly run-of-the-mill new medicine might earn 1million a year, and a very successful new active substance perhaps 50 million per year during its short patent life, it can be seen that each additional month's delay in issuing licences is costing companies thousands, even millions, of pounds annually. And, of course, the tax-payer has an interest in a thriving UK pharmaceutical industry.

2.6 Delays of this order are not confined to the UK but are found in other licensing authorities including those elsewhere in the European Community and in the USA. The EC is taking an increasing interest in the licensing of medicines in preparation for the introduction of a common market in all products including pharmaceuticals which is scheduled for 1992. EC directives already control many aspects of licensing, and in an endeavour to promote harmonisation in member countries, the Community has introduced procedures for multi-state assessment and for the handling of applications relating to novel biotechnical products. The difficulties being encountered with these European initiatives, and the conjectural routes by which the difficulties may in future be overcome, form an important backdrop to our study, to which we return in Chapter 6.

Chapter 3 COMPLAINTS & FINDINGS

3.1 In this and the following chapter we summarise the curren problems in relation to the control of medicines as perceived b those we consulted, and discuss our own findings and conclusion about the strengths and weaknesses of the existing arrangements Many of these conclusions are critical. Necessarily, we give t criticisms full weight and space, for they are the foundation o which we have built our recommendations for improvement: but it is important to remember when reading them that the overall record of medicines control in the UK is a good one, and its reputation stands deservedly high. All countries have problems with delays and bureaucracy, and not withstanding their complaints the consensus of those we consulted was that the UK system is still one of the best in the world - it is by no mea the slowest, and its record in protecting the public without inhibiting therapeutic innovation and progress is second to no What follows, then, is intended as constructive criticism to make a good system better.

3.2 The principal complaints and difficulties made known to us were:-

3.2.1 - by senior management of DHSS
- : increasing workload is causing overload and delays
- : too many applications are incomplete, slovenly or premature
- : imposed constraints (eg the Treasury headcount) forbid taki on nececessary staff
- : difficulty in recruiting suitably experienced professional assessors
- : appeals against licence refusals are very time-consuming

3.2.2 - by "consumer interests"
- : legislation more favourable to health of the pharmaceutical industry than to health of the consumer
- : more medicines are approved than are needed
- : undue secrecy about the nature and working of the medicin control process
- : undue secrecy about the grounds on which licensing decision are taken
- : flaccid enforcement of the legal powers re promotion and advertising

3.2.3 - by the industry
- : delays
- : over-formalised procedures with too little informal communication
- : over-zealous pursuit of unnecessary detail ('nit-picking')
- : professional assessors lack experience
- : frequent errors in documentation

3.2.4 - by the staff of Medicines Division
- : poor quality of many applications
- : lack of secretarial and other support for professional st
- : inadequate computing and unreliable database
- : structure of the division impedes good working and effectiv management

3.2.5 - by others
: the scope of the legislation should be extended to bring additional items under control.

3.3 It was noteworthy that several of those who helped us, including the Association of the British Pharmaceutical Industry and the Pharmaceutical Society of Great Britain outside, and many staff inside Medicines Division (mainly but not exclusively professional staff) told us firmly that the persisting combination of
- staff shortages
- difficulty in recruiting and retaining professional staff, because of uncompetitive salary levels, and
- inappropriate and ineffective management

could not or would not be remedied within the civil service. They advised that the licensing function should be hived off into an independent agency such as a Special Health Authority. Certain points of principle were adduced by others to support the suggestion that responsibility for licensing should preferably not rest within DHSS:-

: the licensing function should be kept separate from sponsorship of the pharmaceutical industry,
: the licensing function should be kept separate from NHS purchasing considerations such as influence the limited list

3.4 Rather to our surprise there were two signficant omissions from the list of criticisms. Even though we gave ample opportunity for the issue to be raised, those we consulted did not particularly condemn the amounts of data required in support of licence applications for new drugs. And we found that althoug many of those we consulted would like to see the Medicines Act 1968 changed in one respect or another (some favouring tightenin its provisions, others the reverse) there was almost universal reluctance to seek its amendment lest more be lost than was gained by disturbing the present balance of conflicting interests.

<u>The principles of control.</u>

3.5 Present day controls on the manufacture and marketing of medicinal products were brought in to protect the public because of the growing power, for good and ill, of modern medicines. In the UK and other countries it was accepted that however principled most commercial manufacturers may be, it was no longe sufficient to leave decisions on the introduction and promotion of medicines to their judgement alone; some kind of oversight of their activities was necessary in the public interest. Even though understanding of the scientific issues underlying the assessment of safety and efficacy has progressed since then, and the discipline of marshalling all relevant evidence is fairly well established, it is inconceivable that the principle of the public control of medicines could be abandoned.

3.6 The most fundamental questioning of the nature and purpose present-day controls on medicine came from the spokesmen for Social Audit when they argued that the arrangements for control are insufficiently stringent because they allow onto the market

many more medicines than are "needed"; the profusion of drugs available is exploited by the industry to the confusion of doctors, the detriment of patients and the impoverishment of National Health Service. It would be better, they said, to licence many fewer drugs - only the best, that is, of all tho becoming available - and to see that they are wisely used.

3.7 While we certainly favour measures to promote the informe and judicious use of medicines by doctors and patients, we do accept the view that this objective is best approached via medicines licensing. Medicines have to be assessed for licens at the very outset of their therapeutic life, when (despite voluminous data about their chemistry and their effect on animals) there is relatively little experience of their actio man. Time, experience in real-life medical practice, and care comparison with other medicines, are all needed before the relative merits and demerits of the newcomer can be seen in proper perspective. We therefore favour continuing the prese approach, whereby any medicine which satisfies the licensing authority on grounds of quality, safety and efficacy should b licensed even if there appear to be similar medicines extant.

3.8 In the UK, every single medicinal product is controlled separately even though there may be many similar products alr on the market. There is therefore a separate licence for ever brand of tetracycline, every brand of aspirin, and so on. Inde there are individual licences for every tablet-strength and formulation of each brand. Hence there are many more licence (and licence applications) than there are active ingredients. The requirement for product licensing in this degree of detail follows from the terms of the Medicines Act, in which quality given equal place to safety and efficacy. Some doctors told us they consider the emphasis on quality to be overstated - a vie not shared by pharmacists. We accept that the quality of a medicinal product is equally as important as its safety and efficacy: indeed, only quality control can ensure that safet efficacy are continued through the shelf life and manufactur history of the product. But we believe an effort should be mad to simplify the licensing of well-established products , especially as it seems to us unlikely that future European Community controls can be exercised product-by-product.

Confidentiality or secrecy?

3.9 Rightly, the law sets out to protect the commercial confidentiality of information supplied by applicants to the licensing authority, and rightly this obligation is taken very seriously. Perhaps for this reason, some have the impression t the control of medicines is shrouded in mystery (para 3.2.2 refers) and that the veil of secrecy is in some way sinister. Although we do not believe there is deliberate obscurity, we accept that currently available literature is not very informative and that, for example, the annual reports of the Medicines Commission and major committees are uncommunicativ There is no reason why the structure and methods of work[illegible] or the licensing system should not be better known, and we RECOMM that steps should be taken to improve public understanding of these matters.

3.10 However, advocates of more openness seek more than information about the system: they ask also for publication of the grounds upon which individual licensing decisions are made. Specifically, they suggested that companies should be required to make public a summary of the evidence and argument supporting their application, and that the licensing authority should similarly make available a summary statement showing why the application was or was not approved. They referred us to practice in the USA, but did not offer any convincing example nor explanation of the advantages which they believe have accrued there. We are not convinced that the claimed advantages of greater public accountability for the licensing system would nearly outweigh the considerable extra effort and expense of preparing and publishing such statements as a routine. Rather, we believe that the need for public accountability on licensing decisions (which need we endorse) is best met by having the best experts available to advise Ministers who themselves are answerable to Parliament. Very occasionally, it may be appropriate to publish the evidence on which particular decisions are taken, but experience suggests (cf the controversy some years ago about pertussis vaccine) that in these rare instances a full account must be given rather than a summary statement.

The Licensing Operation

3.11 The general outline of the UK system for giving effect to the control of medicines, ie a licensing office taking advice from independent expert bodies and reporting to Ministers, seems to be correct. The present arrangments allow, and must continue to allow, licensing decisions to be made on science-based and defensible judgements about the balance of risk and benefits, without undue pressure from industry, politicians, DHSS or Treasury. But our examination of the workings of Medicines Division suggested that within that outline there is room for improvement.

3.12 The delays brought to our notice both by the industry and the DHSS certainly occur and appear to be getting worse, though convincing figures are hard to find. It is fair to say we heard some scepticism expressed about the figures published by DHSS, which are believed by some observers to understate the full impact of current delays. The Association of the British Pharmaceutical Industry told us that the time taken to grant a product licence for a new active substance has increased from some 9.6 months (the mean figure) in 1974 to some 2 years, while the Proprietary Association of Great Britain commented "Over the past two years processing times for abridged applications have been growing longer and it is not unusual for companies to wait to 12 months for even the simplest product licence and some of the simplest applications involve no more than the transfer of a licence from one company to another." It must be remembered, of course, that the growth in processing times coincides with greatly increased workload, and that processing times in several other countries are believed to be even less satisfactory. Moreover, these times are gross, ie they include time taken by applicants to reply to enquiries etc.

3.13 Despite uncertainty about the exact figures, it is clear that relatively few applications (e.g less than one-quarter of abridged applications) are currently being processed within the time limits specified in EEC Directives, viz 120 days unless the application is referred to an advisory committee in which case another 90 days is permitted; that is a total of 210 days. Following an enquiry in 1982 under the aegis of Sir Derek Rayner (now Lord Rayner) DHSS accepted (as we too accept) that it was reasonable to expect applications to be processed within the EC periods. The EC periods of 120 and 210 days respectively, do not include time taken to reply to enquiries and are fully adequate for rigorous assessment of quality, safety and efficacy. There is no suggestion that longer processing times than these are desirable in the public interest.

3.14 Although concern about processing delays is almost endemic, there is no regular information to show where these delays are incurred. Nor is there information to support the claim that delays are often attributable to companies' failure to respond quickly to enquiries. To judge from a pilot investigation carried out at our request, substantially the greatest time is spent in a bottleneck, queueing for professional assessment. The assessment itself may (in the case of new active substances) take several weeks, but a similar period is spent in clerical work before and after assessment. It is unsatisfactory that there is so little information on such a fundamental aspect of the work, and we RECOMMEND that the managers of the licensing operation should at once take steps to monitor the transit of applications.

3.15 Similarly, there is no systematic quality control information available about the incidence of errors in internal documentation and in correspondence, but it appears that minor mistakes at least are common. One small survey suggested that 10% of the files relating to individual licences ("gold files") carried mistakes relevant to the working of the licence. The Association of the British Pharmaceutical Industry also quoted several examples, drawn from their members' experience, of documentary confusion and error. We accept that there is sufficient though unquantified evidence of relatively frequent documentary errors; though none of them is particularly serious in itself, as far as we know, we believe their prevalence should be taken seriously as indicating one or more of

- slipshod working
- overload
- poor morale

and - ineffective management.

