Drug Evaluation by the Therapeutic Goods Administration

Department of Health and Family Services

Performance Audit

Tabled 8 October 1996

Audit Report No. 8 1996-97

Abbreviations / Glossary

ADEC	Australian Drug Evaluation Committee
ADR	Adverse drug reaction
ADRAC	Adverse Drug Reaction Advisory Committee
ADRS	Adverse Drug Reaction System
ANAO	Australian National Audit Office
APMA	Australian Pharmaceutical Manufacturer's Association
ARCS	Association of Regulatory and Clinical Scientists
ARTG	Australian Register of Therapeutic Goods
AUA	authorised user approvals
CANDA	Computer Assisted New Drug Application
CATEGORY 1	evaluation of new chemical entities
CATEGORY 2	evaluation that relates to a drug that, in each of two acceptable countries, had been approved for general marketing

CATEGORY 3	evaluation that relates to variations to the information on a drug already on the ARTG
DART	Drug Applications for Registration and Tracking system
DHFS	Department of Health and Family Services
DHSH	Department of Human Services and Health
DSEB	Drug Safety and Evaluation Branch
EC	European Community
FDA	Food and Drug Administration
GMP	good manufacturing practice
ICH	International Conference on Harmonisation
IGCC	Industry/Government Consultative Committee
IPU	individual patient use
IT	information technology
JCPA	Parliamentary Joint Committee of Public Accounts
KPI	key performance indicator
MAB	Management Advisory Board
MIAC	Management Improvement Advisory Committee
MIAA	Medical Industry Association of Australia

NCE	new chemical entity
NFA	National Food Authority
PBMS	Portfolio Budget Measures Statements
PBS	Pharmaceutical Benefits Scheme
PMAA	Proprietary Medicines Association of Australia
PPS	Program Performance Statements
RAJ	Regulatory Affairs Journal
TGA	Therapeutic Goods Administration
WHO	World Health Organisation

Summary

Therapeutic Goods Administration

1. The Therapeutic Goods Administration (TGA) is a sub-program of the Department of Health and Family Services, with an objective of ensuring that the safety, quality and efficacy of therapeutic goods available in Australia is at a standard equal to that of comparable countries.

2. In July 1991 Professor Peter Baume was commissioned by the then Government to conduct an inquiry to seek improvements in Australia's drug evaluation system operating within the TGA. The main theme of the report was the need to ensure the timely availability of drugs to the public by making the review process more efficient within existing resource limits.

The purpose of the audit

3. The purpose of the audit was to examine the efficiency, effectiveness and accountability of the Therapeutic Goods Administration's performance in evaluating and approving prescription drugs for public use.

4. In particular the audit focused on analysing elements of the regulatory process associated with the evaluation of prescription drugs. In this context the audit reviewed the administrative

operations performed within the Department's Drug Safety and Evaluation Branch, the Australian Drug Evaluation Committee and the Business and Services Branch of the TGA, rather than any processes preceding or succeeding those activities. The audit did not look at processes for non-prescription (over-the-counter) drug products or other therapeutic products evaluated by the TGA.

5. As part of the audit, criteria were determined to consider how well the TGA was performing evaluation of prescription drugs and the effectiveness of its administrative processes. The objectives of the audit are discussed under Audit Objective at paragraph 1.11.

Overall conclusion

6. The audit found that the drug evaluation process was efficient. The TGA could increase the effectiveness of its drug evaluation by giving more attention to the monitoring of adverse drug reactions. Further, although the TGA produced much information for the pharmaceutical industry, it could strengthen its external accountability through provision of clearer information on its activity to Parliamentarians and to consumers of prescription drugs.

7. In relation to the pre-marketing aspects, the ANAO found that the TGA has reduced dramatically the time taken to approve a drug for use. In 1990, the average number of working days required to evaluate and approve a new chemical entity was 702. In 1995, the average number of working days was 106 against the 255 working days allowed under the legislation. This improvement benefited all stakeholders, including drug consumers and the pharmaceutical companies. Notwithstanding this improvement, there was scope for the time taken to be reduced further, particularly in calendar days, with the assistance of pharmaceutical companies.

8. Information technology used by the TGA was not satisfying the needs of users nor were systems adequately integrated. Principal users found a need to use other supporting systems/databases and manual techniques.

9. Furthermore, the ANAO concluded that the TGA should develop an adequate system to assess the cost of its services to the pharmaceutical industry, and improve the low level of reporting of adverse reactions to drugs in Australia.

10. Finally, the ANAO concluded that TGA's performance indicators and performance reporting were not adequately informing the Parliament and consumers of its work.

Recommendations

Set out below are the ANAO's recommendations with Report paragraph reference and DHFS's responses. The ANAO considers that DHFS should give priority to Recommendation Nos. 11, 12, 13 and 14.

Recommendation No.1 Para. 2.13	The ANAO recommends that the TGA: ertakes a review of its requests for additional information from rmaceutical companies to identify common omissions from drug luation applications, and determine whether or not the Australian delines for Registration of Drugs should be amended;

end if necessary the Australian Guidelines for Registration of Drugs;

k with the industry to identify ways of reducing the time taken by them to ond to TGA's requests for information; and

report drug approval times to stakeholders, particularly for new chemical entities, in both working day and calendar day formats.

Response: The TGA agrees with the recommendation.

Recommendation No.2 Para. 2.16

The ANAO recommends that the TGA reviews the definition of Category 1 submissions for evaluation to determine the appropriateness of including evaluations of complex new chemical entities in a category with less complex submissions.

Response: The TGA agrees with the recommendation.

Recommendation No.3 Para. 2.27

The ANAO recommends that the TGA reassess current procedures for production of the Australian Drug Evaluation Committee's minutes so as to meet the 20-day time frame recommended in the Baume report and accepted by the Government. Furthermore, TGA should assess when it can actually meet this timeframe.

Response: The TGA agrees to undertake the reassessment and review.

Recommendation No.4 Para. 2.34

In order to improve the effectiveness of drug evaluation, the ANAO recommends that the TGA reviews the number of working days allocated to each phase of the evaluation process, with a view to giving more emphasis to the evaluation of submissions from the pharmaceutical industry.

Response: While ANAO has acknowledged the very good performance of the TGA in contracting the average number of working days to evaluate and approve a New Chemical Entity from 702 days in 1990 to 106 days in 1995, TGA agrees to review the number of working days allocated to each phase of the process.

Recommendation No.5 Para. 2.37

The ANAO recommends that the TGA reviews consultative arrangements with consumer organisations, to ensure that consumer expectations of drug evaluations are given due consideration.

Response: The TGA has agreed to undertake the review.

Recommendation No.6 Para. 2.41

The ANAO recommends that:

- TGA undertakes a review of the Drug Applications for Registration and Tracking (DART) computer system to make it more effective and user friendly; and

the information technology interfacing project be completed in order to achieve integration of the various computer systems operating within the TGA as soon as possible.

Response: The TGA agrees with the recommendation.

Recommendation No.7 Para. 2.44

The ANAO recommends that the TGA brings all computer system user documentation up to date and promulgate this to users so as to improve overall effectiveness.

Response: The TGA agrees with the recommendation.

Recommendation No.8 Para. 2.54

The ANAO recommends that the TGA:

- expand the use of internal audit programs relating to external evaluators to encompass all relevant evaluation sections within the TGA with the objective of using resources more efficiently; and

develop appropriate training programs for external evaluators and incorporate them into operating procedures.

Response: The TGA agrees with the recommendation.

Recommendation No.9 Para. 2.62

The ANAO recommends that the TGA assesses the cost/benefits of a centralised computerised database which reflects current international regulatory information, such as drug evaluation activities, best practice and useful contacts.

Response: The TGA agrees with the recommendation.

Recommendation No.10 Para. 2.68

The ANAO recommends that, in order to use fully the efforts being undertaken by other regulatory bodies and to reduce the costs to Australia for similar evaluations performed overseas, the TGA considers reassessing its requirements to determine if more evaluations, or parts of them, can be accepted from other international regulatory authorities.

Response: The TGA agrees with the recommendation.

Recommendation No.11 Para. 3.8

The ANAO recommends that, in order to improve further the effectiveness of its drug evaluation processes, the TGA reviews:

- its promotion and encouragement of the reporting of adverse drug reactions;
- the dissemination of information on adverse drug reactions to all relevant health professionals; and
    - the adequacy of resource allocation, within the TGA budget, for adverse drug reactions monitoring.

Response: The TGA believes its Adverse Drug Reaction system compares favourably with those of other developed countries but agrees to undertake a review to ensure that it conforms to international best practice.

Recommendation No.12 Para. 3.27

The ANAO recommends that the TGA strengthens its public reporting to better meet the information needs of Parliament and consumers in the interest of enhanced accountability.

Response: The TGA agrees in principle but notes that TGA is not a separate authority and its formal reporting occurs through the Department of Health and Family Services' reports to Parliament.

Recommendation No.13 Para. 4.16

The ANAO recommends that the TGA:

- identifies international pricing structure options with a view to adopting the most cost effective method for use in Australia; and
    - seeks the co-operation of the pharmaceutical companies in assisting TGA to forecast future workloads with a reasonable degree of confidence.

