THE HON TONY ABBOTT MP
MINISTER FOR HEALTH AND AGEING
Leader of the House of Representatives

22 MAY 2006

Mr Tony Smith MP
Chair
Joint Committee of Public Accounts and Audit
Parliament House
CANBERRA ACT 2600

Dear Mr Smith

I am writing to you in relation to Report No. 404 of the Joint Committee of Public Accounts and Audit (JCPAA).

The JCPAA report made six recommendations (Recommendations 37 to 42 inclusive) to the Therapeutic Goods Administration (TGA), a part of my Department, relating to the regulation of non-prescription medicinal products.

You may recall that I wrote to you on 9 March 2006 providing a report in relation to Recommendation 42, on the establishment and operation of the Australia New Zealand Therapeutic Products Authority – ANZTPA.

The responses to the remaining Recommendations 37 to 41, in the *Executive Minute* format required by the JCPAA and signed by the Secretary of my Department, are attached.

Included with the *Executive Minute* are three attachments relating to aspects of the TGA's regulatory practices and procedures. These attachments contain Commercial-in-Confidence information about specific therapeutic goods manufacturers, and sensitive information relating to the investigation and prosecution activities of the TGA Surveillance Unit.

Accordingly, in order to preserve the confidentiality and sensitivity of the information, I request that the attachments to the *Executive Minute* not be placed on the public record.

Yours sincerely

TONY ABBOTT

Encl (3)

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EXECUTIVE MINUTE

JOINT COMMITTEE OF PUBLIC ACCOUNTS AND AUDIT
REPORT NO. 404

Review of Auditor-General's Reports: Report No.18 of 2004-2005 - Regulation of Non-prescription Medicinal Products - Department of Health and Ageing and Therapeutic Goods Administration

General Comments

The JCPAA's Report made six recommendations to the Therapeutic Goods Administration (TGA), a part of the Department of Health and Ageing. One of the recommendations (Recommendation 42) required responses in February and June 2006. The February response was provided to the JCPAA on 13 March 2006. The responses to the remaining five recommendations are set out below.

By way of overarching comment, the TGA has made significant changes to the management and general governance related to the Good Manufacturing Practice (GMP) audit program by establishing a new branch, the Manufacturers Assessment Branch (MAB), and recruiting an Assistant Secretary to manage and reform the branch's functions.

A new structure has been implemented within MAB, with four audit team managers in place to improve auditor performance, consistency and documentation. In addition an Audit Governance Committee has been established to review and monitor the audit program and processes, and to review, monitor and manage audit consistency across the audit teams.

The TGA's Regulatory Risk Management & Compliance Monitoring Committee meets quarterly to discuss a wide range of risk issues including enforcement actions. In addition, a Post-Market Monitoring and Compliance Coordination Group, which meets monthly, has been established to:

- enhance the operational interface between key post-market activities;
- provide a forum for information sharing and review of the relevant post-market monitoring and compliance activities;
- provide guidance in order to improve the effectiveness and efficiency of post-market operational activities; and
- develop optimal strategies for improving post-market operations.

Five specialist Manufacturing Technical Expert Reference Groups (TERGs) are being established by MAB in partnership with industry to achieve the following outcomes:

- improve the regulatory interface with industry;
- enhance GMP audit and industry practice consistency; and
- collaboratively and proactively address GMP issues.

The TERGs will also include representation from industry associations from both Australia and New Zealand in a move to ensure continuity from the inception of the Australia New Zealand Therapeutic Products Authority.

RESPONSES TO RECOMMENDATIONS 37 TO 41 OF JCPAA REPORT NO. 404

Recommendation 37

The Committee recommends that the TGA provide this Committee with a copy of the audit frequency matrix, and any other documentation linked to determination of audits (such as procedures for undertaking an unannounced audit), when it is completed.

Department of Health and Ageing Response

The Standard Operating Procedure (SOP) Number 303 for Audit Frequency and Programming, incorporating the audit frequency matrix, is the subject of ongoing review. The SOP was revised in January 2005 to reflect the improvements recommended by the ANAO. Copies of the SOP as at September 2004 and January 2005, the latter reflecting the matters raised by the ANAO, are at **Attachment 1**.

In the context of the governance and management reforms associated with the GMP function outlined above, SOP Number 303 is being further reviewed and enhanced to align with, and give effect to, the reforms that are underway.

A copy of the revised SOP will be provided to the JCPAA when it is completed and authorised for implementation.

Recommendation 38

The Committee recommends that the Therapeutic Goods Administration document its procedures for implementation of enforcement action against manufacturers. This should include:

- **a clear definition of different enforcement actions, the circumstances in which they are applied, and manufacturers' rights of submission or appeal;**
- **stipulation of management authorisation for enforcement actions;**
- **a definition of timelines for short-term reporting and TGA assessment of manufacturer reports; and**
- **a requirement that all manufacturers subject to an enforcement action will undergo a follow-up audit within three to six months of the initial action.**

Department of Health and Ageing Response

The TGA has a range of enforcement actions covered by documented procedures that can be taken against manufacturers. These involve a number of different areas of the TGA. At **Attachment 2** is a table summarising the range of enforcement actions. This table includes information about management authorisation, manufacturers' rights of submission or appeal, and the references to the documentation relevant to each enforcement action.

Short term reporting is referred to as 'progress reporting' in the MAB SOP Number 401 – a copy of this SOP is at **Attachment 3**. In general, manufacturers are required to respond to deficiencies within 28 days of the issue of the final audit report, indicating the corrective action that has been implemented or outlining a plan to address the deficiencies.