We RECOMMEND that the managers of the licensing operation should monitor prevelance of errors in correspondence and internal documents. Also,licences are the legal basis on which companies operate, so their detail is important; there is at present some confusion as to which document or documents comprise the licence. Clearly, the licence should be a single document, of which the licensing authority and the company each have a copy, specifying the material points.

3.16 The central core of Medicines Division is the licensing operation, which deals each year with several thousand licence applications of different kinds. The determination of each

application involves a processing component, by which for example, the application is received and registered, a file is opened and its movements logged in and out, and (usually) a judgemental component in which professional staff and/or expert committees take a decision eg on the balance of benefit and risk.

3.17 The processing component is largely but not entirely an "administrative" responsibility, ie it is carried out in the main by clerical staff. Essentially the work comprises repeated operations and lends itself to well-structured procedures, computerisation, and a "conveyor-belt" approach. Most of the present arrangements are manual, labour-intensive and almost Dickensian, and job satisfaction and morale are low. Computerisation is insufficient and unsatisfactory and the database inaccurate and out of date. Repeated transcription of complicated data gives ample opportunity for errors to creep in. We judged the processing of licence applications to be inefficient and crumbling under pressure of workload. Moreover, while some sub-units are attempting to increase their effectiveness, there is little effective management and no evidence of satisfactory overall control.

3.18 In contrast, we are satisfied that the judgemental decisions are generally soundly made. All the evidence, and our own experience and observation, indicate that the quality of the professional and expert judgements made by Medicines Division staff and by the members of the expert advisory committees is very high. This expert competence is in fact the great strength of the UK system, and when recommending change in the present arrangments we have been especially concerned not to weaken its excellence, which has served the public well. There are however sometimes substantial delays in reaching the decisions - delays which are in part attributable to shortage of professional staff though they may also in part reflect the lack of effective management.

3.19 Delays and errors are classic indicators of overload. Our scrutiny of Medicines Division showed that it is indeed overloaded and will require some more resources - some more staff, and computing equipment. But we are convinced from what we have seen and heard that resources alone will not be enough: major changes are required in the way the licensing work is done.

3.20 We were also struck by the lack of sensitivity to the impact of the licensing operation on the commercial fortunes of applicant companies. There seemed to be no consistent attempt to relate the demands of the licensing process to what is needed to safeguard the public, and sometimes the bureaucracy seemed quite disproportionate: it is one thing to hold up introduction of a new active substance to ensure it is rigorously tested and assessed, but quite another to delay a company for many months when it simply wishes to market its established "Brand A" under the additional name "Brand B". Also, the internal procedures within the office - for photocopying, for instance, or for typing letters - seemed designed to save the Division pennies, heedless that the resulting delays might be costing applicants pounds. Both these aspects of the running of Medicines Division reinforced our view that it lacks effective oversight of its

work.

3.21 Our finding that management is unsatisfactory and ineffective does not mean that the managers are of poor quality or not trying: the contrary is generally the case. Rather we believe there are at present several major impediments to truly effective management, for example:

a) computerisation is insufficient and unsatisfactory and the database inaccurate and out of date

b) until the new file-tracking system is properly operational, finding files will remain a nightmare

c) too frequent staff movements

d) there are no relevant performance indicators, nor the ability to judge performance against target

e) divided responsibility, which makes for complexity, delay and inaction.

3.22 All these difficulties can be traced back to three fundamental weaknesses which, in our view, handicap Medicines Division in the exercise of its very specialised responsibilities:

i) as is usual in the policy areas in DHSS headquarters, the staff are structured in separate hierarchies representing the professional disciplines making up the workforce - in this case hierarchies of administrators, doctors and pharmacists respectively. As the structure and subdivisions of the different hierarchies differ from each other, with no common relationship to the several "businesses" into which the work of the Division can be divided, it is difficult to design simple operational policies and almost impossible to engender any feeling that staff are working together to a common purpose.

ii) for the same reason, there is no unified management of the Division as a whole nor of its several "businesses". Thus there is no one person in control of the applications for New Active Substances, for example, nor of adverse drug reaction work. It follows that no one manager is accountable for the delays complained of, nor (without complex and often unproductive liason) is he able to put into effect measures to correct the situation.

iii) also in common with other parts of DHSS headquarters, the senior staff tend to value "policy" matters more highly than routine management such as the design and monitoring of procedures for processing licence applications.

3.23 Whatever the historical origins of Medicines Division, we believe it is a mistake nowadays to regard it as a policy division in any way similar to those elsewhere in DHSS headquarters. The dominant activity is the control of medicines within the framework of existing legislation, and the greater part of this is the processing of licence applications along set lines. The analogue should be the factory, with a number of production lines, rather than a think-tank. The organisational characteristics i) to iii) above may well have countervailing merits in other circumstances, but they are inappropriate to the running of the licensing factory and its production lines.

3.24 In opposition to this view, some officers put forward the claim that we had underestimated the importance of policy issues and that the latter rightly dominate the time and energies of senior staff. We looked into the case made, but cannot accept it. It seems to us that most of the so-called policy issues handled in Medicines Division would be seen in commercial circles as natural and inevitable consequences of the business: spin-offs which need to be dealt with but which should not monopolise attention. Examples quoted to us, which we would put into this category, include:

> advising on membership of committees; consideration of extensions to the scope of UK or EC legislation; deciding how to move forward on the monitoring of adverse drug reactions.

Another argument referred us to the intensity of "top-of-the-office" and, sometimes, Ministerial interest in events likely to attract Parliamentary attention or that of the media or national bodies. An example might be the decision to withdraw a product licence because of reports of serious adverse reactions. We recognise that knowledge of any such event will be of concern eg to the Chief Medical Officer, who may have to field questions from medical organisations and the media, and to Ministers.... just as they may have to answer for the operational activities of a district health authority.

Questions of handling and presentation are important and have to be dealt with sensitively, but they are essentially secondary to the principal responsibility, which is the control of medicines via such routine work as processing of licence applications, the Medicines Inspectorate, and enforcement. In chapter 5 we make recommendations designed to improve the discharge of this primary responsibility.

Chapter Four: STAFFING & EXPERT ADVICE.

4.1 Responsibility for the control of medicines rests on the Licensing Authority, ie on the UK Health and Agriculture Ministers, but necessarily in practice the staff of Medicines Division carry the major load. They are civil servants, being members of the DHSS headquarters staff. Alongside them, and crucially important to their work on the assessment of licence applications, are the Medicines Commission, the expert advisory Committees set up under Section 4 of the Medicines Act, and thei subcommittees. The chairmen and members of these bodies are not part of the staff of Medicines Division but are drawn from outside the civil service - mostly from universities. This chapter reports our findings on staffing and personnel matters and on the advisory bodies.

4.2 In general, it is difficult to recruit staff to Medicines Division. For clerical and secretarial staff the work is specialised and unremitting; job satisfaction is impaired becaus of the highly fragmented subdivision of labour, and the Market Towers offices (though pleasant as DHSS accommodation goes) are set in a windswept wasteland. All these factors accentuate the problem the civil service has of competing for labour in central London. In consequence, most of these staff are drafted in from elesewhere in DHSS headquarters, and hurry away as soon as they can.

4.3 The more senior administrative staff are accustomed to beir moved around during their civil service careers (some two or three years in each post being the norm) and they can afford to be stoical about a move to Market Towers. We were told that usually they try to resist being posted to Medicines Division bu come to like it when they get there. However, the frequent changes are disconcerting to pharmaceutical companies and their associations, and irritating to members of the advisory bodies. As we note elsewhere, the administrative ethic traditionally favours 'policy' to the detriment of good management. We feel that the control of medicines requires fewer generalist administrative staff who should stay in post for longer periods.

4.4 Inevitably, from the nature of the work, doctors and pharmacists are the heart of Medicines Division: only they (with the assistance of similar professionals on the advisory bodies) can assess the factors relating to quality, safety and efficacy of medicines around which all control measures revolve. Hence their number and their calibre are crucial. Yet two very senior officers told us that their dominant memory of medicines control work since its inception is of persisting anxiety about the numbers of doctors and/or pharmacists and their quality.

4.5 Shortage of professional staff has an obvious effect: it causes formidable bottlenecks (as now) in the assessment of licence applications. There is quite close correlation over many years between problem periods (with mounting delays) and professional staff vacancies. The influence of the calibre and quality of these professionals is more difficult to recognise bu perhaps even more important. All those we consulted agreed that top-class staff (by which they meant senior doctors and

pharmacists, adequately trained in an appropriate specialty, with good experience relevant to the control of medicines and personal qualities of judgement and balance) could significantly cut the time and labour required for assessments compared with less excellent staff. The latter -

: toil more slowly
: take refuge in formal procedures as they lack the confidence to disuss matters informally with companies
: pursue unnecessary detail obsessively, for lack of confidence to put them on one side as unimportant
: do not see as quickly to the heart of a case.

Members of the advisory bodies agreed that the calibre of the assessors is all-important. DHSS management told us that for several years it has been increasingly difficult to recruit and retain top-class professional staff for work on medicines; sometimes the worse problems have been with doctors, sometimes with pharmacists. And the Association of the British Pharmaceutical Industry told us that in their opinion the excellence of DHSS professional staff had declined in recent years, and that they were confident their member companies would agree to pay higher fees for the licensing authority to employ top-class professionals. We RECOMMEND that steps be taken to increase the numbers and more especially the calibre of professional staff engaged in the control of medicines.

4.6 The problems with professional staffing detract from the operations of medicines control. The causes appear to be:

a) restraint on staff numbers such as the Treasury headcount
b) difficulty in recruiting because of -
   : small pool of expertise outside to draw upon
   : unpopularity of the civil service to professionals
   : salaries too low relative to the market
   : protracted procedures for advertising and filling vacancies via the Civil Service Commission
   : ignorance of the work of Medicines Division and absence of a clear 'image'
c) dissatisfaction of those in post, because of -
   : uncompetitive salaries
   : absent or inadequate secretarial etc support
   : frustration at the inability to bring about change, because of the organisational and managerial obstacles (see para 3.22)
d) loss of staff in post due to-
   : move to better paid employment outside, usually with a pharmaceutical company
   : transfer (with or without promotion) elsewhere in DHSS (rarely applies to pharmacists).

Many of the recommendations in chapters 5 and 6 are directed towards alleviation of these factors.

4.7 A common factor underlying many of the above is the rigidit of civil service rules and practice compared with competing employers outside the public sector:-

: central restraint on numbers (though the headcount rules have recently been relaxed for Medicines Division, and will in any case shortly be subsumed into budgetary control)
: uncompetitive salaries, held down by public sector pay policy and the need to keep in step eg with other grades and departments.
: irritating restrictions on support staff and collaborative working because of work patterns common to other parts of the service.