Response: The TGA agrees with the recommendation.

Recommendation No.14 Para 4.23

The ANAO recommends that:

- the TGA, consistent with Government policy, introduces a method of calculating the industry-related costs of its operations to enable it to recover those costs; and
- include in its annual report to Parliament the extent to which its costs were recovered.

Response: The TGA agrees in principle with this recommendation. TGA has already completed an activity based costing of its manufacturer auditing and licensing functions, and studies in other areas (including the DSEB) are either underway or planned for completion before the end of the year.

1. Introduction

This Chapter introduces the Therapeutic Goods Administration. The audit objective and methodology are also discussed.

The Therapeutic Goods Administration (TGA)

1.1. The TGA is a sub-program of the Public Health Division of the Department of Health and Family Services (DHFS). The objective of the sub-program is to ensure the safety, quality and efficacy of therapeutic goods available in Australia at a standard equal to that

of comparable countries, and to ensure that pre-market assessment of therapeutic goods is conducted within a reasonable time frame. With respect to pharmaceutical drugs, the TGA is responsible for their evaluation and approval for use by the public. In 1995-96, the TGA made decisions about 803 prescription drugs.

1.2. The Table below summarises TGA's financial information for 1995-96:

Table 1
Summary Of Financial Information For 1995-96

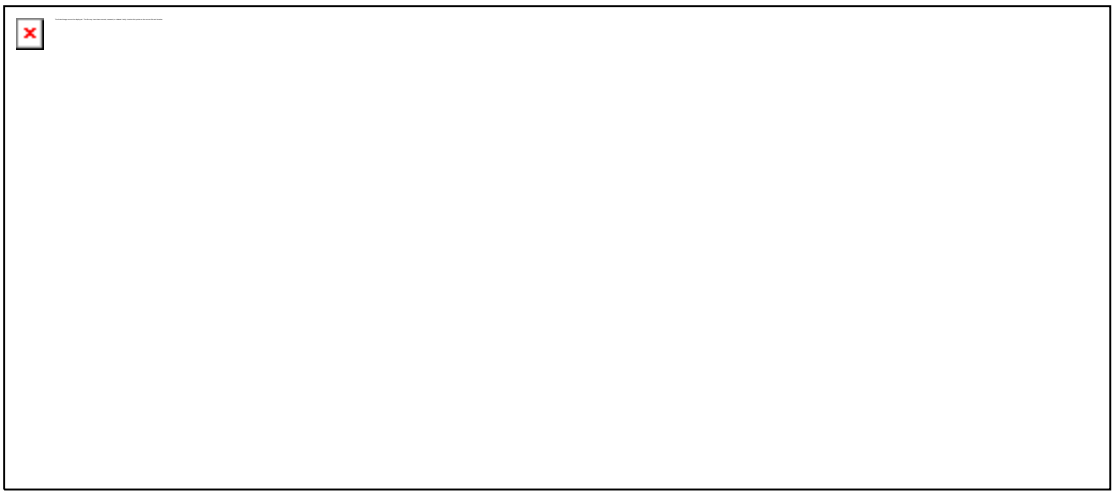
ITEM	$ MILLION
REVENUE	
Annual Appropriations	21.76
Special Appropriation [1]	5.97
Fees from pharmaceutical companies	17.31
TOTAL REVENUE	**45.04**
EXPENSES	**39.64**

1.3. The Government has proposed that, by 1998-99, TGA will recover 75 per cent of its operating costs from industry via fees and charges.

1.4. The TGA's organisational structure is illustrated in the following diagram:

Figure 1

Therapeutic Goods Administration



The Baume Report

1.5. In 1991, the Minister for the Aged, Family and Health Services, stated that:

'The purpose of drug evaluation is to protect the public from unsafe, ineffective and poor quality drugs. However, this needs to be balanced against the public's interest in gaining access to new and possibly life-saving medications. ... Streamlining should be seen as maximising public access to improved drugs in the minimum time ensuring the public interest is paramount in regards to safety, quality and efficacy.' [2]

1.6. In March 1991 the Minister announced an inquiry to seek improvements in Australia's drug evaluation system operating within the TGA. Professor Peter Baume from the University of New South Wales was commissioned in July 1991 to conduct the inquiry. The resultant report was titled *A Question of Balance: Report on the Future of Drug Evaluation in Australia* [3]. The report is referred herein to as *the Baume report.*

1.7. The principal changes proposed in the Baume Report encompassed various aspects of the evaluation and approval process of pharmaceutical drugs. The main theme of the report was the need for the timely availability of drugs to the public by making the review process more efficient within existing resource limits. Major recommendations included:

- restructuring and management of change of the Therapeutic Goods Administration;
- adoption of the European Community (EC) format for drug submissions;
- wider use of overseas data to speed up evaluations; and
- strict timetables for evaluating applications for drug approval.

1.8. Professor Baume concluded that Australia could increase its efficiency in drug evaluation by means of greater use of overseas evaluation reports and cooperative arrangements with other countries. Professor Baume also devoted a section of his report to post-marketing surveillance of pharmaceutical drugs, with suggestions for improvements in reporting of adverse drug reactions.

1.9. The Government accepted all 164 recommendations posed by Professor Baume. The report led to the amendment of the Therapeutic Goods Act to include the timely availability of therapeutic products as a goal, and the introduction of evaluation deadlines in relation to the TGA's activities. If the evaluations are not completed within the required time frame, then the pharmaceutical company which submitted the application for approval of the drug need pay only 75 per cent of the application fee.

1.10. As a result of the Baume report, the TGA management accepted that the organisation must change its culture to achieve these goals. Its Strategic Management Plan for 1994 to 1997 states that:

'In accepting and endorsing the Baume recommendations the Government has recognised that risk management must be accepted as part of the regulatory process.

TGA must develop and accept new administrative policies and procedures which will lower the workload. This will involve trust in, and acceptance of, summary reports and overseas evaluation reports without a need to check everything back to how it used to be done. It will also involve using international standards and harmonisation with other regulatory authorities. Streamlining techniques, especially applied to the lesser tasks, must be incorporated into practice. This will involve the introduction and use of new electronic technologies.

Change of this nature is far more important than structural change. Continued energy must be devoted to cultural change as a first priority.'

Audit objective

1.11. The objective of the audit was to assess the efficiency, effectiveness and accountability of TGA's evaluation and approval of prescription drugs for public use.

1.12. Specifically, the audit reviewed the efficiency and effectiveness of the following areas within the TGA:

- the drug evaluation and approval process;
- information technology systems, i.e. Australian Register of Therapeutic Goods (ARTG) and the Drug Application and Tracking System (DART);
- use of external evaluators;
- the processes around the Australian Drug Evaluation Committee (ADEC) and the Industry/Government Consultative Committee (IGCC);
- cost recovery and fees;
- adverse drug reactions monitoring and reporting; and
- performance information.

Audit methodology

1.13. The ANAO focussed on analysis of the following elements of the regulatory process associated with the evaluation of prescription drugs:

- evaluation;
- administrative effectiveness;
- adverse drug reactions reporting; and
- cost recovery.

1.14. While the audit included reviews of selected operational and administrative aspects of the TGA, it did not seek to assess the technical and scientific processes surrounding drug evaluation. The scope of the audit was contained to the administrative operations performed within the Drug Safety and Evaluation Branch, the Australian Drug Evaluation Committee and the Business and Services Branch of the TGA rather than any processes preceding or succeeding those activities. The audit did not look at processes for non-prescription (over-the-counter) drug products or herbal products, multivitamins, nutritional supplements or other therapeutic products evaluated by the TGA. As part of the audit, criteria were determined to consider how well the TGA was performing evaluations of prescription drugs and the effectiveness of their administrative processes.

1.15. The audit involved:

- documentation and review of the work flows through the TGA, including the Drug Safety and Evaluation Branch (DSEB) which is responsible for evaluation and approval of applications, and post-marketing/adverse drug reaction reports;
- examination of the Australian Register of Therapeutic Goods (ARTG), the entity which enters the approved application onto the Register;
- reviewing the functions of the Australian Drug Evaluation Committee (ADEC) which advises departmental delegates about prospective approvals for registration, and the Industry/Government Consultative Committee (IGCC); and
- interviews of key stakeholders (i.e. industry and industry representatives, consumer groups, medical professionals) in Sydney and Melbourne. These interviews highlighted a number of issues relating to the pre-marketing and post-marketing of registered drugs.

1.16. The audit was conducted in conformance with ANAO Auditing Standards and cost $321 018. Fieldwork was undertaken in 1994 and 1995.

Conclusion

1.17. In relation to the pre-marketing aspects, the ANAO found that the TGA has reduced dramatically the time taken to approve a drug for use. In 1990, the average number of working days required to evaluate and approve a new chemical entity was 702 while in 1995, the average number of working days was 106 -against 255 working days allowed under the legislation. This improvement benefited all stakeholders, including drug consumers and the pharmaceutical companies. Notwithstanding this improvement there was scope for the time taken, particularly in calendar days, to be reduced further, with the assistance of pharmaceutical companies.

1.18. Information technology used by the TGA was not satisfying the needs of users nor were systems adequately integrated. Principal users found a need to use other supporting systems/databases and manual techniques.