In most instances objective evidence will be provided with the response to the Audit Report and will be evaluated as part of the audit close out. Each response is thoroughly and objectively assessed by the Lead Auditor.

In some circumstances, implementation of corrective action for non-critical deficiencies, may for many practical reasons involve a time frame beyond 28 days. Provided that the audit response details the corrective and preventive action that will be taken, and a reasonable time frame for completion, such deficiencies will be closed out. Progress reports may be provided by the manufacturer on a monthly or quarterly basis, however, the specific timeframe is determined on a case by case basis. All progress reporting and timelines must be agreed by the Audit Team Manager.

All manufacturer audit reports must be prepared and reviewed by the Audit Team Manager and signed by the Lead Auditor within the following target times - 2 weeks from the date of the Lead Auditor's return to the office for a domestic manufacturer and within 3 weeks from the date of the Lead Auditor's return to the office for an overseas manufacturer. If it is necessary to refer the audit report to a Review Panel, these times may need to be extended.

SOP 401 requires that a manufacturer's response to the Audit Report must be critically reviewed within 4 weeks from the date of receipt of the response. Each response is assessed by the Lead Auditor.

As identified in the summary table at **Attachment 2**, manufacturers are subject to a range of enforcement actions including requirements to undertake corrective and preventative action, conditions being placed on the licence, through to suspension or revocation of a manufacturing licence. Where there are significant manufacturing deficiencies that may pose imminent public health risks there is provision to instruct the manufacturer to immediately cease production and quarantine the relevant products.

The interval for a follow-up audit is dependent upon the specific enforcement action. The audit frequency matrix is used to determine the audit interval based on the risk of the product and the level of compliance. When a GMP compliance rating is unacceptable, or the enforcement action is significant, the audit interval may be significantly reduced and is determined on a case by case basis. In extreme circumstances a dedicated GMP Auditor and/or TGA technical specialist may be assigned to undertake frequent audits on a single manufacturer. For example, monthly or quarterly surveillance audits could be implemented.

Recommendation 39

The Committee recommends that the Therapeutic Goods Administration increase its post-market laboratory testing for non-prescription medicinal products from overseas manufacturers, particularly with an emphasis on products from manufacturers who have not been subject to certification or audit in the past 18 months.

Department of Health and Ageing Response

Post-market laboratory testing for non-prescription medicinal products is undertaken by the TGA Laboratories in close collaboration with the TGA's Non-Prescription Product Regulator. Service Level Agreements are in place between the TGA Laboratories and the Non-Prescription Medicines Product Regulator.

An appropriately risk and intelligence based sampling and testing program is determined in advance between the TGA Laboratories the Drug Safety and Evaluation Branch and the Non-Prescription Medicines Branch.

There is a number of factors that are taken into account in the sampling program, including:

- intelligence and scientific reports;
- products recalls;
- adverse drug reaction reports;
- surveillance reports and any relevant international literature that may have identified potential quality problems related to a product;
- GMP compliance information from the Manufacturer Assessment Branch or overseas regulators; and
- GMP audit risk assessment, if an overdue audit occurs.

The TGA Laboratories adjusts their sampling program accordingly to address any acute issues that are identified by any of the factors outlined above.

In the instance where an audit interval exceeds the recommended period determined by the audit frequency matrix, the Chief Auditor completes a GMP risk assessment. This risk assessment is one input into a review by the TGA's Regulatory Risk Management & Compliance Monitoring Committee that is intended to ensure that all regulatory and public health risks are adequately addressed. A possible outcome is an increased and targeted sample testing activity to mitigate a particular concern.

As indicated the TGA Laboratories actively manage their testing priorities based on risk factors; audit frequency is one factor. An additional testing program has resource and cost recovery implications, which will result in an additional fiscal impost on industry; therefore consultation with industry will be necessary before any significant increases in the testing program are implemented.

Recommendation 40

The Committee recommends that the Therapeutic Goods Administration urgently review its information management systems, including documentation of key decisions and correct electronic and hard copy filing of relevant documents. The importance of maintaining accurate and up-to-date records should also be communicated to all TGA staff.

Department of Health and Ageing Response

The TGA has thoroughly reviewed its management systems, including documentation practices and procedures, and is implementing a new TGA-wide Records Management System. The system will enable the identification and provision of information relevant to all product and manufacturing regulators.

Records management education and awareness sessions are provided to all staff in an ongoing cycle to promote the importance of maintaining accurate and up to date records.

Recommendation 41

The Committee recommends that the Therapeutic Goods Administration continue with its re-accreditation process for ISO 9000 and National Association of Testing Authorities (NATA) standards. When the TGA achieves these standards this information should be promulgated to manufacturers and other industry bodies.

Department of Health and Ageing Response

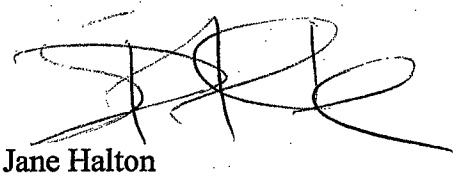
Within the TGA, the MAB is revising and enhancing its internal quality system in preparation for re-certification to ISO9001:2000. A new Quality Systems Manager was appointed in February 2006.

In addition, MAB have established a Quality System Implementation Committee to:

- revise the current MAB quality systems;
- review and monitor compliance with quality system requirements; and
- provide reports and recommendations to the MAB Executive and Branch Head as necessary.

In mid to late 2006, MAB's quality system will be independently assessed by Health Canada's quality system experts in the context of a quality system equivalence agreement.

The TGA Laboratories are accredited by NATA to ISO 17025.



Jane Halton
Secretary
Department of Health and Ageing

May 2006