We encountered several other instances where the size and rigidity of the present arrangements operate to the disadvantage of medicines work-

: slowness in anticipating and filling vacancies
: obstacles to taking on temporary staff, such as computer keyboard operators, to help with bottlenecks
: rules allegedly related to the completion of annual reports on staff, such as that a clerical assistant cannot report to a clerical officer (the next senior grade).

Overall we were given the impression of an overcomplex organisation (Medicines Division within DHSS within the Civil Service) hog-tied by personnel rules . We strongly RECOMMEND introducing much more flexibility in personnel matters, especially by relating pay to the nature of work and the market.

The Section 4 Committees

4.8 We examined the work of all the Section 4 Committees (except the Veterinary Products Committee, which lay outside our terms of reference) and their subcommittees, and judge them to be well-run and highly expert bodies. Their chairmen and members carry considerable responsibility and a heavy burden of paper-work in preparation for meetings, and the country is much indebted to them for their labours.

4.9 The Committee on Safety of Medicines (CSM) is in a pivotal position in that no licence can be refused by the Licensing Authority on grounds of quality, safety or efficacy, without reference to the Committee. There is also an appellate function which we discuss later. We commend the activities of the CSM and its subcommittees (on Safety, Efficacy and Adverse Reactions, on Chemistry, Pharmacy and Standards and on Biologicals respectively) and the sub-sub-committee, the Adverse Reactions Group of SEAR.

4.10 The Committee on the Review of Medicines (CRM) appears to be well on course to complete its remit by the European Commission deadline in 1990. We RECOMMEND that it should continue in being with full vigour until that year, when it should be wound up. (There may be some residual activity thereafter, but we believe the task can be subsumed by the CSM and its subcommittees.)

4.11 In all these committees, the chairmen and members have to be vigilant to avoid spending time and effort over interesting

but inessential details. We RECOMMEND that the Medicines Commission, should give advice from time to time to help all concerned to concentrate on points of substance.

The Medicines Commission.

4.12 The Commission has a rather different task, being broader and less technically specialised than the Section 4 committees. Whilst its terms of reference are very wide (easily encompassing our own, for instance) it must inevitably have difficulty in pursuing many matters in any depth because of practical limitations on the time of its members and secretariat. Moreover, the membership of the Commission has steadily been expanded to an unwieldy degree in the endeavour to strengthen its competence as an appellate body. We RECOMMEND that Ministers should progressively reduce the permanent membership of the Commission and take powers (by secondary legislation) to enable the appointment of sufficient temporary members for the satisfactory hearing of appeals.

4.13 If our recommendations are implemented, we expect them to lead to a vigorous Medicines Directorate (see para 5.25) under tighter and more effective management: the expert decisions however will still be made, as now, by assessors and advisory committees working in close partnership. It is always possible, in such a situation, for the standards of quality, safety or efficacy demanded to creep up to unreasonable levels beyond what is justified to protect the public interest. Conversely, it is possible (though we believe less likely) for complaisant experts unduly to relax standards . The contribution which the Commission is uniquely able to make, by virtue of its statutory pre-eminence and broad composition, is that of overseeing the whole system - assessors and committees together - to ensure that a fair balance is held between the interests of industry and the public, and between the benefits and dangers of new medicines.

Appeals

4.14 The Act is generous in its provision for appeals by companies against refusal of a licence (though as we were reminded, there is no reciprocal provision for public interest groups to appeal against decisions to grant a licence). Appeals are quite frequent as Table 5 shows, and this puts a considerable strain upon the Medicines Division, the Committee on Safety of Medicines, and the Medicines Commission. Several witnesses suggested that the right of appeal should be curtailed, especially appeal to the Medicines Commission which they saw as a less expert body which ought not be allowed to override judgements reached by the Committee on Safety of Medicines. The industry, of course, saw the rights of appeal as a necessary safeguard against error, misunderstanding, and the possibility of encountering a committee member with a bee in his bonnet. We sat through several appeals and are satisfied that the present rights of appeal are fully justified and should remain, but we believe it is possible and desirable to modify their impact as the following paragraphs show.

4.15 When matters go to appeal it is customary to have the data

re-assessed by fresh medical and pharmacist assessors; if there is further appeal to the Medicines Commission, two new assessors are brought in, making six in all. This is done in the interests of natural justice, but is very expensive in professional staff time and it delays the other work the new assessors would otherwise have been doing. We RECOMMEND that companies should be charged a fee for appealing. We further RECOMMEND that at each appeal stage companies should be offerred the choice whether or not to have the data reassessed by new assessors, and that where appropriate the fee charged should reflect the extra cost of reassessment.

4.16 Companies often produce new evidence for the appeal, which was not available earlier or which expands upon those points which caused difficulty. (Some observers believe that some companies quite cynically put forward inadequate or premature licence applications in the expectation that they can be amplified later on appeal. If this is true, the practice while reprehensible is probably a consequence of the current long delays in processing licence applications: companies try to stake a place in the queue, as it were, with a premature application. In para 5.7 we recommend the weeding-out of grossly inadequate applications.) Provided the new evidence can be assessed properly and considered by members beforehand, the Committee on Safety of Medicines can assimilate such new data without difficulty: but it is not satisfactory for the CSM to be presented with new oral or written data at the hearing. If this happens, we suggest the hearing should be adjourned and reconvened at a later date. We RECOMMEND that when hearing appeals the Committee on Safety of Medicines should decline to take account of any new evidence without having the opportunity for members and assessors to consider it adequately beforehand. The same point applies more forcibly to hearings by the Medicines Commission. In our view it is not sensible to allow companies to adduce new evidence before the Commission without giving the Commission and if necessary the CSM the opportunity to study it beforehand. We RECOMMEND that the Medicines Commission, if presented with new data relating to an appeal, should normally seek the views of the Committee on Safety of Medicines upon that data before the Commission reaches a conclusion on the appeal.

4.17 When hearing appeals, the Committee on Safety of Medicines and the Medicines Commission are acting in a quasi-judicial as well as a professional and scientific capacity, but even so we were suprised to find their proceedings on these occasions so stilted. Apparently they have adopted certain formal procedures so as to make it demonstrably apparent that their actions are governed by the principles of natural justice. We fully accept the absolute need for natural justice, which in a professional context such as this could, we suggest, be defined as fair play with the opportunity for all relevant considerations to be looked at openly and fully. In the event, we suspect that the present procedures inhibit proper professional discussion. We were told that on at least one occasion an appelant company put forward arguments at a hearing which one of the assessors knew to be contradicted by the company's own written data; yet the assessor felt precluded from drawing the committee's attention to the discrepancy. Clearly, procedures have to be fair, but they must

not inhibit exploration of all relevant issues. We understand there is authority for the proposition that " the general requirements of fairness" as applied to hearings such as these, "are likely to fall at the very lowest end of the scale in terms of the degree of formality.....required". This encourages us to believe that these hearings could be conducted in a more medical/scientific vein. We RECOMMEND the Medicines Commission and Committee on Safety of Medicines should review the manner in which they hear appeals, so as to encourage full professional discussion whilst abiding by the tenets of natural justice.

Where should medicines control be located?

4.18 At the beginning of this chapter we mentioned the difficulties which the location of Market Towers poses for staff recruitment. So far as the staff are concerned, we see every reason for relocating this work somewhere well outside London and SE England. To move the office in this way would however pose major problems for the work of the advisory committees, whose numerous members come from all parts of the UK. There seem to us to be only three ways of reconciling these conflicting interests, and none of them is entirely satisfactory -

: stay in London near the airport and main termini (good for committee members but poor for recruitment, at least of junior staff, and for quality of life).
: move somewhere else with an airport and road/railway links. (the Birmingham area comes to mind.)
: move without regard to transport, and arrange to hold the committee meetings in London. This would probably be the best solution for recruitment both to staff and the committees, but would entail substantial and continued expenditure on moving the assessors and other staff to the meetings. It would not be satisfactory greatly to curtail the attendance of staff at the committee meetings as so much depends on the close mutually -instructive relationship of staff and outside experts.

We RECOMMEND DHSS to examine the costs and benefits of relocating the Medicines Directorate, having regard particulary to-

a) the recruitment of staff
b) the work of the expert advisory committees
c) the opportunity which re-location would give to create a strong new image for the Directorate.

Chapter 5: WAYS OF IMPROVING.

5.1 Our study suggests that the UK approach to the control of medicines is sound, and the legislative framework satisfactory. Thanks to the contribution of assessors and advisory committees, its intellectual and judgemental qualities stand high. Medicines Division of DHSS has coped quite well with rising workload over a number of years, but is now showing signs of overload with increasing delays and minor documentary errors. There is chronic difficulty in recruiting the best professional staff, and computing support is antedeluvian. The complex organisational structure prevents effective management, and overall the Division is unduly constrained from without and lacks resilience within. In this chapter we detail a number of ways by which we believe the situation can be improved, and in the next chapter we discuss the financial and constitutional changes needed to secure these improvements.

Modern Technology

5.2 The thousands of current and previous licence applications are moved around the office in cardboard folders, the so-called gold files. It is astonishing that there is no reliable way of finding files within the building. Some months ago, DHSS introduced a file-tracking system in which staff read-off bar codes into a central computer, but it is not yet comprehensive nor fully operational. File-tracking is an essential tool not only for finding and linking files but also for monitoring the transit of work through the organisation. We RECOMMEND that a high priority be given to completing and developing the file-tracking system.

5.3 There is urgent need for more and better computerisation of the office processes relating to licence applications, and to the monitoring of adverse drug reactions. DHSS is at present considering recommendations of a study they commissioned by Arthur Young Management Consultants into an information technology strategy for the next 5 - 10 years. Their recommendations seem sensible to us but we have no expertise in this field. Our study convinces us however that there are lessons to be learned from previous experience. For example we were told :-

a) the usefulness of the present system was impaired and quality control broke down because the users of the system had insufficient oversight of its design and operation
b) it is not enough to put in new technology to assist unsatisfactory patterns of working. First the working practices need to be reorganised on rational lines.
c) some of the faults in the present system are due to unwise pruning of the initial budget for software.

Conceptually, the processing of licence applications is a simple task and well suited to the use of information technology, with very considerable potential for increased efficiency and reliability and for saving of staff. We RECOMMEND that modern information technology be introduced as a priority to assist in

the processing of licence applications and adverse drug reaction data, providing always there are earlier or concomitant improvements in working practice.

5.4 The same does not apply to what we have called the judgemental component of medicines work (para 3.16 refers). We believe it would be premature to attempt widespread application of Information Technology to the task of the professional assessment of data for quality, safety and efficacy. Huge amounts of data are submitted for study and assessors differ in the way they prefer to go about their work; some of them find it easier to work with paper-based data than with visual display screens. In time, it may be appropriate to accept or require the submission of data in electronic form, on computer tape etc, and possibly assessors may be allowed to interrogate company-held data : but we RECOMMEND only limited experimentation along these lines, and low priority.