1.19. Furthermore, the ANAO concluded that the TGA needs to develop an adequate system to assess the cost of its services to the pharmaceutical industry.

1.20. The TGA also needs to implement changes to improve the low level of reporting of adverse reactions to drugs in Australia.

1.21. Finally, the ANAO concluded that TGA's performance indicators and performance reporting were not adequately informing the Parliament and consumers of its work.

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2. Drug Safety and Evaluation

This Chapter reports on the drug evaluation processes and provides audit observations and recommendations on the TGA's performance. The ANAO found that the TGA had reduced the time frame to complete evaluations since the July 1991 Baume report. The recommendations in this Chapter address how TGA can further streamline its operations.

Drug Safety and Evaluation Branch

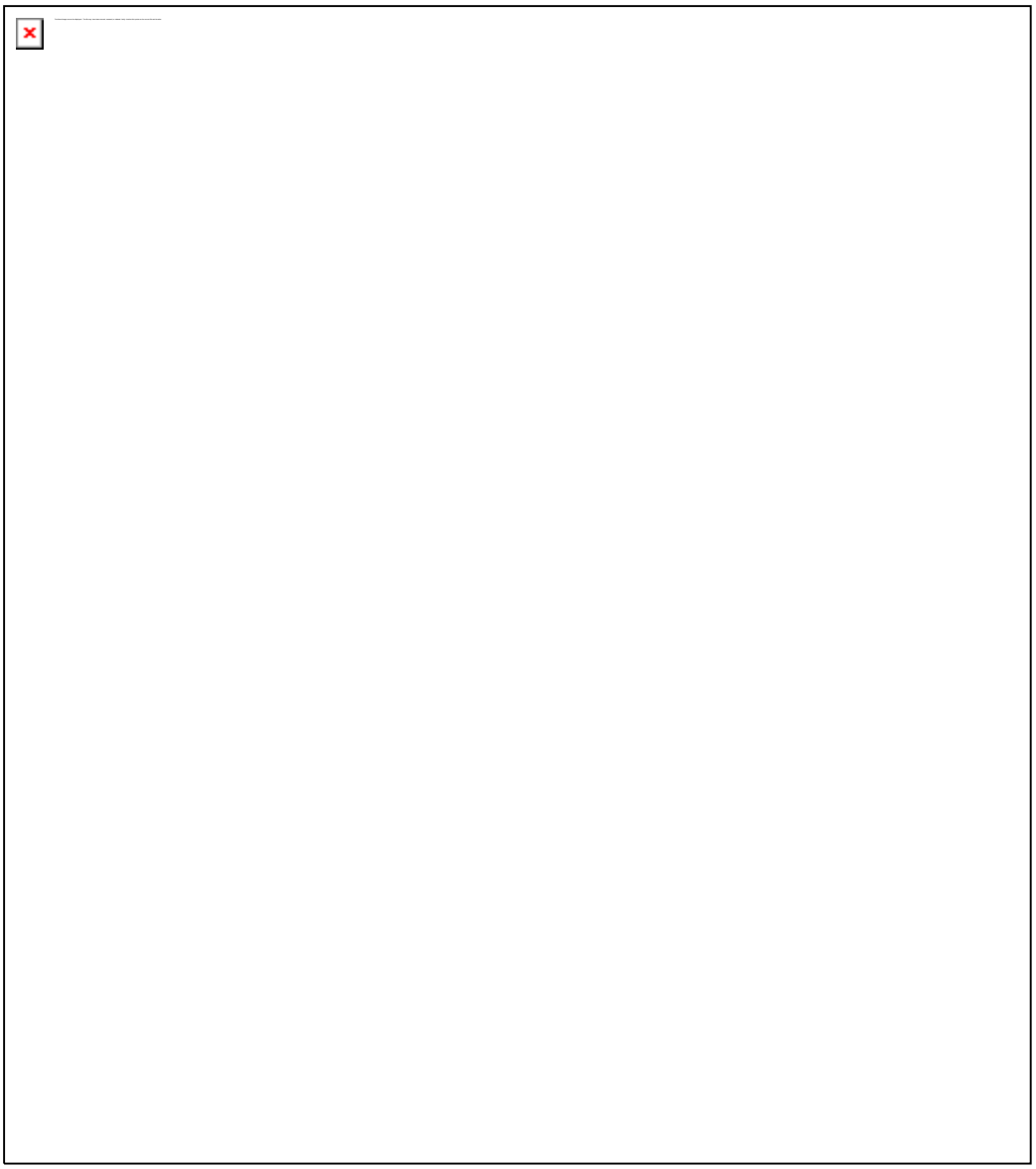
2.1. The TGA's Drug Safety and Evaluation Branch (DSEB) is responsible for the evaluation and registration of prescription drugs. The Branch evaluates, within prescribed time limits, applications for registration from Australian sponsors of new drugs and prescription drugs to ensure that they meet acceptable standards of quality, safety and efficacy. Changes to existing products, such as the updating of product information, are also evaluated and approved.

2.2. Figure 2 shows the movement of the application from the pharmaceutical company sponsor through the DSEB to the delegate's decision and inclusion on the ARTG. Delegations for approving registration of drugs are held by the senior medical officers in the DSEB who decide whether the pharmaceutical product will be included on the ARTG. Time frames to evaluate the various categories of submissions are specified in the Therapeutic Goods Regulations in accordance with recommendations of the Baume Report, i.e:

- category 1 new chemical entities (NCEs), 255 working days;
- category 2 where the evaluation relates to a drug that, in each of two acceptable countries, had been approved for general marketing, 175 working days; and
- category 3 variations to the information on a drug already on the Register, 45 working days.

2.3. Categories 1 and 2 relate to applications for which there needs to be a consideration of clinical and/or toxicology data. That is the differentiating point between Categories 1 and 2 on the one hand and Category 3 on the other. The latter relates solely to chemistry and quality control matters.

Figure 2
Application for registration of a new chemical entity



2.4. The processes from receipt of the application to approval for the drug to be listed on the ARTG are, in summary:

- a pharmaceutical company's application is received with appropriate fee by the TGA;
- a TGA professional officer is assigned the task of examining the application for correct formatting in accordance with the Australian Guidelines for the Registration of Drugs;
- the application is examined by the relevant component evaluators, such as clinical, toxicology and pharmaceutical staff;
- recommendations are made to the evaluation manager by the evaluators;
- a recommendation is made by the Evaluation Manager to the Australian Drug Evaluation Committee (ADEC);
- pre-ADEC response is sought by industry (ten days);

- ADEC examines the submission and recommendations;
- ADEC considers the DSEB recommendations and makes recommendations for approval or rejection to the Minister and the Secretary;
- the TGA delegate (Evaluation Manager) approves the drug for listing on the Register;
- the drug is listed on the ARTG.

2.5. Since the Baume Report, the TGA has increased approvals and decreased rejections of evaluation reports submitted through the ADEC. The role of ADEC is explained later in this Chapter.

2.6. In 1990, the average number of working days to perform an evaluation was 702. This can be compared with an average of 106 working days in 1995 for approving a Category 1 application. The Therapeutic Goods Regulations allow 255 working days to complete a Category 1 approval. This was close to the European Community (EC) standard of 240 days.

2.7. The ANAO testing of Category 1 submissions approved between 1 August 1994 and 1 August 1995 found that 98 per cent of these were completed within the legislated 255 working day time frame, with an average of 106 working days which is equivalent to 258 calendar days. Calendar days can be significantly greater than elapsed days because the count of elapsed days stops whenever TGA requires additional information from a pharmaceutical company.

2.8. The Therapeutic Goods Regulations (section 16A (2)) make allowance for the TGA to query or request information from an applicant or sponsor. The time taken by the applicant or sponsor to respond to the request is outside the time frame in which TGA must complete the evaluation process, in other words the clock is stopped. Only some of the calendar days were weekends or public holidays. A substantial proportion of the calendar days was when industry was gathering more information requested by the TGA.

2.9. ANAO found that 28 per cent of the Category 1 applications approved between August 1994 and August 1995, the sample selected for testing, had taken more than 365 calendar days to be approved.

2.10. Of note is that the cost to the pharmaceutical industry to fully commercialise a new drug is around $200 million. It is in everyone's interest that a drug is approved as soon as possible since the sooner a safe drug is on the market, the sooner patients can use the drug and the sooner the industry starts recouping costs. This is not to suggest that safety aspects should be compromised but simply that the administrative effectiveness of the evaluation process can be improved.

2.11. The ANAO considers that in order to reduce the elapsed time it takes for a drug to be approved, the TGA needs to examine ways to reduce the time taken for industry to respond to TGA requests for more information. The examination could identify areas where efficiencies in time can be realised. Discussions with industry representatives should be included in the review.

2.12. One method, that has been successful overseas, is to have the sponsor provide a presentation before submitting the application to the DSEB. This forum would provide the opportunity for interaction between TGA and industry, and could reduce the need for the TGA to 'stop the clock' later in the evaluation phase.

Recommendation No.1

2.13. The ANAO recommends that the TGA:

- undertakes a review of its requests for additional information from pharmaceutical companies to identify common omissions from drug evaluation applications, and determine whether or not the Australian Guidelines for Registration of Drugs should be amended;
- amend if necessary the Australian Guidelines for Registration of Drugs;
- work with the industry to identify ways of reducing the time taken by them to respond to TGA's requests for information; and
- report drug approval times to stakeholders, particularly for new chemical entities, in both working day and calendar day formats.

TGA response

2.14. The TGA agrees with the recommendation.

New chemical entities

2.15. As mentioned earlier, ANAO testing of Category 1 submissions approved between 1 August 1994 and 1 August 1995 revealed the norm for completing evaluations to be 106 working days compared to the 255 days allowed under the legislation. This is because there are submissions received under Category 1 that do not require anywhere near the maximum amount of evaluation time required by the more complex new chemical entities. TGA's performance reports reflect these figures and could be misleading to readers. However, the ANAO considers that, although it was legitimate to include the 'simple' or less complex submissions in the category, the legislated time frame for completing these submissions could be set lower having regard to TGA's performance.

Recommendation No.2

2.16. The ANAO recommends that the TGA reviews the definition of Category 1 submissions for evaluation to determine the appropriateness of including evaluations of complex new chemical entities in a category with less complex submissions.

TGA response

2.17. The TGA agrees with the recommendation.

Australian Drug Evaluation Committee

2.18. In the wake of the thalidomide tragedy, the Australian Drug Evaluation Committee (ADEC) was formed in 1963 to advise the then Minister for Health on matters relating to the safety of therapeutic substances.

2.19. The ADEC was established by Regulation 36 of the Therapeutic Goods Regulations. ADEC presently comprises 25 members with 6 or 7 core members and at least 10 and not more than 20 associate members. As core members, at least three are medical practitioners eminent in the medical profession, and at least two of these are specialists in clinical medicine. There must be at least one person who is a pharmacologist or holds qualifications in pharmaceutical science. Associate members must include at

least one pharmaceutical chemist, one toxicologist, and a medical practitioner currently engaged in general practice; and other medical practitioners with specialist qualifications in a field of medicine that complement the expertise of core members with medical qualifications.

2.20. The functions of the ADEC as defined in the Regulations are to:

(a) make medical and scientific evaluations of any drugs that the Minister or the Secretary of DHFS refers to it for evaluation;

(b) make medical and scientific evaluations of other drugs if, in the opinion of the Committee, it is desirable that it should do so;

(c) make medical and scientific evaluations of such therapeutic devices that the Minister or the Secretary refers to it for evaluation;

(d) advise the Minister or the Secretary on the importation into, the exportation from and the manufacture and distribution within Australia of therapeutic goods that have been the subject of evaluation by the Committee; and

(e) provide advice similar to that given to the Minister or the Secretary under paragraph (d) to persons or bodies as the Minister may direct.

2.21. The ADEC is able to appoint sub-committees to inquire into any matter within its function. There are presently three such sub-committees:

- Adverse Drug Reactions Advisory Committee (ADRAC);
- Pharmaceutical Committee; and
- Sub-Committee on Emerging and Niche Drugs.

2.22. The ADEC currently has two working parties which have a finite life and are established for specific projects:

- the Medicines and Pregnancy working party; and
- the working party on Registration of Drugs in Children.

2.23. The ADEC meets every eight weeks and resolutions that flow from the meetings are used by the delegates in the TGA in approving drugs for registration.

2.24. Professor Baume considered that 'A summary record of action to be undertaken is essential to allow efficient management of follow-up tasks, particularly where the formal minutes of meetings are 60-100 pages in length.' [4] Notwithstanding this, as the resolutions from the ADEC are such an important step in the approval process, Professor Baume recommended that full minutes of each ADEC meeting be available within 20 working days of the meeting, and should contain a clear summary of action required.

2.25. The ANAO appreciates that there is a requirement for detailed minutes to be produced to enable the ADEC to support its decisions and to make recommendations. TGA advised that its delegates are presented with detailed ratified recommendations (resolutions) from the Committee on or about day six after the ADEC meetings. The detailed minutes are sent to many bodies such as State Health Departments, the Pharmaceutical Benefits Branch and the Drugs and Poison Schedule Committee. They are also sent to approximately forty-five countries, and there are

indications that they are highly valued.

2.26. While the ANAO was advised that the delays were due to a lack of adequate resources, the ANAO considers that there may be other avenues that the TGA should consider in producing appropriate and timely minutes, such as employment of contractors.

Recommendation No.3

2.27. The ANAO recommends that the TGA reassess current procedures for production of the Australian Drug Evaluation Committee's minutes so as to meet the 20-day time frame recommended in the Baume report and accepted by the Government. Furthermore, TGA should assess when it can actually meet this time frame.

TGA response

2.28. The TGA agrees to undertake the reassessment and review.

2.29. The evaluation process in the DSEB is undertaken in a number of different phases, each of which is allocated a certain number of days: for example, as indicated earlier, evaluations of new chemical entities (NCEs) must be completed within 255 working days. This is disaggregated as follows:

- 135 days for evaluation;
- 80 days for ADEC; and
- 40 days for the delegate's decision.

2.30. These periods were established after the Baume report in 1991 and the TGA has been operating to them since then. The ADEC process consumes 31 per cent of the process; whereas the evaluation process has been allocated 53 per cent with the delegates' decision taking 16 per cent balance of time.

2.31. The figure of 80 days for ADEC represents a maximum figure, as would occur if the evaluation reports for a Category 1 product were available on the day after the closing date for an ADEC meeting, (i.e. they would need to wait to go to the next ADEC meeting). In fact, it is usual that fewer days are taken by the ADEC process and these days are already available and, on occasions, used for the evaluation phase.

2.32. The ANAO considers that the evaluation process should be allocated the optimum amount of time, and suggests that the TGA should review the times allocated to each step in the process to ensure that they are appropriate.

2.33. The ANAO suggests that the TGA considers having eight or ten ADEC meetings a year rather than the six as at present in order to reduce the time between meetings and potentially the time taken to complete the evaluation processes.

Recommendation No.4

2.34. In order to improve the effectiveness of drug evaluation, the ANAO recommends that the TGA reviews the number of working days allocated to each phase of the evaluation process, with a view to giving more emphasis to the evaluation of submissions from the pharmaceutical industry.

TGA response

2.35. While ANAO has acknowledged the very good performance of the TGA in contracting the average number of working days to evaluate and approve a New Chemical Entity from 702 days in 1990 to 106 days in 1995, TGA agrees to review the number of working days allocated to each phase of the process.

2.36. A number of stakeholders expressed concern that appropriate consumer organisations were not allowed to attend ADEC meetings. There was a feeling that they should at least have observer status. In the USA, consumer organisations have an opportunity to put their case before the Food and Drug Administration, albeit at a different time from when the relevant committee discusses the application and makes a final decision. While the ANAO does not believe that the TGA should necessarily adopt the USA model, the TGA, in the interests of accountability, may wish to consider making the meetings more open to relevant consumer organisations. Or, if this course is not appropriate, the TGA should strengthen consultative arrangements with appropriate consumer organisations.

Recommendation No.5

2.37. The ANAO recommends that the TGA reviews consultative arrangements with consumer organisations, to ensure that consumer expectations of drug evaluations are given due consideration.

TGA response

2.38. The TGA has agreed to undertake the review.

2.39. The ANAO further suggests that the TGA monitor the incidence of evaluations being sent to the ADEC more than once, and introduce procedures whereby evaluations are only formally considered by the ADEC on the one occasion, except where there is a special reason for the evaluation to be reconsidered by ADEC.

Information technology

2.40. Information technology is integral to TGA's operations. During the audit, the ANAO observed functions and practices associated with the Drug Applications for Registration and Tracking System (DART) and the Australian Register of Therapeutic Goods (ARTG). The ANAO found that:

- TGA's IT systems were not considered efficient, effective or user-friendly by the users: for example, principal system users used supporting systems/databases and manual techniques other than the standard applications because the latter did not meet their needs;
- the principal systems used by the TGA, ie, the DART, ARTG and ADRS, were not integrated; and
- TGA terminated a review of the efficiency of interfacing systems at the TGA.

Recommendation No.6

2.41. The ANAO recommends that:

- TGA undertakes a review of the Drug Applications for Registration and Tracking

(DART) computer system to make it more effective and user friendly; and

- the information technology interfacing project be completed in order to achieve integration of the various computer systems operating within the TGA as soon as possible.

TGA response

2.42. The TGA agrees with the recommendation.

2.43. The ANAO found that procedures associated with the drug evaluation and adverse drug reactions (ADR) processes were not necessarily systemic. The deficiencies included a lack of internal documentation of administrative operating procedures, which were current, written, standard and consolidated with automated access. User documentation supporting IT systems (eg., DART System, ADRS, ARTG) was incomplete, outdated or non-existent.

Recommendation No.7

2.44. The ANAO recommends that the TGA brings all computer system user documentation up to date and promulgate this to users so as to improve overall effectiveness.

TGA Response

2.45. The TGA agrees with the recommendation.

External evaluators

2.46. The ANAO noted that TGA in 1994-95 collected $12.7 million or 27 per cent more than the Budget estimate of $10.6 million. The main source of the extra revenue was from an increased number of applications for registration of drugs. With constant staff levels the TGA, and in particular the DSEB, found it difficult to process the additional workload within the legislated time frames.