Simplification of Procedures & Removal of Unnecessary Work

5.5 Smooth and speedy processing of licence applications must depend in part on the intelligibility and completeness of the application, yet it is generally acknowledged that many applications are muddled or incomplete. Sometimes this may result from ignorance of the requirements. The DHSS handbook "Guidance Notes on Applications for Product Licences" (MAL 2) is out of date and obscure. We RECOMMEND it be rewritten. Newcomers to the UK system of control, especially small companies, can be helped by consultancy firms, and we RECOMMEND that they are encouraged to seek such help.

5.6 None of the recommendations we have made can compensate for poor quality applications. The fact that 10% of applications are sent back as inadequate even by the present rather perfunctory validation process, and that many others are judged to be unsatisfactory later, is a telling criticism of the industry. Too many applications are premature or are 'fishing expeditions', hoping the expert committees will identify the salient points for them; others are rambling and repetitious, or have sections which are illegible or not translated into English. Under our recommendations, good applications should be dealt with expeditiously; those of poor quality will get shorter shrift. We RECOMMEND companies to ensure, by supervision and training (in which the industry associations can play a useful part) that their applications are satisfactory.

5.7 Applications for product licences are examined by DHSS for prima facie completeness, a step called 'validation'. It is at present a very crude filter,but even so about 10 % of applications are now being returned to companies as too incomplete to warrant assessment. Clearly it is foolish to waste professional time, still less that of the expert committees, on seriously deficient applications; they should be sent back, and quickly. We are introducing a new step called triage (see para 5.9 below) at which a senior pharmacist reviews the applications and can reject any which are seriously unsatisfactory. This more effective professional filtering means that "validation" as a separate step can be reduced to a quick check by clerical staff

that all categories of information required have been supplied. We therefore RECOMMEND that seriously deficient applications should be returned at or before triage.

5.8 In theory, companies seeking some minor change in an existing product licence might do so via a Notification to the licensing authority. More significant changes have to be pursued by applying for a Variation. In practice, companies rarely procede via notification, apparently because there is no clear guidance on the distinction between changes requiring a variatio and those for which a notification will suffice. We RECOMMEND th licensing authority to define the criteria for Notifications and Variations, making clear the distinction between them.

5.9 The category of Abridged applications covers a wide range o complexity. At one extreme the applicant may wish only to change the name of his branded product; at the other he may wish to begin promoting its use for some new medical indications, thus exposing many more patients to its effects. It is unsatisfactory to have all these caught in the same queue so that trifling matters are held up for months. What is required is a way of sorting out applications on receipt, so that each can be given appropriate treatment thereafter. We RECOMMEND triage of all Abridged and New Active Substance applications, and Variations, in which a senior pharmacist assessor should review applications on receipt, to determine their subsequent handling. (The name triage is taken from the analogous procedure for sorting casualties after major accidents and the like.) Often, the officer carrying out triage will himself be able to complete all the professional assessment that is needed. The aim should be to deal then and there with all simple applications, and to specify clearly what further action is needed on the more complex applications - for example those needing medical assessment or more prolonged pharmaceutical assessment. To achieve this aim it is essential that senior and experienced staff are used for triage duties: they alone have the competence and self-confidenc to work quickly and reliably, and to carry the responsibility.

5.10 To assist the officer carrying out triage, we RECOMMEND that companies should be required to submit with each product licence application a very simple statement (not exceeding one page in length) signed by a responsible individual such as the registration manager, specifying what is sought and certifying that the necessary data accompanies the application. For example :

> "We seek to market under the brand name BRAND-B our effervescent analgesic tablets which are already licensed (Product Licence No.....) under the name BRAND-A. The active ingredient is Aspirin 300mg. Apart from the change of name and packaging, the application is identical to PL No.... "I certify that in my belief all necessary data accompany thi application."

5.11 Though we believe triage should greatly speed up handling of the simpler applications, there would still - under present arrangements - be large amounts of data for scrutiny. We believe it should be possible greatly to simplify the process where

well-established ingredients are concerned. Formerly, it was sufficient for the applicant applying for a licence for his brand of, say, soluble aspirin to answer many of the questions with a simple " conforms to the British Pharmacopoeia", without more. This is no longer possible because of the terms of EC directives which require all applications to be accompanied by full supporting data. And so we were told of the pharmaceutical assessor who had to check line-by-line an application transcribed from the Pharmacopoeia against the official text. We RECOMMEND the licensing authority should look for and adopt administrative devices which remain within the directives but simplify their application. We have discussed two possible approaches, as outlined in the following paragraphs.

5.12 The Statement of Acceptable Specification. In this approach, the licensing authority would publish a Statement of Acceptable Specification (SAS), for instance for ibuprofen tablets. The statement would incorporate all or almost all the data judged to be required; a prototype for such a SAS would be the documents on analgesics issued in 1978 by the Committee on the Review of Medicines. Applicants wishing to market a product conforming to the SAS would have to submit only a copy of the SAS itself, to abide by the directives, together with such limited extra data as the SAS states is necessary. (For example, data on stability of the product may be appropriate, as stability depends on the packaging to be used.). This approach could readily be applied to the simpler and best-established products, the over-the-counter medicines. It is possible it might be applied later to other products, such as generic prescription medicines, but it may prove difficult to draw up a useful statement of Acceptable Specification early in the therapeutic life of a drug, not least because of commercial confidentiality relating to the synthetic route, which is relevant to the impurity profile and so to safety. Also bioavailability data , which relate to efficacy, will probably continue to be needed for these medicines. We RECOMMEND that the licensing authority should publish Statements of Acceptable Specification beginning with over-the-counter medicines and possibly extending to others later.

5.13 At the very least it must be possible to obviate line-by-line checking of standard texts. The licensing authority could if necessary supply official copies of pharmacopoeial monographs, Statements of Acceptable Specification, existing product licences (to their holders) and the like. Such official copies (stamped, as are official copies of probate documents) would be acceptable without further scrutiny. This alone would simplify assessment and enable more applications to be determined at triage stage. We so RECOMMEND.

Better communications

5.14 DHSS and the pharmaceutical industry agree that communication between officials and applicant companies has become more formal in recent years, with more reliance on written notices referring to terms of the Medicines Act. All parties agree that informal communication, by telephone, letter and meetings, help to remove misunderstanding and aid the smooth despatch of business. Various reasons are put forward for the

drift towards formality : inexperience of professional assessors; shortage of staff; defensiveness in an age of increasing litigation. Although some formal communication must continue eg under S.21 of the Act when a licence is to be refused, we RECOMMEND that both parties should take steps to encourage informal communication. Such steps should include those taken to improve the capability of staff - a point to which we return later.

5.15 Specifically, we RECOMMEND

a) The applicant and the DHSS should each nominate a contact point for enquiries, eg as to the progress of the application
b) Enquiries for further data in support of an application should usually be passed informally as well as by "Section 44 letter".
c) In those cases where one or more of the subcommittees of the Committee on Safety of Medicines decide to advise the CSM against approval of an application in the terms sought, there should be an interval of, say, 4 weeks to allow informal discussion with the company before the application is considered by the CSM.

5.16 In paragraphs 5.5-5.15 we have suggested some ways in which working practices and procedures might usefully be modified. More generally, we RECOMMEND that the management of the Medicines Directorate should explicitly review its procedures periodically to see what further simplification can be made. Unless this is done, it is almost inevitable that the consideration of applications will ossify and unnecessarily elaborate procedures persist.

Staffing and Personnel Matters

5.17 As will be clear from earlier chapters, we regard the staffing and personnel arrangements as major determinants of the standard of work on medicines control. We believe there is need to free them from some of the constraints inherent in the present rules and practice of the larger organisational groupings of which Medicines Division is a part, ie the constraints currently associated with the civil service and the DHSS.

5.18 Specifically, we RECOMMEND :-

a) the frequency of movement of administrative, executive and clerical staff between Medicines Division and other parts of DHSS should be reduced. The aim should be to leave many staff for 5 years or more, and to encourage some officers to stay even longer
b) more flexibility for managers to take on temporary staff without lengthy consultation with trades unions or outside personnel management
c) fostering of job-satisfaction by promoting 'whole-job' and team working, and reducing organisational frustration
d) modest increase in numbers of professional staff
e) modest overcomplementing of pharmacists and doctors, to help reduce delays arising while posts are vacant

f) simplification and speeding-up of professional recruitment. Advertising, short-listing, and setting up the arrangements for interviewing selected candidates should all be undertaken in-house rather than through the Civil Service Commission
g) exceptionally, and as an experiment, external assessors to be employed to help cope with bottlenecks
h) better clerical and secretarial support for professional staff, preferably by introducing team working (see below)
i) increased emphasis on training, especially for professional staff, in specialised aspects of medicines control work. The aim should be, over time, to give all relevant staff the opportunity to train for the Diploma in Pharmaceutical Medicine.
j) increased opportunity for learning about industry eg by visits and temporary placements. Reluctantly, we accept that secondment -in and -out is likely to be possible only rarely, but we recommend discussion with the industry about provision of some joint training.

5.19 Important though the above recommendations are, we consider it even more relevant to improve the attractiveness of medicines control work to senior experienced professionals. The changes we recommend below in working methods and management should help in this respect, but will not be sufficient in themselves. There is urgent need for more flexibility in pay and grading, so that certain posts can be made significantly more attractive. Measures to this end should include -

: greater use of individual or merit promotion
: flexible pay arrangements so that an individual's pay is related to the prevailing market rate for the work undertaken and responsibility carried

5.20 Taken together, these recommendations point to the desirability of having special personnel arrangements for staff engaged on the control of medicines. Essentially, we seek greater flexibility for those managing medicines control to decide upon and then implement pay and staffing matters in ways most appropriate to the problems facing them, with a minimum of external constraint.

Improved organisation

5.21 It is useful to consider work on the control of medicines as being made up of a number of distinct "businesses". (This way of thinking about the work of a department is now customary in the civil service and can be applied very straightforwardly to Medicines Division because of the overwhelming preponderance of repetitive processing activities. Thus for example-

- the New Active Substances business,
- the Abridged Application business, and
- the Adverse Drug Reaction business,

can readily be identified. Yet these 'businesses', conceptually easy to recognise, are not reflected in the existing organisation and management structure of the Division. To take one example,

the monitoring of adverse drug reactions is an obvious and coherent 'business' and an important and continuing task. The work is carried out by administrative/clerical staff, pharmacist and doctors scattered amongst 11 rooms over 3 floors of the office; their computing support is 40 miles away, in Reading. Even though efforts have been made to create a sense of identity and common purpose (much more than in other parts of the Division), it is uphill work. While some of the 30-odd staff have close working contacts, and senior administrators, pharmacists and doctors engaged in this work meet every fortnight, responsibility is diffused between three separate lines of command with no overall coincidence of responsibility below the Permanent Secretary. Working procedures are complex and difficult to change; there is elaborate demarcation of simple tasks but no possibility of effective responsibility for the whole, and indeed no possibility of managing the 'business' in a business-like way.