2.47. In an effort to overcome these problems TGA used external evaluators to supplement DSEB's staff resources.

2.48. Professor Baume reported that:

'While external evaluators have primarily been recruited to overcome person shortages within the TGA, the practice is a highly desirable one and is a useful strategy for improving the quality of evaluations, maintaining professional standards and important in the strategic development of a regulatory professional status for professional people working within the TGA and outside.' [5]

2.49. Although external evaluators are used by the TGA to assist with evaluations, the quality of reports by external evaluators was found to be variable. This meant that certain areas of the DSEB saw a need to evaluate the evaluations.

2.50. The ANAO found that the training of external evaluators was almost non-existent, but noted that the Pharmaceutical Chemistry Evaluation Section provides regular feedback to the external evaluators it uses.

2.51. The ANAO noted that the Pharmaceutical Chemistry Evaluation Section in the DSEB introduced an audit program to examine evaluations undertaken by external evaluators. The section does not cross check all externally generated evaluations against the data submitted except according to the

predetermined audit frequency. Notwithstanding, although the ANAO had not tested that approach, this practice should provide an efficient basis for internal and external drug evaluation.

2.52. The TGA advises that the Pharmaceutical Chemistry Evaluation Section has chosen to follow a generally standard format and reports are much briefer than toxicology or clinical evaluations. This more readily lends itself to the use of audit programs.

2.53. The Pharmaceutical Section has developed operating procedures to standardise its approach to evaluations. The ANAO considered that the operating procedures were sound and should be formally developed and used throughout the DSEB.

Recommendation No.8

2.54. The ANAO recommends that the TGA:

- expand the use of internal audit programs relating to external evaluators to encompass all relevant evaluation sections within the TGA with the objective of using resources more efficiently; and
- develop appropriate training programs for external evaluators and incorporate them into operating procedures.

TGA response

2.55. The TGA agrees with the recommendation.

International cooperation

2.56. Professor Baume considered that Australia needed to maintain its sovereign decision making capacity, but that there were opportunities to streamline the drug evaluation process by harmonising data requirements and cooperating in the evaluation process with other countries. Professor Baume defined the advantages of harmonisation/cooperation as:

- a reduction in the costs of regulation, including costs to the sponsor in the preparation of applications and costs of the evaluation process itself;
- a reduction in the time involved in regulation with no loss of safety, so that important new therapies were made available to consumers more quickly;
- access to overseas expertise in the newer areas of therapeutics, eg., biotechnology, where Australian expertise might be scarce; and
- access to new ideas as to how evaluation processes can be improved.

2.57. Professor Baume also identified a number of difficulties, including:

'There are some areas in which unique Australian requirements are justified, e.g. Australia's harsh climatic conditions mean that we need access to stability data on pharmaceutical products in excess of normal overseas requirements.

...it is necessary to exercise caution in using overseas evaluation reports of products sponsored by local companies.

Language barriers present a potential problem but most regulatory agencies with which Australia is likely to enter into any agreement use English as their reporting language.

It is important to ensure, in using an overseas evaluation report, that the report is based on the same data that have been presented to the Australian agency. It is not uncommon, for example, for a drug to be marketed in various formulations of a particular dosage form throughout the world and for evaluation in different countries to be carried out on different strengths or different forms of a drug.

There are difficulties in identifying suitable agencies with similar standards to ours. Time is required for the building of mutual confidence in each other's agencies and processes and in this respect regular staff exchange could be of enormous benefit. Assessments need to be standardised and it will be necessary to audit regularly those agencies with which reciprocal agreements are reached.

It is necessary to ensure that in any scheme of mutual recognition, particularly one involving more than two agencies, standards are not reduced to some lowest common denominator. Australia's high standards of regulation must not be rendered unsatisfactory by harmonisation, although there may be instances where Australia's standards are unnecessarily high and some adjustment could be beneficial.' [6]

2.58. The scope of the audit did not extend to an examination of other regulatory authorities. However, research undertaken during the audit suggested that evaluation practices, procedures and standards operating in a number of countries aligned with those operating in Australia.

2.59. The TGA has cooperated with similar bodies overseas in regard to regulatory standards and practices. The following are examples of particular relevance:

- participation as a member of the Pharmaceutical Evaluation Report (PER) Scheme. This is for the mutual recognition of evaluation reports on pharmaceutical products, and involves exchanging assessment reports with 15 European countries, Canada and South Africa;

- acceptance of evaluation reports from the US, the UK, Canada, Sweden and the Netherlands;
- adoption of European Community (EC) format for drug submissions;
- participation in continuing negotiations with the proposed European Union Mutual Recognition Agreement and the Trans-Tasman Mutual Recognition Arrangement; and
- participation in international regulatory conferences, including the International Conference on Harmonisation (ICH) meeting in Brussels in 1991 and in Orlando in 1993, where the development and adoption of harmonised guidelines were discussed in detail. Also, most recently, TGA participated in the Association of Regulatory and Clinical Scientists (ARCS), and in the International Conference on National Medicinal Drug Policies (sponsored by the Australian Government and the World Health Organisation).

2.60. In May 1996 a conference was held in Canberra on International Regulatory Trends in the Pharmaceutical Industry. Of particular interest was the support and participation from both the TGA and its USA counterpart, the Food and Drug Administration. A conference theme was that there is a trend towards global regulation of good manufacturing practices of pharmaceutical products.

2.61. It is important that the TGA responds appropriately to international trends in drug evaluation. To assist the TGA a formal internal knowledge base of current, global regulatory information on the structure and administration of other regulatory authorities or the evaluation practices in other countries could be maintained. While certain international standards could be provided informally by particular individuals at the TGA, the ANAO could not find any evidence where global information was disseminated throughout the organisation. Availability of such information would assist the TGA to perform its responsibilities in an even more consistent and efficient manner.

Recommendation No.9

2.62. The ANAO recommends that the TGA assesses the cost/benefits of a centralised computerised database which reflects current international regulatory information, such as drug evaluation activities, best practice and useful contacts.

TGA response

2.63. The TGA agrees with the recommendation.

Low number of sponsor applications with international reports

2.64. The ANAO examined relative performance statistics to determine whether or not the TGA was using international reports to speed up the evaluation process, as advocated by Professor Baume. The ANAO found that the number of sponsor applications mentioning international evaluation reports was low.

2.65. Performance statistics show minimal and decreasing exchanges of international evaluation reports during the evaluation process.

2.66. During the first half of 1994-95, the TGA received only one Category 2 submission (see paragraph 2.2), compared with 156 Category 1 submissions during the same period. The underlying reason for the low return was that Category 2s must reflect those applications for drugs with the same formulation, dosage and indications in two acceptable countries and for which two independent evaluation reports were available. Because drug applications falling within Category 2 were evaluated overseas before submission to the TGA, the target duration of the regulatory process was 175 working days compared with 255 working days for Category 1s.

2.67. It is difficult for sponsors to comply with Category 2 requirements, particularly the requirement that the application must have been accepted by two countries recognised by the TGA. A major problem is that by the time two other countries have undertaken and accepted the application, the time difference between a category 1 and 2, ie, 80 working days, would have been exceeded. Sponsors may as well have submitted their proposal as a Category 1 application. It is also difficult for sponsors to obtain evaluation reports from some countries.

Recommendation No.10

2.68. The ANAO recommends that, in order to use fully the efforts being undertaken by other regulatory bodies and to reduce the costs to Australia for similar evaluations performed overseas, the TGA considers reassessing its requirements to determine if more evaluations, or parts of them, can be accepted from other international regulatory authorities.

TGA response

2.69. The TGA agrees with the recommendation.

Risk management

2.70. The ANAO Audit Report No. 12 1995-96 recently examined Commonwealth consumer product safety regulators and the TGA was one of the agencies examined. That audit addressed a 'whole of agency' approach to risk management, as advocated by the Management Advisory Board/Management Improvement Advisory Committee (MAB/MIAC). This MAB/MIAC approach involves risk management being systematically applied to all organisations and to all functions and activities within an organisation; with the approach being integral to the agency achieving its goals and objectives.

2.71. In relation to the TGA that audit found:

'The TGA has adopted risk management in relation to surveillance and investigation activities and problem reporting schemes. But it has not adopted structured risk management in relation to other post-market regulatory activities reviewed. A "whole of agency" approach to risk management has not been adopted.' (page 16).

2.72. The audit recommended that the agencies'... adopt and use a structured "whole of agency" strategically-based risk management approach, involving a systematic, data driven approach to identifying, analysing and ranking risks, and assessing treatment options.' (page 16).

2.73. The TGA agreed with the recommendation. A risk management approach to its operations has been sanctioned by management through its 1994 to 1997 Strategic Plan as follows:

'TGA must adopt a risk management approach in the interest of efficiency and in the streamlining of operations to work within available resources. The Baume report highlighted the reform required to streamline the evaluation and related processes within the Drug Evaluation Branch; this attitude must be adopted across all of TGA.

In adopting the Baume report the Government has adopted as a policy the risk management approach to drug evaluation and, by reference, to the overall operations of TGA. This means that TGA must streamline its operation to the maximum while maintaining a high level of effectiveness to ensure the quality of our work and the quality, safety, efficacy and availability of therapeutic goods in Australia.

The TGA management will encourage staff to streamline all operations and will inform the Departmental Executive and Minister's Office of the approaches being taken. The organisation as a whole must accept that risk management could lead to some unforeseen dangers but these will hopefully be identified with experience and through good post-marketing surveillance.'

2.74. TGA has advised that pre-market assessment procedures are intended to identify potentially high-risk therapeutic goods, such as prescription pharmaceuticals. For products identified to be of lower risk, less rigorous assessment is conducted in the pre-marketing phase for all therapeutic products.

2.75. TGA's strategy for risk assessment of evaluating prescription pharmaceuticals is based on perceived risk, scientific and other relevant data and actual risk if known, e.g. experience with the product marketed elsewhere. The full extent of actual risk may not be apparent until the product has been in the market for some time and post-market monitoring plays a part in quantifying this risk.

2.76. Chapter 3 identifies some potential problems in the post-marketing surveillance of drugs. In the light of this and the observations of ANAO Audit Report No. 12, the ANAO endorses the moves by the TGA to introduce risk management practices into its operations. Periodic monitoring of operations, to ensure that

they are adapted to reflect changes in the working environment, should form a part of the risk management process.

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nitoring and Accountability

apter examines how the TGA monitors the success of the evaluation processes. The Chapter also looks at eporting mechanisms to satisfy stakeholders' expectations.

arketing surveillance of registered drugs

Post-marketing surveillance of drugs occurs mainly through the reporting of adverse drug reactions (ADRs). number of Adverse Drug Reactions to drugs approved by the TGA is a basis for assessing the success of the g evaluations process within the TGA. A small number of adverse drug reactions would suggest a robust pre-keting drug evaluation regime.

A World Health Organisation (WHO) international drug monitoring project, the WHO Adverse Reaction nitoring Scheme, was established in 1968 for the purpose of identifying rare serious reactions by pooling of rnational data. Twenty-seven countries participate in the program, of which Australia is one. Adverse drug orting in Australia is voluntary, while other countries such as France and Sweden have a mandatory reporting em.

Within the TGA there is an Adverse Drug Evaluation Section responsible for reporting ADRs to an ADEC -committee, the Adverse Drug Reaction Advisory Committee (ADRAC).

The ANAO observed that:

- the methods of monitoring and detecting ADRs through trend analysis were difficult due to deficiencies with the Adverse Drug Reaction System (ADRS): for example, it was not possible:
  - ☐ to produce a trends analysis on the different classes of drugs over time;
  - ☐ to produce the most recent necessary reports in order to identify any trends on reactions to a specific drug; and
  - ☐ to list all those adverse reactions in the last month.

3.5. These deficiencies led to greater reliance on elaborate, manual techniques.

3.6. The ANAO also noted that:

- the extent and effectiveness of reporting ADRs including by drug manufacturers was uneven, leading to doubts over the reliability of reporting and whether safety has been compromised.
  - The reporting and tracking of ADR by the TGA was slow: for example, it takes about six weeks for TGA to enter data from a card received by TGA advising of an ADR.
  - It is generally accepted that reporting of ADRs is low in Australia. If the TGA could ascertain the reasons for the low or variable reporting in Australia it would be able to target an education strategy. Notwithstanding this, TGA affirmed that there was no evidence to suggest that under reporting has led to significant problems, such as the

failure to identify important drug safety signals.

- Photocopies of individual, originating ADR reports, rather than computerised summaries, are directed to committee members for further checks at the regular ADRAC meetings. There are approximately 1000 reports per meeting every six weeks. Each member has access to all reports but individually they are only required to look at around 200. This situation indicates a deficiency with the ADRS in its ability to summarise automatically the necessary information and the need to streamline the process.

- Pharmacoepidemiological research is used to determine the nature and extent of risk of a drug. This research is important because it can identify the incidence of ADRs and causes of reactions, and detect diseases such as cancer that may occur from long-term ADRs. An active role and future direction for the TGA in pharmacoepidemiological research has not been defined. In the ANAO's view, greater emphasis should be placed on the importance of pharmacoepidemiological research and long-term studies into the effects of drugs, the incidents and causes of reactions and long-term diseases. Professor Baume recommended that ADRAC be supported by a budget to enable it to commission a small number of necessary studies of this kind to determine the nature and extent of risk of some drugs. There has only been one recent study of the kind he recommended, and financial support appeared to be insufficient for valid and credible research. The prospect of financing this function by industry could be considered as a way of implementing the Government's acceptance of Professor Baume's recommendations on a resource neutral basis.

- Professor Baume recommended that:

  - *'...a scale, relating ADR reports to the level of use, should be designed in concert with industry'*. This was to assist the quantification of risk for drugs considered by the ADRAC to pose a significant public health risk. After discussing the issue at a number of meetings, the ADRAC concluded that such a scale was not appropriate or feasible;

  - *'From 1 July 1992, the consumer education program,...should include a component on how consumers can assist their practitioners to report ADRs through the existing voluntary reporting system.'* A four point plan was developed and presented to ADRAC. Three of the points have been implemented while the final point is being addressed;

- Baume generally supported the exclusion of consumers from making direct reports to the TGA because this was*'...not an efficient means of collecting the technical, medical data needed to identify ADRs'*. He recommended that consumers be educated to assist their practitioners to report ADRs, and that information be distributed to consumers through pharmacies. This recommendation appears not to have been implemented.

3.7. The TGA distributes the Adverse Drug Reactions Bulletin to health professionals, and safety-related issues are reported to the community through mechanisms such as the Bulletin of Australian Recalls and Corrections.

Recommendation No.11

3.8. The ANAO recommends that, in order to improve further the effectiveness of its drug

evaluation processes, the TGA reviews:

- its promotion and encouragement of the reporting of adverse drug reactions;
- the dissemination of information on adverse drug reactions to all relevant health professionals; and
- the adequacy of resource allocation, within the TGA budget, for adverse drug reactions monitoring.

TGA response

3.9. The TGA believes its Adverse Drug Reaction system compares favourably with those of other developed countries but agrees to undertake a review to ensure that it conforms to international best practice.

Performance reporting

Requirements for performance reporting

3.10. The requirements for departmental reports, issued by the Department of Prime Minister and Cabinet and approved by the Parliamentary Joint Committee of Public Accounts, state that the principal formal accountability mechanisms to the Parliament are:

- annual reports;
- Portfolio Budget Statements; and
- Portfolio Additional Estimates Statements.

3.11. The annual reporting requirements were designed to emphasise program performance, the achievement of program objectives and to focus on results. Recently the requirements were amended such that departments and agencies now only need to provide details of their most significant developments. The Parliament, however, is to be provided with sufficient information to allow it to make an informed judgment about a department's or agency's performance.

3.12. As well as the formal requirement to report program objectives and results to the Parliament, TGA has a responsibility to report to its clients and stakeholders. These include the pharmaceutical industry, the Government, drug consumers and the public. The TGA's Strategic Management Plan for 1994 - 1997 specifically mentions performance reporting and gives a commitment to inform stakeholders of TGA's progress in meeting their expectations, as follows:

'The program performance statement at the Departmental level will serve the government, industry, consumers and the international community and inform them of our progress in meeting their expectations.'

3.13. The expectations of the client groups as set out in the TGA Strategic Plan are as follows:

'Government

- assurance of safety of goods on the market
- minimum delay in approval of goods

- technical advice and information
- a well managed regulatory control authority
- demonstrable cost benefit

Industry

- justification of regulations
- minimum interference in commerce
- cost-effective regulatory operations
- consistency of application of legislation
- identification and development of areas for co-regulation with industry
- facilitation of the export of therapeutic goods from Australia

Consumers, including health providers

- timely availability of necessary goods
- goods that are safe
- goods that are effective
- accurate advice to consumers
- the international community
- co-operation between control authorities
- shared regulatory information
- contribution to technical aspects of regulation
- harmonisation of regulations
- optimal access to international markets through both import and export.'

3.14. TGA's Strategic Plan commits it to reporting stakeholders' expectations in the Portfolio Budget Statements (PBS). However, only Budget initiatives and significant changes in appropriations are now included in the PBS. Therefore it is important for the TGA to review its reports to stakeholders in order to reflect their expectations.

3.15. Performance information should be provided to all stakeholders on a regular basis, in accordance with TGA's Strategic Plan.

Reporting by the Therapeutic Goods Administration

3.16. The ANAO looked at the relevance and validity of the data produced by the DART system and examined numerous publications, both Australian and overseas, to determine the extent of TGA's

reporting.