5.22 All these inappropriate working practices should be swept aside. We RECOMMEND that the staff of all disciplines should be organised into functional teams, each related to a specific "business" or sub-set of a business. We further RECOMMEND that one member of each team , the Team Leader, should carry unambiguous responsibility for the quantity and quality of the work of the team. Thus to take the previous example, the clerical, pharmacist and medical staff concerned would be restructured as members of the Adverse Drug Reaction Team responsible to the ADR team leader. So far as possible members of the team should be grouped into adjacent rooms.

5.23 We see the reorganisation of work into functional teams as the key to better working practices and effective management. The main lines of the new structure are easy to define but further work will be needed on the details. In defining the teams, we believe the main criteria should be:

- : teams to relate to a function which it is sensible to run, supervise and plan as a unity
- : most teams will be multidisciplinary
- : regard should be had to the use of information technology
- : the teams to be small enough to be managed by the team leader, preferably without single-discipline sub-managers.

Thus, we tentatively suggest (subject to further study by the Director) there should be teams for -

- : New Active Substance applications
- : Abridged applications (see below)
- : Variations & Notifications
- : ADR monitoring
- : Clinical Trial certificates & Clinical Trial Exemption certificates
- : Review of Medicines
- : Medicines Inspectorate & Enforcement
- : Export certificates & other licences
- : central functions eg finance (including fees) and management of the Directorate.

At present about 29 people work on Abridged applications, so it is possible that more than one team will be needed. In our view, it would not be appropriate to subdivide the handling of each individual application between a number of teams each responsible for a portion of the process. Rather, it is preferable to apportion the various applications between teams, so that each application is the responsibility of one team from start to finish. This might for example be done by therapeutic group, putting cardiovascular drugs to one team, central nervous system drugs to another and so on. Or, it could be done by companies, putting applications from companies 1,2 and 7 to one team, 3,4 and 5 to another, etc. Subject to further detailed consideration by management, we conclude that the latter, allocation by company, is probably the method of choice because we are told it simplifies the information technology requirements.

5.24 We RECOMMEND that the managerial superstructure above the teams should be light and, again functional. It will be necessary to ensure consistency of standards between teams, but there should not be parallel management hierarchies, nor even "dotted lines" of unidisciplinary relationships. For example the multidisciplinary teams engaged on Abridged applications should be accountable to a single manager. There should however be provision for staff to seek counsel from a senior member of their own discipline, to obtain advice about their career, ethical dilemmas and the like. There is also need to keep staff fresh and to promote their training and career experience by giving them the opportunity to change teams periodically.

5.25 We RECOMMEND that a single Director be appointed to head all the work relating to the control of medicines. He or she should control the work, head up the staff, and promote the identity and self-esteem of Medicines Division which we rename the Medicines Directorate. This senior and important post, Director of Medicines Control, would carry greater responsibility than either of the Grade 3 posts at present heading up the Division, and the first holder in particular would face a most challenging task in carrying through the reshaping of working practices and the introduction of modern information technology. Clearly, the Director must understand the problems and requirements of medicines control work; the crux of the task lies in preserving the highest standards of professional and scientific judgement while dealing expeditiously with routine processing of applications. Leadership qualities and the ability to guide an organisation through a period of change would also be requisite. It is probable that the Director will be medically qualified. We RECOMMEND that the post should be advertised, perhaps initially with a 5-year contract. The team leaders and other managers should be selected for their managerial and leadership abilities and relevant experience, and not primarily for their specialist qualifications or professional discipline; some of these posts should also be advertised.

5.26 Rearrangement of the organisation into functional teams with a unified management structure will open the way to many improvements in management. Firstly, we RECOMMEND that team leaders should

: use staff flexibly within their teams, on 'whole-job' principles
: develop streamlined procedures and ensure they are followed within the team
: apply performance indicators relating to quality as well as quantity of work done.

Secondly, we RECOMMEND that the Director and his senior staff should audit the working of teams and the performance of the whole Directorate using performance indicators and other measures (such as transit times for the handling of applications) developed for the purpose. It is their responsibility too to see that thought is given from time to time to innovation, so that new ways are found for coping with the workload. Thirdly, we RECOMMEND that the Director himself should be accountable for all aspects of the performance of the Directorate. This would include accountability for its budget, and for reaching operational targets set. Overall, the emphasis should be on the development of explicit quantified management illuminated by relevant information. Managers at all levels should be given maximum flexibility, within budgets, for carrying out the work reliably and efficiently.

Management of Change

5.27 Taken together, our recommendations for new information technology, organisational change and managerial reform amount to a revolution in the working practices of the staff engaged on control of medicines. The whole culture of Medicines Division will be altered. This amount of change is considerable and its introduction needs firstly to be planned and secondly to be implemented. We RECOMMEND that the Director should seek advice on the management of change (which is available through DHSS and the NHS, and from central departments). In the next chapter we examine what other constitutional and financial steps are needed to make these changes happen.

Chapter 6 THE ORGANISATIONAL FRAMEWORK

6.1 In previous chapters we have examined the strengths and weakness of current arrangements for the control of medicines in the UK, and have proposed a number of recommendations for improvement. Four major questions arise, which we address briefly before setting out our further recommendations -

- will EC developments make changes here unnecessary?
- does the future workload warrant this degree of disruption?
- given the inertia of large organisations, how can change of this nature be accomplished? (Should there be a Special Health Authority, for instance?)
- what will the changes cost, and how should they be paid for?

How can the necessary changes be achieved?

6.2 The overall framework of control of medicines in the UK is now determined by European Community legislation, though decisions on individual products are still taken nationally. The necessity for industry to seek so many authorisations to market their products across Europe, and the occasional contradictions in the various national decisions, pose a major impediment to the EC goal of achieving a common market in pharmaceuticals by 1992, the more so as attempts to move towards harmonisation of decision-taking have not been very successful. Many observers feel that the pursuit of harmonisation between 12 largely autonomous regulatory authorities will continue to be unproductive, and that the Commission and the EC will be forced to move towards some kind of centralisation of decision-taking, perhaps in a supranational regulatory authority. We believe that some such developments in the EC will quite probably supplement and then possibly supplant national licensing systems, but we expect the changes to be introduced gradually over the next 5 to 10 years. While attempts to predict what form a future European system would take must largely be guesswork, we were impressed with the suggestion made by the Proprietary Association of Great Britain. In their view, progress is most likely to be made via European monographs similar to the Statements of Acceptable Specification we propose in paragraph 5.12 above. This would entail decisions in principle at EC level, with follow up action in member states to licence products conforming to the monographs or S.A.S..Whether this prediction proves to be correct or not, we anticipate that a UK licensing operation will be needed for at least 10 to 15 years, and perhaps much longer. We see it as important to keep that national operation strong and effective, not only to do its job properly but also to influence the eventual European system.

Future trends in workload

6.3 Whilst the introduction of New Active Substances may slacken off a little (though this is uncertain), activity on generic medicines is expected to continue at least at the present rate. The nature of the licensing system, by which every new product licence generates a flow of notifications, variations and renewals, means that the number of applications will in any case

continue to grow. If - as seems likely - the growth in applications continues at much its present rate, the total to be dealt with may easily be 50% greater than now, and perhaps even double, before any future EC authority could have much impact. Many of these extra applications will be relatively minor, which serves to emphasise the value of triage and the need to streamline procedures; however, the complexity of major Abridged applications and those for New Active Substances is rising steadily as new delivery systems are introduced for example, and new products based on biotechnology. There are also other factors tending to increase the workload, not all of which are resistable. As we note elsewhere, the field of adverse drug reaction monitoring seems poised to develop; there are pressures too to extend medicines controls in other ways, for example in relation to blood products, homeopathic medicines, and certain dental and surgical materials. We conclude that the workload relating to medicines control seems likely to continue to grow, and that action along the lines we have indicated will indeed be needed.

6.4 As we mentioned in paragraph 3.3, we met powerful support for the proposal that control of medicines should be removed from DHSS and vested instead in a Special Health Authority. The suggestion rested on four arguments, as follows -

a) public sector pay policy is too tight to allow civil service salaries to be raised to compete with the market rate
b) central controls on public expenditure and civil service numbers would preclude expansion to the extent thought necessary
c) the changes sought in organisation and structure (ie functional team working and unified management) are too far different from those elsewhere in the civil service or in DHSS to be accepted
d) the degree of management flexibility sought for the Director and his senior managers exceeds that attainable in large organisations such as the DHSS.

We examined these propositions carefully in relation to the four main options we identified for our proposed Medicines Directorate, viz:

: privatisation
: a quango, more properly referred to as a non-departmental public body, or NDPB
: a new Government department,
: to remain within DHSS but with considerably more flexibility of action.

Privatisation

6.4.1 In our view, the control of medicines is too important to the public health, and of too great an interest to Parliament, to be taken out of the public sector. We RECOMMEND the control of medicines should remain under Parliamentary scrutiny and Ministerial responsibility.

Non-Departmental Public Body

6.4.2 There is a wide variety of non-departmental public bodies, and a similarly wide variety in their freedom of action. Certain NDPBs enjoy substantial autonomy because they are exempt from gross running cost controls; however the advantage of such exemption is not confined to NDPBs, and forms an important aspect of our own proposals, below. In general though, NDPBs enjoy much less autonomy in pay and personnel matters than their advocates apparently believe. In particular, Special Health Authorities (SHAs) are just as constrained by public sector pay policy, public expenditure controls and public sector manpower controls as is DHSS itself, and they operate undr close supervision from that Department. SHAs are expected to apply NHS terms and conditions, which would mean in practice that if the Medicines Directorate were a SHA, some medical staff might be eligible for higher pay (but only via the Distinction Award system), but pharmacists would not. On this analysis, the only advantages to be gained from reconstituting the Medicines Directorate as a NDPI would flow from a measure of greater organisational and management freedom, but this would still have to be exercised within the framework of public sector policy generally.

6.4.3 On the debit side, we were influenced by the fears expressed by experienced chairmen and members of some of the advisory committees, that distinguished experts would be less willing to spend their time and efforts advising a quango. In their view, to distance medicines control from Ministers and the DHSS would risk imperilling the excellence of the Section 4 Committees and the Medicines Commission. There were two other practical points militating against reconstitution as a NDPB. Firstly, we were advised that the change would almost certainly require primary legislation. Secondly, it is by no means certain that approval would be given since the published guide-lines do not allow bodies to be constituted as NDPBs just to escape civil service pay etc constraints. (The legitimate reason for seeking NDPB status is to distance the organisation from Ministers, whic in our view is not a desideratum.)

6.4.4 On balance we concluded that there is not sufficient advantage to be gained from removing the control of medicines into a Special Health Authority or other NDPB.