3.17. The ANAO examined the TGA's annual reports from 1992 to 1995, the TGA News for 1990 to 1995, the Australian Prescriber from 1992 to 1995, the US Regulatory Reporter from 1994 to 1995, the Regulatory Affairs Journal from 1991 to 1995 (produced in the UK), and other publications either produced or contributed to by the TGA, to ascertain the extent of performance reporting. The ANAO found limited reporting of TGA's performance that would satisfy its stakeholders as envisaged in their Strategic Plan. An example can be found in the annual report for 1994-95. While the TGA is complying with the reporting requirements with respect to coverage the ANAO is of the opinion that some of the information can be misleading to the reader. Following are two examples taken from the 1994-95 annual report:

- *'all deadlines have been met for decisions on prescription drugs'* (page 52)
- *'the adverse drug reactions section receives between 600 and 700 reports of adverse reactions to drug products each month'* (page 54)

3.18. While the first dot point is a true statement, figures extracted during the audit revealed that the average time taken to evaluate a Category 1 (NCE) was around 106 working days against a target of 255. Chapter 2 commented that the ANAO considered that the time frames were conservative in certain instances.

3.19. The second dot point is also true. However, it does not, in the ANAO's opinion, go far enough or provide an explanation as to what the figures mean as suggested in paragraph 3.6.

3.20. The TGA each quarter produces 32 different performance reports, using its DART system. The reports are primarily used by the TGA in presenting performance data to the Industry/Government Consultative Committee (IGCC) which meets twice yearly. The reports provide detailed performance information on TGA's operations expressed in working days, and include the Registration of Prescription Drugs (Report 1), and the Listing of Drugs for Supply in Australia (Report 8). (A full list of the Reports produced is at Appendix 1.) The IGCC comprises the Departments of Industry, Science and Tourism, and the Department of Finance, as well as the four peak industry associations (APMA, PMAA, NFA, MIAA).

3.21. The ANAO examined the reports and found that they were a very good source of information; enabling industry to assess TGA's performance and to gain an appreciation of the varying workloads that occurred from one period to another. By providing the reports to the IGCC, TGA was partly satisfying its responsibilities to the pharmaceutical industry. The ANAO considered that the TGA could produce a summary or abridged version of its quarterly reports that could be used by all stakeholders to provide details of their performance.

Key performance indicators

3.22. The ANAO suggests that a shortened version of reporting, such as in TGA's Program Performance Statements (PPS) prepared for the Senate Estimates Committees in 1992-93, would provide appropriate and relevant information for stakeholders. In subsequent years the information was not, in the ANAO's opinion, as informative. The information in the 1992-93 PPS was reported at a higher level than TGA's current performance reports. In 1992-93, TGA's performance outcomes were reported against seven indicators, as follows:

- Indicator 1 The number of new therapeutic products judged to be safe, efficacious and of appropriate quality reaching the community, the total number of goods assessed with the

level of assessment being linked with the potential risk of the goods

- Indicator 2 Time taken to evaluate new products
- Indicator 3 Level of compliance by manufacturers of therapeutic products with good manufacturing practice
- Indicator 4 Level of coverage achieved in testing products in the market place
- Indicator 5 The number of harmful or sub-standard products found to have reached the Australian population
- Indicator 6 Provision of information and assistance
- Indicator 7 Level of international co-operation in regulation

3.23. The indicators are reflected in the reports provided to the IGCC but are not easily identifiable. The seven mentioned above are the key indicators that allow stakeholders to assess TGA's performance. In the ANAO's view this level of reporting is easier to understand, succinct and relevant.

3.24. The ANAO considered that the TGA's performance information should be reported in such a way that it reaches the majority of stakeholders, for example, in professional journals.

3.25. The TGA advised that a set of outcomes based performance indicators for TGA relating to efficiency, effectiveness and quality devised in the latter part of 1995 to meet departmental reporting requirements was accepted by the Department of Finance. These indicators were reported in the Department of Health and Family Service's annual report. For 1996-97, an indicator relating to equity has been added.

3.26. The ANAO considered also that information to allow clients to compare the performance of the TGA over a period of time should be included as a matter of course. Generally, TGA's stakeholders, such as drug consumers, were unaware that the delay in a drug being approved could be related to the time a pharmaceutical company took to respond to requests for additional information. The ANAO considers that TGA should be relaying details of times taken by all parties to stakeholders, and promoting the fact that it performed within legislated time frames.

Recommendation No.12

3.27. The ANAO recommends that the TGA strengthens its public reporting to better meet the information needs of Parliament and consumers in the interests of enhanced accountability.

TGA response

3.28. The TGA agrees in principle but notes that TGA is not a separate authority and its formal reporting occurs through the Department of Health and Family Services' reports to Parliament.

4. Cost Recovery and Fees

This Chapter reviews the fees and charges imposed by the TGA, the methods for calculating them and the recovery of industry related costs from the pharmaceutical companies.

Cost recovery and fees

4.1. At the time of the Baume review, the TGA complained that a lack of resources had contributed to a considerable backlog in evaluations. Among other things, Professor Baume proposed that the TGA implement the recommendations from his review in a way which would be cost neutral to government. One way of achieving this was to increase the fees industry paid for TGA's services. Professor Baume recommended that they be increased by 20 percent on those current at the time, i.e. July 1991.

4.2. The ANAO charted TGA's budget allocations, outlays and revenue for the period from the Baume report, namely from 1990-91 to 1995-96. The ANAO found that TGA operated in a cost neutral way to government. Table 2 below reveals that there had been a reduction, in real terms, of the cost to the Government in running the TGA since the Baume report. The main reason was that pharmaceutical companies were contributing a higher percentage of TGA's costs.

4.3. Professor Baume also reported:

'Industry agreed to the introduction of fees because it understood that the TGA was unable, with its existing staff levels and resources, to provide a reasonable service or to remove or reduce the delay in evaluations. The agreement with the therapeutic goods industry is for 50% cost recovery of all TGA activities (ie, not limited to those identified as services to industry). It is therefore reasonable for industry to expect that it will get the improved service for which it is paying.' [7]

4.4. As mentioned earlier, the cost to the pharmaceutical industry to fully commercialise a new drug is around $200 million. Any means of hastening the evaluation process, even if there were a small charge for the service, would serve TGA's stakeholders, ie, industry and consumers.

4.5. As described in Chapter 2, TGA's performance to process a submission for a new chemical entity has increased dramatically, with a decrease from an average of 702 working days (pre-Baume) to an average of 106 working days (at the time of the audit). The ANAO noted that this improvement was accompanied by an increase in industry fees and charges.

Table 2
Comparison of Appropriations and Running Costs for TGA 1990-91 to 1995-96 [8]

ITEM	1990-91 $m	1991-92 $m	1992-93 $m	1993-94 $m	1994-95 $m	1995-96 $m
REVENUE						
Annual Appropriation	27.85	19.96	26.58	21.33	21.37	21.76
Sub-total	**27.85**	**19.96**	**26.58**	**21.33**	**21.37**	**21.76**
Fees received from industry [9]	-.02	8.46 2.37	8.21 2.69	8.83 3.56	12.16 4.76	17.31 5.97
priation [10]						

TOTAL REVENUE	**27.87**	**30.79**	**37.48**	**33.72**	**38.29**	**45.04**
EXPENDITURE						
Salaries	12.39	15.99	17.07	17.46	18.18	22.58
General Administration	8.25	14.92	15.62	15.05	16.00	17.06
TOTAL EXPENDITURE	**20.64**	**30.91**	**32.69**	**32.51**	**34.18**	**39.64**

4.6. 1991-92 was the first year TGA was to recover 50 per cent of its costs from industry. However, substantially less than the expected $17 million was collected. The TGA provided a number of reasons for the poor performance:

- the introduction of the fees and charges;
- the recession;
- poor initial estimates of the units of work to be undertaken; and
- the initial setting of the fees and charges was too low.

4.7. The TGA realised that in order to achieve a 50 per cent recovery rate from the pharmaceutical industry, there would need to be substantial rises in some base charges. As a result of concerns raised by industry and after considerable discussion between the Departments of Health, Prime Minister and Cabinet, Finance, Industry, Technology and Commerce and the industry, it was agreed that a 50 per cent recovery rate from industry would be phased in over a five year period. When this commenced in 1992-93 with a recovery rate of 32.7 per cent it was expected to grow to 50 per cent in 1996-97. Subsequently, this was to change to the TGA recovering 100 per cent of industry related costs (see comments in paragraph 4.19). Of note is that the Government proposes that, by 1998-99, TGA will recover 75 per cent of its operating costs from industry via fees and charges.

Estimating fees

4.8. In determining the fees to be applied to submissions for drug evaluations in the following year, the TGA estimates the number of applications expected to be received. At each November meeting of the IGCC, a timetable for consultation with the industry is presented and the IGCC agrees to the proposed timing. A meeting, usually in March of each year, is held with key industry bodies. The May meeting of IGCC ratifies the fees and charges which are gazetted before being promulgated from 1 July.

4.9. There is a number of categories of fees and charges established by the Therapeutic Goods Act and the Therapeutic Goods (Charges) Act, namely:

- charges - annual charges for the listing and registration of drugs and devices on the Australian Register for Therapeutic Goods (ARTG). These are prescribed in the Therapeutic Goods (Charges) Regulations;
- licences - manufacturing licences for premises to manufacture therapeutic goods;

- application fees - fees for sponsors to submit applications to market therapeutic goods in Australia. These are listed in Schedule 9 of the Therapeutic Goods Regulations; and

- evaluation fees - these are to cover the evaluation process for the applications accepted for evaluation by the Drug Safety and Evaluation Branch.

4.10. The ANAO understands that in preparing estimates of workloads TGA receives little indication of the expected numbers of submissions to come from industry, because of commercial sensitivities. The TGA advises that consultations with industry representatives about estimates of workloads have not been very useful in assessing workloads because of the limited information available to industry organisations.

4.11. Until 1994-95, the TGA was relatively successful in estimating the number of submissions received and thus the amount of revenue to be collected. In 1994-95, however, the TGA estimated that it would receive approximately $10 million, but in fact it received $12.7 million or 27 per cent more than anticipated.

4.12. The TGA's estimate of 'units' of work is derived by the DSEB and Budget Management Unit based on historical data for fees and the number of drugs on the register for the charges. It is easier to determine the annual charges (based on drugs already on the Register) as they are based on known factors, while fees (paid on submission of an application) are based on historical data available to the TGA.

4.13. An alternative system is used by the UK and Sweden and is based on annual fees, that are large when compared to their application fees. It is easier to administer and the need for accurate estimates of likely workloads is not as imperative. The main disadvantage would be to the industry in that sponsors already having drugs on the ARTG, and paying annual charges, would be subsidising those sponsors submitting applications. A phased introduction of a change to a fee structure such as that existing in the UK or Sweden would alleviate this. Of note is that industry representatives are vigorously opposed to TGA having a larger proportion of fixed fees.

4.14. The TGA has recognised that the subject of fees and charges is complicated and that there is no quick fix solution. At the 11th meeting of the IGCC in May 1994, the National Manager advised that '...(TGA) was to undertake in the near future a comparison of the fees and charges of overseas regulatory agencies with the aim of identifying possible options.' The ANAO was unable to locate any further reference to this review.

4.15. TGA advised that it planned for the manager of the Business Management Unit to visit overseas organisations late in 1996 for discussions on mutual issues relating to fees and charges. The options put forward as a result of these meetings will be central to a review of TGA's pricing structure from 1 July 1997.

Recommendation No.13

4.16. The ANAO recommends that the TGA:

- identifies international pricing structure options with a view to adopting the most cost effective method for use in Australia; and

- seeks the co-operation of the pharmaceutical companies in assisting TGA to forecast future workloads with a reasonable degree of confidence.

TGA response

4.17. The TGA agrees with the recommendation.

4.18. The operation of an efficient, effective and equitable costing system is fundamental not only to the TGA as it seeks to recover costs in accordance with Government direction but also to industry concerned about its investment.

4.19. Professor Baume recommended that total costs be shared on a 50/50 basis between TGA and industry. However, in November 1992 the Government agreed to a proposal to recovery from industry 100 per cent of industry-related costs. The rationale behind the move was to make the relationship between the fees paid and the service received by the industry much clearer. This was a change from the previous arrangement that sought to recover 50 per cent of TGA's costs from industry.

4.20. The Government also believed that industry should not be subsidising 'public interest' activities which should be paid for from the Budget.

4.21. The ANAO considers that if the TGA is to recover the costs of providing a service to the pharmaceutical industry the TGA needs to ascertain with a greater degree of accuracy what those costs are. The TGA must be able to measure the costs to be sure that they will be recovered. The ANAO noted that evaluation staff worked extra hours in order to complete evaluations within required time frames. These hours, although not a direct cost to government, are a cost to completing the evaluation. However they were not costed and, therefore, were not recovered from industry.

4.22. TGA advised that it had undertaken an activity based costing project on the costs of licencing drug and device manufacturers. A report on licence activities was completed recently and distributed to industry for comment. A proposal to commence a project in the DSEB is under consideration.

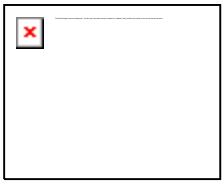
Recommendation No.14

4.23. The ANAO recommends that:

- the TGA, consistent with Government policy, introduces a method of calculating the industry-related costs of its operations to enable it to recover those costs; and
- include in its annual report to Parliament the extent to which its costs were recovered.

TGA response

4.24. The TGA agrees in principle with this recommendation. TGA has already completed an activity based costing of its manufacturer auditing and licensing functions, and studies in other areas (including the DSEB) are either underway or planned for completion before the end of the year.



Canberra ACT
4 October 1996

P. J. Barrett
Auditor-General

1

$5.97 million received in annual charges from industry was paid into the Consolidated Revenue Fund and then drawn down through Special Appropriations.

2

Address to the International Conference on Drug and Device Regulations (Towards Global Cooperation) by the Honourable Peter Staples, 4 March 1991.

3

Baume, Peter, *A Question of Balance*, AGPS, Canberra 1991.

4

Baume, Peter, *A Question of Balance,* AGPS, Canberra 1991, p94.

5

Baume, Peter, *A Question of Balance,* AGPS, Canberra 1991, p175.

6

Baume, Peter, *A Question of Balance,* AGPS, Canberra 1991, p17.

7

Baume, Peter, *A Question of Balance,* AGPS, Canberra 1991, p58.

8

Amounts adjusted for 1995-96 constant prices using the Consumer Price Index.

9

Industry commenced paying fees in 1991-92.

10

Annual charges from industry were paid into the Consolidated Revenue Fund and drawn down through Special Appropriations.

Appendix 1 - Performance reports produced by the TGA

Report 1	Registration of Prescription Drugs - Workflow of Submissions
Report 2	Registration of Prescription Drugs - Decisions made on Submissions
Report 3	Registration of Prescription Drugs - Processing times
Report 4	Registration of Prescription Drugs - Applications and Submissions not finalised as at 31 December 1994
Report 5	Registration of Non-Prescription Drugs - Workflow of Applications
Report 6	Registration of Non-Prescription Drugs - (II) Processing times
Report 7	Registration of Non-Prescription Drugs - (III) Applications not finalised
Report 8	Listing of Drugs for Supply in Australia
Report 9	Listing of Drugs for Export Only
Report 10	Registration of Therapeutic Devices
Report 11	Listing of Therapeutic Devices
Report 12	GMP Audit - Standard of Australian Manufacturers
Report 13	Licensing of Australian manufacturers
Report 14	TGA Laboratory Testing of Therapeutic Goods

Report 15	Testing of Therapeutic Devices
Report 16	Clinical Trials - Drugs
Report 17	Clinical Trials - Therapeutic Devices
Report 18	Export Certificates - Drugs
Report 19	Export Certifications - Therapeutic Devices
Report 20	Special Access Scheme - Drugs
Report 21	Individual Patient Use (IPU) and Authorised User Approvals (AUA) - Therapeutic Devices
Report 22	Drug Recalls and Problem Investigations
Report 23	Therapeutic Device Recalls
Report 24	TGAL Evaluation of Chemistry, QC and Manufacturing data
Report 25	GMP standard of Overseas Manufacturers
Report 26	Adverse Drug Reaction Problem Investigations
Report 27	Therapeutic Device Problem Investigation
Report 27(a)	Resolution of Non-Compliance Complaints - Therapeutic Devices
Report 28	TGAL - Projects and Method Development
Report 29	Surveillance - Enforcement of the Therapeutic Goods Act
Reprot 30	Australian Register of Therapeutic Goods
Report 31	Provision of Information to Clients

Appendix 2 - Performance audits in the Health and Family Services Portfolio

Set out below are the titles of the reports of the main performance audits by the ANAO in the Health and Family Services Portfolio tabled in the Parliament in the past three years.

Audit Report No.42 1993-94
Mind the Children
The Management of the Children's Services
Department of Human Services and Health

Audit Report No.19 1994-95
Efficiency Audit
Validation of Nursing Home Funding
Department of Human Services and Health

Audit Report No.5 1995-96
Provision of Hearing Services

Australian Hearing Services

Audit Report No.12 1995-96
Risk Management by Commonwealth Consumer Product Safety Regulators

Audit Report No.14 1995-96
The Sale of CSL
Commonwealth Blood Product Funding and Regulation

Audit Report No.18 1995-96
CETP
Department of Health and Family Services

Audit Report No.24 1995-96
Impact of Sunset Clause on Investigatory Powers Health Insurance Commission

Other relevant audit reports

Audit Report No.6 1993-94
An Audit Commentary on Aspects of Commonwealth-State Agreements

Audit Report No.17 1993-94
Underperforming Officers in the APS - A Question of Efficiency

Audit Report No.21 1993-94
Department of Finance
Australian Government Credit Card - its Debits and Credits

Audit Report No.22 1993-94
Cash Management in Commonwealth Government Departments

Audit Report No.28 1993-94
Department of Veterans' Affairs
Use of Private Hospitals

Audit Report No.32 1993-94
Accrual Reporting: Are Agencies Ready?

Audit Report No.41 1993-94
The Australian Government Credit Card - Some Aspects of its Use

Audit Report No.16 1993-94
Pay for Performance
Performance Appraisal and Pay in the APS

Audit Report No.16 1994-95
Follow-up Audit
Accrual Reporting - Are Agencies Ready?

Audit Report No.21 1994-95
Project Audit
Specific Purpose Payments to and through the States and Territories

Audit Report No.30 1994-95
Efficiency Audit
Commonwealth Government Information and Advertising