A smaller Department

6.4.5 We also considered whether it might be advantageous to reconstitute the Medicines Directorate as a separate small Government department, responsible directly to the Secretary of State for Social Services but not being part of DHSS. (We took a analogue the Office of Population Censuses and Surveys.) Certainly, the smaller organisation offers some advantages, notably flexibility, freedom of action and speed of respo se, bu the Medicines Directorate is really too small to be credible in this form and would have problems over the grading of its senio staff, for example.

Autonomy within DHSS

6.5 While the arguments for moving medicines control into a Special Health Authority or separate Department did not stand up well to scrutiny, we were encouraged to be told that the prospects for attaining satisfactory flexibility and freedom of action within DHSS and the civil service are much more promising than critics had supposed, for the following reasons -

: new developments in pay policy allow much more flexibility of pay in relation to grading. We RECOMMEND that the pay of pharmacists and doctors in the Medicines Directorate should be determined flexibly so as to allow recruitment and employment of senior experienced staff at market rates
: simplistic controls on civil service numbers (eg the headcount) are giving way to control via the budget
: following the principles of the Financial Management Initiative, much progress has been made towards freeing up management
: most importantly: if, as we believe, the Medicines Directorate can be made to qualify for exemption from gross running cost controls under Treasury and Public Expenditure Survey rules, it will be much easier to allow substantial organisational change and managerial autonomy and flexibility within DHSS.

6.6 There are of course substantial benefits for keeping the control of medicines within DHSS, to set against the contrary arguments reported in paragraph 3.3.

- it facilitates easy access to DHSS expertise and to the NHS
- senior DHSS staff help to link with the professions, especially the medical organisations. These links are especially important when licences have to be withdrawn on grounds of safety
- the control of medicines by licensing etc is only one aspect of DHSS concern with the use and pricing of medicines, and with the pharmaceutical industry. There is advantage in considering broad policy in these matters together
- similarly, there are many aspects of common policy relating to the EC, to medical and surgical appliances etc etc.

6.7 For these reasons, we RECOMMEND that the Medicines Directorate should remain within DHSS. We assume that the Director will be accountable to a Grade 2 officer, and for reasons given earlier we believe it is preferable to avoid dual lines of accountability within parallel hierarchies. We therefore RECOMMEND the Director of Medicines Control should be managerially accountable to the appropriate Deputy Secretary (ie, the chairman of the Budget Committee (see below) and of the Medicines Policy Committee). However, the Chief Medical Officer and his relevant Deputy will need to be involved in many issues especially those arising from the Medicines Commission and the Section 4 Committees, and the latter officer will presumably act as the professional career adviser to senior medical staff of the Directorate (para 5.24 refers). The Chief Pharmaceutical Officer will have a similar role in respect of pharmaceutical staff.

Exemption from Gross Running Cost Controls

6.8 Without going too far into the arcane details of Public Expenditure Survey rules, we can say that we believe the key to satisfactory progress in the control of medicines is to achieve exemption from gross running cost controls status for the Medicines Directorate. As explained earlier, the receipts from fees for licensing are at present classed as negative public expenditure and not netted against the expenditure on Medicines Division. Providing certain conditions are satisfied, it is possible for the Medicines Directorate to be exempted from gross running cost controls, whereby the receipts are netted against expenditure. On such a footing, there is appreciable relaxation from the rigidities of public expenditure controls. The principal conditions, over and above those already met, are that i) the receipts should cover the whole of the gross revenue expenditure, and ii) especially in a monopoly situation such as obtains in medicines licensing, there should be some mechanism for satisfying those who pay (in this case, the pharmaceutical industry) that the scale of expenditure proposed is reasonable. Both these conditions will be met if our report is implemented, and we RECOMMEND that DHSS should apply for the Medicines Directorate to be exempted from gross running cost controls, to take effect as soon as possible.

Financing the changes

6.9 Under our proposals, the cost of medicines control will go up in the short term because of -

: modest increase of staff, say +10% at most
: more pay for a few selected posts
: capital expenditure on information technology.

In the longer run, when the managerial and information technology changes we have recommended come into effect, we expect the real cost to fall to present levels or below.

6.10 The receipts from industry currently cover only about 62% of the revenue expenditure on Medicines Division, seemingly because industry has not been charged the cost of certain so-called 'policy' work. Leaving aside the work associated with the British Pharmacopoeia, which is discussed further in the next chapter, we consider that all the work of Medicines Division (including the so-called policy work) can reasonably be regarded as relating to the control of medicines. We RECOMMEND that the full cost of the Medicines Directorate (ie, of Medicines Division as strengthened by our recommendations, but less the British Pharmacopoiea) should be charged to the pharmaceutical industry.

6.11 Charges are levied both on licence applications and on company turnover, the latter currently accounting for some 89% of receipts. We RECOMMEND that the balance should shift from turnover towards fees for processing licence applications and appeals, so far as this is consistent with year on year stability. We RECOMMEND too that fees for the different

categories of work (NASs, Abridged, CTXs, appeals etc) should relate to the approximate proportionate cost of carrying out that category of work.

6.12 We are confident that the changes we have recommended should reduce the burden of delays and bureaucracy that the licensing system places upon the pharmaceutical industry, without in any way impairing the protection of the public. We believe that industry will be willing to pay the increased cost, in the interests of a better service. To ensure cost-effective management of the Medicines Directorate, we RECOMMEND that a Budget Committee (comprising representatives of the Association of the British Pharmaceutical Industry, DHSS, H.M. Treasury, and the Proprietary Association of Great Britain, under the chairmanship of DHSS) should meet say twice each year to monitor the cost and efficiency of the Directorate, to set the budget for the succeeding year, to set operational targets, and to review performance against those targets. The terms of reference of the Budget Committee must specifically preclude its having any influence over the licensing etc decisions of the Directorate, for the reputation of the UK Licensing Authority depends upon remaining free from the influence of industry.

6.13 To begin with, the performance yardsticks and operational targets will need to relate to such measures as -

: proportion of New Active Substance applications determined within the European Community defined periods,
: ditto Abridged applications, etc etc
: arithmetic mean times for determination of licence applications, by category,
: median times, ditto.

Information is available now to compile any of the above. Some targets will also relate to internal management goals, such as achieving a fully-functioning file tracking service and developing systems for internal quality control. Performance yardsticks such as these are requisite for the Director's use and that of the Budget Committee but quantitative measures alone do not give the whole picture; the excellence of the judgemental decisions taken to protect the public must continue to be the first consideration. So much time is being wasted now while files wait for attention, and in clerical operations, that significant speeding-up is attainable without in any way impairing the thoroughness of assessment and expert consideration. As performance improves towards the figures specified in EC directives, more sophisticated measures will be needed to guarantee that fully adequate time remains available for professional and committee assessment; only time wasted in queuing or in clerical operations is superfluous. The Budget Committee will be concerned to see that the Director develops management tools appropriate to the task.

6.14 It is relevant to point out that the ability and willingness of industry to carry the considerable costs of the licensing and other arrangements for the control of the quality, safety and efficacy of medicines must depend in the end on the returns from their trade; and the flow of new, safe and efficacious medicines

depends upon research. The restoration of the patent life of medicines would help to improve the rewards for pharmaceutical innovation; it would also reduce the pressure for quick licensing, which is partly responsible for premature and incomplete applications.

Chapter 7: OTHER ISSUES

7.1 In this chapter we discuss a number of issues related to our main theme, but without attempting to comment on all the points raised with us during the review.

The British Pharmacopoeia

7.2 Despite its distinguished history, we felt that the British Pharmacopoeia (BP) is in some respects an anachronism. Sooner or later it is due to be replaced by the European Pharmacopoeia, to which the BP makes a considerable input. Even if an official UK compendium of pharmaceutical monographs is still needed (which some commentators doubted, given that the licensing authority draws up similar monographs on many products, currently unpublished and sometimes differing from the BP monographs), it seems doubtful if it is necessary to print it in several volumes, handsomely bound and handsomely subsidised. We note that at least one other national pharmacopoeia, that of the United States of America, operates as an independent business and we believe it would be preferable to put the British Pharmacopoeia too on a more commercial basis, recouping substantially the whole of its costs from publications.

7.3 That opinion is strengthened by the evidence from several sources that the BP does not greatly benefit from its apparent closeness to the licensing operation. Unlike the other expert advisory committees, the British Pharmacopoeia Commission has, and needs to have, members drawn from the pharmaceutical industry, who clearly cannot be party to licensing information; this necessarily inhibits what might otherwise have seemed an opportunity for useful interchange. Certainly, the pharmacopoeial work does not sit easily alongside the licensing operations which will dominate the Medicines Directorate; by contrast we note that the Pharmaceutical Society of Great Britain already undertakes some statutory responsibilities for pharmaceuticals and is engaged in publishing, eg the British National Formulary. We RECOMMEND that the DHSS should consider transferring responsibility for the British Pharmacopoeia to the Pharmaceutical Society of Great Britain; there should then be opportunity to rationalise laboratories. The British Pharmacopoeia Commission should remain a statutory committee under Section 4 of the Medicines Act.

Adverse Drug Reaction Monitoring

7.4 As is well known, no amount of laboratory testing of medicines, nor controlled clinical trials of their use, can suffice to reveal all possible adverse reactions. In the UK and elsewhere much thought is being given to ways of developing the monitoring of adverse reactions occurring in ordinary clinical practice, more especially in the early months and years after release onto the market. The 'yellow-card' scheme, foundation of UK information on adverse reactions, remains important but is not in itself enough. Various schemes of post-marketing surveillance have begun or are under discussion. We are not competent

suggest in detail what should be done, but we RECOMMEND -

a) proportionately more effort should be devoted to work on adverse drug reaction (ADR) monitoring. (This is an aspect the Medicines Commission might take an interest in.)
b) ADR monitoring, and oversight of the arrangements for post-marketing surveillance should remain the responsibility of the Medicines Directorate and the Committee on Safety of Medicines, for the information so obtained is crucial to the continuing assessment of safety. In our view it would not be appropriate to devolve the central responsibility to an outside body, though many or all of the studies can be carried out by others.
c) information on adverse drug reactions should be made available (without identifying particulars) to bona-fide researchers and to relevant pharmaceutical companies. For example, the Medicines Directorate should send an anonymised copy of each yellow-card report to the company or companies concerned.
d) The Medicines Directorate should continue and improve upon the arrangements for exchange of information with authorities overseas, and should encourage international initiatives for retrieval of library and other ADR data.

Alternative Medicines

7.5 We understand that various parties are considering whether the arrangements currently made for controlling orthodox medicines would also be appropriate for controlling homeopathic and similar alternative medicines. The essence of product licensing, as applied to orthodox medicines, is the assessment of quality, safety and efficacy using various science-based procedures such as controlled clinical trials. We consider it is fruitless to require product licences for products whose quality, safety or efficacy cannot be judged by the standard science-based criteria, and we RECOMMEND that insofar as control is needed, other methods should be used, eg perhaps inspection of manufacture.

The Medicines Inspectorate

7.6 We were impressed by the evidence of the regard in which the Medicines Inspectorate's work is held, and agree that it is appropriate to sustain and reinforce this well-run organisation. There may be opportunity, in the new structure of the Medicines Directorate, to aggregate other responsibilities (eg enforcement, perhaps) with the Inspectorate, and to devolve them to the regional offices. (We are not suggesting that enforcement is only a matter of inspection or prosecution; control of advertising, for example, is best pursued via codes of practice)

The Future in Europe

7.7 It will be clear from previous chapters that in the longer term the future pattern of public control of the manufacture and marketing of medicines is likely to be determined within the European Community, in concert with other member states and the

Commission. Britain has much to contribute to the European consideration of these issues, as witness the initiatives on control of biological materials made by the Director and staff of the National Biological Standards Board. We believe the development of EC policy should remain a priority for officers of the Medicines Directorate.

7.8 Looking ahead, we are confident that the invigoration of medicines control work when our recommendations are implemented, the improving efficiency of the Medicines Directorate, and the already high opinion in which UK assessments are held, will put the Directorate in a strong position to share in the licensing work for Europe.

CFB/1833L/61

ANNEX 1

STUDY OF CONTROL OF MEDICINES

DR. N. J. B. EVANS CB
P. W. CUNLIFFE CBE

c/o Department of Health and Social Security
Room 1029
Market Towers
1 Nine Elms Lane
London SW8 5NQ
Tel: 01 720 2188 ext GRO-C

STUDY OF CONTROL OF MEDICINES

You may have heard that we have been asked by Ministers to examine issues relating to the control of medicinal products. Our terms of reference are:

> "To examine the issues for DHSS arising from the continued increases in licence applications and other work under the Medicines Act and to recommend ways of dealing expeditiously with this work, while maintaining adequate standards for the safety, efficacy and quality of human medicines in the United Kingdom".

I enclose a copy of an extract from Hansard for 11 March with the relevant Parliamentary Question and answer.

We would be grateful if you would kindly let us have any observations the [name of organisation] may wish to give relating to the subject of our study.

It is difficult at this stage, the outset of our study, to specify what topics we would particularly wish you to cover. We anticipate that the areas will include:

a. the strengths and weaknesses of the present licensing and other control arrangements;

b. ways of improving throughput by improving efficiency, eg. by minor or major procedural or organisational changes;

c. whether the volume of evidence asked for and its assessment, are appropriate to the various kinds of applications received;

d. workload and other issues arising from the organisation of the licensing authority and its staff and their relationship with the Medicines Commission and the Section 4 Committees relating to human medicines, the Committee on Safety of Medicines, the Committee on Dental and Surgical Materials, the Committee on the Review of Medicines and the British Pharmacopoeia Commission;

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e. international comparisons

f. mutual recognition and other opportunities for collaboration.

These headings are not intended to be exhaustive; we would welcome observations on any or all of them, and on any other matters you consider relevant. Please indicate clearly any material which you wish to remain in confidence.

It would be helpful to have your reply (3 copies, please) by the end of May. We are writing in similar terms to those listed on the attached sheet.

N J B EVANS

P W CUNLIFFE

ANNEX 2

LIST OF THOSE WHO GAVE THEIR VIEWS

WRITTEN

Association of British Dispensing Opticians
The Association of the British Pharmaceutical Industry
Professor D N Baron
Beecham Pharmaceuticals
Professor C L Berry
BIOS (Consultancy & Contract Research) Ltd
British Association of Pharmaceutical Physicians
The British College of Ophthalmic Opticians (Optometrists)
British Dental Association
The British Herbal Medicine Association
British Homoeopathic Association
The British Institute of Regulatory Affairs
Dr D M Burley
Dr J D Cash - Scottish National Blood Transfusion Service
Ciba-Geigy Pharmaceuticals
Consumers' Association
Professor P H Elworthy
Ethical Pharmaceuticals Ltd
The Faculty of Homoeopathy
Federation of Independent British Optometrists
Professor A T Florence
Glaxo Pharmaceuticals Ltd
Professor D G Grahame-Smith
Dr B J Hunt
Imperial Chemical Industries PLC
Dr D R Jones
Professor M J S Langman
Professor D H Lawson
Professor K MacMillan
National Institute for Biological Standards and Control
The Natural Medicines Group
The Natural Medicines Society
The Patients Association
The Pharmaceutical Society of Great Britain
Proprietary Association of Great Britain
Professor A Richens
Roussel Laboratories Ltd
The Royal College of General Practitioners
Royal College of Physicians
Royal College of Physicians - Edinburgh
Royal College of Physicians and Surgeons of Glasgow
The Royal College of Surgeons of England
Royal Society of Chemistry
Social Audit Ltd
Professor J B Stenlake - The British Pharmacopoeia Commission
Dr I Turner
UM Research Data Corporation
Dr G R Venning
Dr R J Walden

ANNEX 2 continued

ORAL

Professor A W Asscher
Mrs G T Banks
P Benner Esq
Civil and Public Servants Association
Dr Joe Collier
Professor Sir Abraham Goldberg
Dr A Herxheimer
H M Treasury
Professor Rosalinde Hurley
The Institute of Professional Civil Servants
Management and Personnel Office
Society of Civil and Public Servants
R N Williams Esq

DHSS Staff

Sir Donald Acheson
Mrs J Alderman
Mrs C Barratt
Mr J St L Brockman
Mr A C Cartwright
Mr G V Chugg
Miss J Clarke
Mrs M Clarke
Mr R T Clay
Miss R Coulson
Mr R G B Cox
Mrs M Dow
Dr L K Fowler
Mr G G W Franks
Mr R Freeman
Mr B K Gilbert
Miss K Good
Mr J Grimshaw
Mr M Hack
Mr D O Hagger
Mr N M Hale
Miss A Harpley
Dr E L Harris
Mr B Hartley
Dr J Hilton
Dr D Jefferys
Dr W J Jenkins
Dr C A Johnson
Dr G Jones
Miss C A Kennedy
Miss V Luttrell
Miss J Male
Mr M C Malone-Lee
Dr R D Mann
Dr B R Matthews
Mr J G Mayne
Dr J A Nicholson
Mr P C Nilsson
Miss S A Norton
Mr M O'Connor
Ms D Palmer
Mr J E Parnwell
Mr M J Partridge
Miss A-M Pittaway
Dr J Purves
Dr J Raine
Mr B R Rayner
Mr P Rescorla
Miss D Richards
Dr J C Ritchie
Dr A R Rogers
Dr R Rotblat
Miss J Shipton
Miss A Simkins
Mr J S Sloggem
Dr D Slovick
Mr A G Stewart
Miss A Tuplin
Mr J L Turner
Mr M R Watson
Dr B A Wills
Mr C H Wilson
Dr S Wood

VI LICENSING OF MEDICINAL PRODUCTS

The Scope of Control

20. The Medicines Act controls medicinal products. These are defined as substances or articles (not being instruments, apparatus or appliances) which are used for administration to human beings or animals for the purpose of treating or preventing disease, of diagnosis, of inducing anaesthesia, of contraception or of preventing or interfering with the normal operation of a physiological function. Ingredients to be used in the preparation of medicines for dispensing in hospitals or pharmacies or by practitioners are also medicinal products, Ingredients are however exempt from detailed licensing control by an Order made in 1973.

21. There are also powers under the Act to extend control to articles and substances which are not medicinal products but which are used for medicinal purposes, or as ingredients in the manufacture of medicinal products, or which might constitute a potential health hazard. Under these powers, control has already been extended to cover surgical sutures and certain other surgical materials; certain substances which are used as active ingredients in medicinal products and which cannot be fully assayed chemically; antibiotics when used for both medicinal and non-medicinal purposes; and intra-uterine contraceptive devices. Control has also been extended to contact lens fluids; and preparations are being made for the licensing of contact lenses. Provisions of the Act have also been applied to dental filling substances.

Types of Licence

22. Licences or certificates are required in the following circumstances:

a. Medicines may not be imported, marketed or manufactured except in accordance with a Product Licence. The licence is normally held by the person responsible for the composition of the product (this is usually the manufacturer or, in case of contract manufacture, the person or company to whose order the product is manufactured) or by the importer of the product.

b. A Clinical Trial Certificate is necessary in order to authorise the supply of a medicinal product for the purpose of a clinical trial in human beings unless a Clinical Trial Exemption is granted.

c. Manufacturers Licences authorise the holder to manufacture or to assemble medicinal products. (Assembly means enclosing the product in a container, and labelling it after manufacture).

d. Wholesale Dealers Licences are required for the sale of medicinal products to anyone other than the ultimate users.

IX CONTROLS ON THE RETAIL SALE OF MEDICINAL PRODUCTS

45. The retail sale or supply of medicines is controlled under Part III of the Medicines Act 1968 which was brought into operation on 1 February 1978. The underlying principle of the controls is that medicines should normally be sold through pharmacies, though the Act does empower Ministers to make Statutory Instruments modifying this principle in relation to particular products or substances. In general, the legislation divides medicines for human use into three categories for the purpose of retail sale or supply: 'General Sale List', 'Pharmacy' and 'Prescription Only'. There are special provisions for herbal and homoeopathic medicines.

General Sale List

46. The purpose of the General Sale List (GSL), which was drawn up on the advice of the Medicines Commission, is to specify the medicinal products which can be sold, with reasonable safety, otherwise than by, or under the supervision of, a pharmacist. Such sales must be made from places which can be closed so as to exclude the public; this prohibits sales from stalls in street markets or from vehicles. There is a separate list of those GSL medicines which are allowed to be sold by means of automatic machines.

Pharmacy

47. Pharmacy medicines may be sold or supplied only in a registered pharmacy by or under the supervision of a pharmacist. All medicines fall automatically into the pharmacy category unless expressly included in one of the other 2 categories.

Prescription Only

48. Prescription only medicines (POM) may be sold or supplied only from a registered pharmacy, by or under the supervision of a pharmacist, and in accordance with a prescription issued by a doctor or dentist. The substances which the Medicines Commission has advised should be so restricted are those whose use in treatment needs to be supervised by a practitioner because they may produce either a toxic reaction or physical or psychological dependence, or may endanger the health of the community.

Drugs Liable to Misuse

49. Medicines liable to misuse and to produce dependence are subject to complex legislation in addition to that applying to medicines in general. The Misuse of Drugs Act 1971 is the main legislation governing dangerous and addictive drugs, and this is administered by the Home Office. The United Kingdom is party to a number of United Nations agreements on the control of narcotic drugs, and this Act was prepared in the light of these.

Registration of Pharmacies

50. The Medicines Act requires the registration with the Pharmaceutical Society of Great Britain (PSGB) of all premises from which retail sales of medicines not on the General Sale List are made. The Society employs Inspectors who visit all registered pharmacies in Great Britain. The Act empowers Ministers to lay down requirements as to the suitability, construction, maintenance, cleanliness, of any premises where medicinal products are to be sold, and to certify that premises whose registration as a pharmacy has been applied for are unsuitable for registration by reason of failing to satisfy those requirements.

Compliance with Standards

55. Pharmacopoeial standards were given statutory force in the United Kingdom by the Medicines Act which made it an offence to sell or supply medicines which are ordered or prescribed by reference to a name which is at the head of a monograph, unless the medicine complies with the standards in that monograph. It should be noted that although specifications for the pharmaceutical quality of medicinal products are included in licences, these are specifications for the quality of the product when it is sold by the manufacturer. They are additional to and do not replace those of the Pharmacopoeia since the latter provides requirements that should be met at any time during the lifetime of the product.

XI LABELLING, LEAFLETS AND PACKAGING

Labelling Regulations

58. It is an offence under the Medicines Act to sell or supply in the course of a business any medicinal product in a container or package which is labelled in such a way as to describe the product falsely, or to be likely to mislead as to its nature, quality, uses or effects.

Leaflets

64. As with labelling, the Medicines Act makes it an offence to supply a leaflet with a medicinal product where that leaflet falsely describes the product or is likely to mislead as to its nature, quality, uses or effects. Ministers are also empowered to make regulations. The Medicines (Leaflets) Regulations which became operative on 15 July 1977 apply only to leaflets supplied with proprietary medicinal products, a limitation reflecting their origin as part of UK implementation of Council Directorate 75/319/EEC.

Packaging

66. Regulations have been made under the Medicines Act for

a. fluted bottles. These supersede Rule 26 of the Poison Rules. They impose a prohibition on the sale or supply of certain liquid medicinal products for external use unless contained in bottles which are recognisable by touch; and

b. child safety. These relate to the sale or supply of aspirin and paracetomol in child-resistant containers.

General Advertising Controls

67. Under the Medicines Act it is an offence to issue false or misleading advertisements relating to medicinal products, or to make false or misleading oral representations. Advertisements or representations involving a recommendation for the use of a product not specified in the product licence are also forbidden. Advertisements must only be issued with the consent of the product licence holder. The Licensing Authority may ask to see all advertisements which have been issued in the previous 12 months.

68. Standard provisions for product licences enable the Licensing Authority to exercise controls over advertisements for particular products, either by requiring all advertisements to be submitted in advance or by requiring that certain particulars should be included, or by requiring that an individual advertisement be amended or withdrawn.

69. In addition to these general controls, regulations directed at advertising to the public and at advertising to medical and dental practitioners have an important role (see 71 below).

Advertising to the Public

70. Regulations made under the Medicines Act control the advertising to the public of medicinal products and provide that:

a. it is an offence to advertise any medicinal product for the treatment of certain serious diseases such as venereal disease or cancer;

b. the advertising of medicinal products which are available only on prescription from a doctor or dentist is prohibited;

c. representations and advertisements in respect of certain specified diseases or conditions which are considered unsuitable for self-treatment are prohibited. Limited exemptions are provided for herbal, homeopathic, and other "traditional" medicines.

Advertising to Practitioners

71. In addition to the general controls mentioned above, any advertisement sent or representation made to a medical or dental practitioner concerning a medicinal product must be accompanied by a data sheet, or preceded by one sent not more than 15 months before the issue of the advertisement or representation. A data sheet is a statement in a set format about the product and its uses, and any information in it must be in accordance with the product licence. Most data sheets are published in an annual compendium published by the Association of the British Pharmaceutical Industry (ABPI).

72. Regulatory controls on advertising to practitioners stipulate that product information consistent with that provided in the data sheet must appear as part of most written representations in journal advertisements, advertisements addressed personally to doctors, etc. The information that must be given includes the name and address of the product licence holder and the product licence number; an indication of the active ingredients; one or more of the authorised indications for use; side effects, precautions and contra-indications (summarised); dosage and method of use (summarised); the basic cost. The unqualified use of the word "safe" is prohibited, as are misleading graphs and tables.

73. The regulations permit abbreviated advertisements in certain circumstances. They must not exceed 420cm^2 in size, and may only include a minimum of information about the product. An abbreviated advertisement is primarily a reminder that the product is available.

XII ENFORCEMENT OF THE ACT

75. The Act creates a number of criminal offences, some of which relate to the marketing, production and wholesaling of medicinal products and others to their retail sale, which the appropriate Ministers in England, Scotland, Wales and Northern Ireland respectively, are under a duty to enforce. This can present problems, the Act therefore also imposes duties of enforcement, concurrently with the appropriate Minister, upon other bodies, such as the Pharmaceutical Society or local authorities. The appropriate Minister may also require such bodies to share the duties of enforcement with him.

Medicines Inspectorate

76. The activities of the Medicines Inspectorate are concentrated on the inspection of manufacturing establishments at home and abroad of wholesaling establishments in the United Kingdom. Inspections are necessary to ensure that the licence holder continues to comply with the conditions of the licence and with the relevant provisions of the Act; to ascertain whether conditions of manufacture, storage and so forth are in accord with the licence as granted and to assess the suitability of manufacturing and wholesale arrangements generally for the purpose of considering applications. Thus their visits are carried out on behalf of the licensing and enforcement authorities.

77. During visits to manufacturers', wholesalers' and other premises Medicines Inspectors may take samples for analysis. Normally these are analysed by the Pharmaceutical Society's Laboratory in Edinburgh or by the Laboratory of the Government Chemist.

78. An experienced member of the Medicines Inspectorate is engaged full-time in the important task of examining the manufacturing methods and in-process controls for biological products. In this he works in close association with the National Institute for Biological Standards and Control and with the professional staff assessing applications for licences for such products. He may be assisted in his inspection work by personnel from both these areas as well as by others of the Medicines Inspectorate and thus plays a part in assessing both manufacturers and Product Licence applications.

79. When an inspection results in the discovery of the manufacture or importation of unlicensed products or unsatisfactory arrangements at the manufacturers' or wholesalers' premises, the report will be submitted to the responsible group in Medicines Division, who will decide on the further action to be taken. This may include revocation, suspension or variation of licences or prosecution.

TABLE 1

MEDICINES DIVISION BALANCE SHEET

STATEMENT OF INCOME AND ESTIMATED EXPENDITURE FOR MEDICINES DIVISION (EXCLUDING THE BRITISH PHARMACOPOEIA - SEE OVER) - 1.9.86 - 31.8 87

ESTIMATED EXPENDITURE

	£,000	£,000
Staff costs (Administrative, and clerical)*	3,589	
Staff costs (Pharmacists)*	1,863	
Staff costs (Medical)*	1,314	
Other costs (including payments to PSGB labs, S.4 Committees and library etc)	1,960	
IT costs	149	
	8,875	8,875
ESTIMATED EXPENDITURE - Legal costs		
Staff*	224	
Prosecutions	95	
	319	319
TOTAL ESTIMATED EXPENDITURE (EXCLUDING BPC)		9,194
INCOME FROM FEES		5,728
Shortfall of Income over Expenditure		3,466

(Income covers 62% of estimated expenditure)

* Including overheads.

TABLE 1 (cont'd)

STATEMENT OF INCOME AND EXPENDITURE FOR THE BRITISH PHAMACOPOEIA COMMISSION

ESTIMATED EXPENDITURE	£000	£000
Staff cost*	777	
Laboratory consumables	67	
Fees, travel, subsistance	50	
Other costs	70	
	964	
TOTAL ESTIMATED EXPENDITURE		964
INCOME		
Gross Income pa from sale of BP	350	
Gross Income pa from sale of BP chem. ref substances	88	
TOTAL INCOME	438	438
Shortfall of Income over Expenditure		526

(Income covers 45% of estimated expenditure)

Notes * - Including overheads.

1 - Excludes printing and publishing costs at present incurred by HMSO

2 - Averaged over the approximately seven year cycle and received currently by HMSO

TABLE 2

LICENSING STATISTICS APPLICATIONS RECEIVED	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987
New Product Licenses	762	660	835	922	1180	1043	1282	1158	922	1365	1217	1073
Product Licence Renewals		480	256	252	216	243	606	465	499	419	830	1294
Variations, Product Licences, Product Licences of Right and Clinical Trial Certificates	4788	3968	3945	5130	7007	7297	7384	5940	6421	7887*	8534*	10564*
Clinical Trial Certificates and CTC renewal	123	224	260	214	296	177	211	155	121	107	94	97
Clinical Trial Exemption Certificates						208	232	252	263	233	249	217
Clinical Trial Exemption Certificates: Variations and renewals									978	1500	2833	
Manufacturers' Licences, Renewals and Variations	211	777	91	124	118	290	780	481	609	683	739	939
Wholesalers Dealers Licences, Renewals and Variations	62	847	146	115	832	264	816	507	462	829	592	829
Product Licence Parallel Imports									1624	665	939	113
Export Certificates	7921	7656	11181	11157	10948	12439	11389	11956	10903	12330	13380	12373

* - includes PLPIs

MEDICINES DIVISION STAFFING

Staff in Post at 31 March

	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987
Administrative Staff	127	125	120	120	117	134	128	142	145	154	165*
Professional Staff	92	93	94	95	98	95	93.5	107.5	117.5	119	125*
TOTALS	219	218	214	215	215	229	221.5	249.5	262.5	273	290*

* at 1 December 1987

TABLE 4A

MEDIAN TIME TAKEN TO GRANT LICENCES GIVEN IN MONTHS[1]

Column 1	Column 2	Column 3
Year	Established Drug Substance Applications (L.A. only)	Established Drug Substance Applications seen by S.4 Committee
1982[2]	5	12
1983[3]	4	16
1984[2]	4	16
1985[2]	5	16
1986[2]	8	17
1987[4]	11	25

note 1. Months are equivalent to periods of 30.5 days.
note 2. Figures published in MAIL.
note 3. Calculated for this table.

note 4. figures are not yet available — interim calculations for the period 1st January to 30th June.

TABLE 4B

MEAN TIME TAKEN TO GRANT LICENCES GIVEN IN MONTHS[1]

Column 1	Column 2	Column 3
Year	Established Drug Substance Applications (L.A. only)	Established Drug Substance Applications seen by S.4 Committee
1982[2]	7	14
1983[3]	4	21
1984[2]	5	16
1985[2]	6	18
1986[2]	8	19
1987[4]	11	23

note 1. Months are equivalent to periods of 30.5 days.
note 2. Figures published in MAIL.
note 3. Calculated for this table.

note 4. figures are not yet available — interim calculations for the period 1st January to 30th June.

NB Licensing times for NAS's not included as the numbers are small and the variables too great to make the results reliable.

TABLE 5

APPEALS

	1982	1983	1984	1985	1986	1987
Medicines Commission						
Hearings	10	13	10	5	11	13
Written	-	2	1	7	9	11
Committee on Safety of Medicines						
Hearings	25	22	14	11	15	12
Written	23	39	39	30	21	24
Committee on the Review of Medicines						
Hearings	4	4	5	13	8	13
Written	5	36	25	26	34	22
Committee on Dental and Surgical Materials						
Hearings and written representations	25	77	20	19	9	30
TOTALS	92	193	114	111	107	124