



White Paper

Preparing for GMP audits

As a GMP licensed manufacturer, you should always be ready for an audit – regulators can ‘drop-in’ at any time. This White Paper provides some hints for preparing for a GMP audit.

Whilst this White Paper focuses on TGA GMP Audit readiness, it provides useful tips for other authorities as well.

Before the audit

As a Therapeutic Goods Administration (TGA) GMP licensed manufacturer, you should always be ready for an audit - regulators can perform 'unscheduled' audits at any time. First impressions count and it's important to convey to the auditors that you have everything under control and that you know what you are doing.

The TGA uses a risk management approach for the frequency of auditing facilities. They take into account the type of products manufactured, results of previous audits, product recalls, adverse reaction reports, complaints and significant changes within the company.

As a general rule of thumb, the following periods for re-auditing apply:

Risk category	Frequency of re-audit (months)			
	A1	A2	A3	Unacceptable rating
High (e.g. sterile medicines)	24	18	12	Internal review panel decides
Medium (e.g. OTC medicines)	30	20	12	
Low (e.g. vitamins)	36	24	12	

A1 = good compliance (<10 'other' deficiencies)

A2 = satisfactory compliance (1-5 'major' and <11 'other' deficiencies)

A3 = basic compliance (>5 'major' deficiencies)

Unacceptable = unacceptable compliance (1 or more 'critical' deficiencies)

Do some research

The lead auditor will notify you of a scheduled audit. Your company can ask to see the audit plan; this will give you the best indication of what the auditors will be looking for. It is also a good idea to review previous audit reports (your own and other companies) to gain some insights.

You may also like to gain some 'intelligence' on the auditors to find out their areas of expertise and focus; you can request copies of their CVs. The web also provides some information and the following links may be useful:

<http://www.tga.gov.au/docs/html/auditmed.htm>

<http://www.tga.gov.au/docs/html/gmpcodes.htm>

<http://www.tga.gov.au/docs/html/gmpcodqa.htm>

Know your documentation

Prior to an audit, ensure that your team has reviewed any documentation that an auditor is likely to request. Make sure they are accessible and that all circulated documents are 'controlled copies' and up to date.

Typically, the auditor will review the following documents before arriving on your site:

- **Site Master File** (if the auditor is new to your site)
- **Validation Master Plan**
- previous audit findings and your responses
- complaints and adverse events.

Site Master File / Validation Master Plan

We believe that when you have been notified of an audit, you should review the content of your Site Master File (SMF) and Validation Master Plan (VMP). If appropriate, the updated SMF should be sent to the authority prior to the audit.

The following link provides useful guidance on preparing SMFs:

<http://www.tga.gov.au/docs/html/siteinfo.htm>

'The message that you want to display during an audit is that you have everything under control and that you know what you are doing'

Define tour routes

It is useful to define routes through the facility during the 'audit tour'. Ensure that you have designated 'hosts' for each area and that they are capable of answering auditors' questions. To prepare your hosts you may like to prepare some mock questions for them to answer.

Train personnel

Before an audit, you should train personnel on how to conduct themselves in front of an auditor. Personnel should always be polite and helpful but shouldn't:

- try to second guess the next request
- be obstructive or argumentative
- say something when being given the 'silent treatment' from the auditor.

It is also a good idea to train personnel on the different audit techniques that an auditor may use. This will help them be more proactive and help them to anticipate the next step in the audit process. Techniques likely to be used include:

- trace forward – start with the raw material and follow the production flow
- trace backwards – start at the final product of a specific batch and go backwards
- random – start at points that appear significant (e.g. complaint, CAPA, change control, training).

Be pro-active

GMP auditors will be impressed to see early implementation of expected changes to the 2002 Code of GMP. The TGA has announced that they will be adopting the most current version of the PIC/S GMP Guide at a later date, so it's a good idea to get audit ready now.

Recent and expected changes to GMP guides and codes include:

New GMP requirement	EU GMP Guide	PIC/S GMP Guide	Australian Code of GMP
Product quality review	October 2005	January 2006	?
Ongoing stability program	October 2005	June 2006	?
Counterfeiting	December 2005	August 2006	?
Reference and retention samples	December 2005	April 2007	?
Quality risk management	February 2008	?	?
Clean-room classification	February 2008 ¹	?	?
Media fill simulations	February 2008 ¹	?	?
Bio-burden monitoring	February 2008 ¹	?	?
Capping freezer dried vials	February 2008 ²	?	?
Adoption of ICH Q9	February 2008	?	?

¹ To commence March 2009

² To commence March 2010

During the audit

It is critical to make a good impression as the auditors arrive on-site. Security personnel should check the identification of the auditors and ensure that they register them in the visitor's book and provide them with appropriate ID badges.

You will also need to ensure that you have a room dedicated to the auditors for the duration of the audit.

Opening meeting

The lead auditor will chair the opening meeting. The content of the opening meetings is likely to include:

- introduction of the audit team
- confirmation of the audit scope and objectives
- confirmation of the audit plan
- discussion of the methods and procedures to be used during the audit
- discussion of the communication links during the audit
- confirmation that the resources and facilities are available
- establishing a tentative time and date for the closing meeting.

It is a good idea to request a summary session at the end of each day. The lead auditor may or may not include this during the opening meeting.

During the opening meeting, you should advise the auditors about the:

- company policy on health, hygiene and safety
- company policy on photographs, video and sound recording
- normal operating hours (e.g. 8am to 5pm)
- the set time for lunch, breaks etc.

The Ops room

The Ops room supports the personnel fronting the auditors. Senior personnel should be in charge to support staff during the audit. The role of the Ops room is to:

- keep track of the auditors location
- keep the schedule on time
- provide an area to hold documents likely to be requested by the auditors
- line up the experts
- follow-up question that can't be answered immediately
- provide an area to review documents before submission.

Senior personnel in charge of the war room should also be responsible for reporting to senior management the progress of the audit, and any areas of attention of significant deficiency.

Conduct the audit

During the audit, ensure that all photocopies provided to the auditor for review are marked as 'uncontrolled' or 'commercial in confidence' as necessary, and provide the correct version.

If any deficiencies are observed during the audit, you should attempt to correct these immediately – this may impress the audit team. You can also ask the auditors to acknowledge such actions in their final audit report.

Some other helpful hints to remember during the audit are:

- when a document is requested, provide this and no more
- do not volunteer information
- do not guess an answer
- allow auditors to question any staff member (i.e. do not steer the auditor away)
- do not hide information
- do not argue or display anger towards the auditor
- never cause a deliberate delay
- always deliver something you have promised
- look confident and smile!.

'A key to success during any audit is preparation'

Closing meeting

At the closing meeting, the lead auditor will give an overview of the audit and its outcome. The scribe should attend the closing meeting to compare the deficiencies presented by the lead auditor to those recorded during the audit, and discuss any discrepancies.

If during the closing meeting you do not understand the deficiencies, ask the lead auditor to clarify them. If any deficiencies are clearly wrong, suggest that these are re-visited or documented as such.

It is important to be co-operative and to commit to providing a written audit response to the audit findings. If the auditors are taking an intimidating approach or are likely to request a product recall or report a critical deficiency, it's a good idea to invite your legal representative to the closing meeting.

After the audit

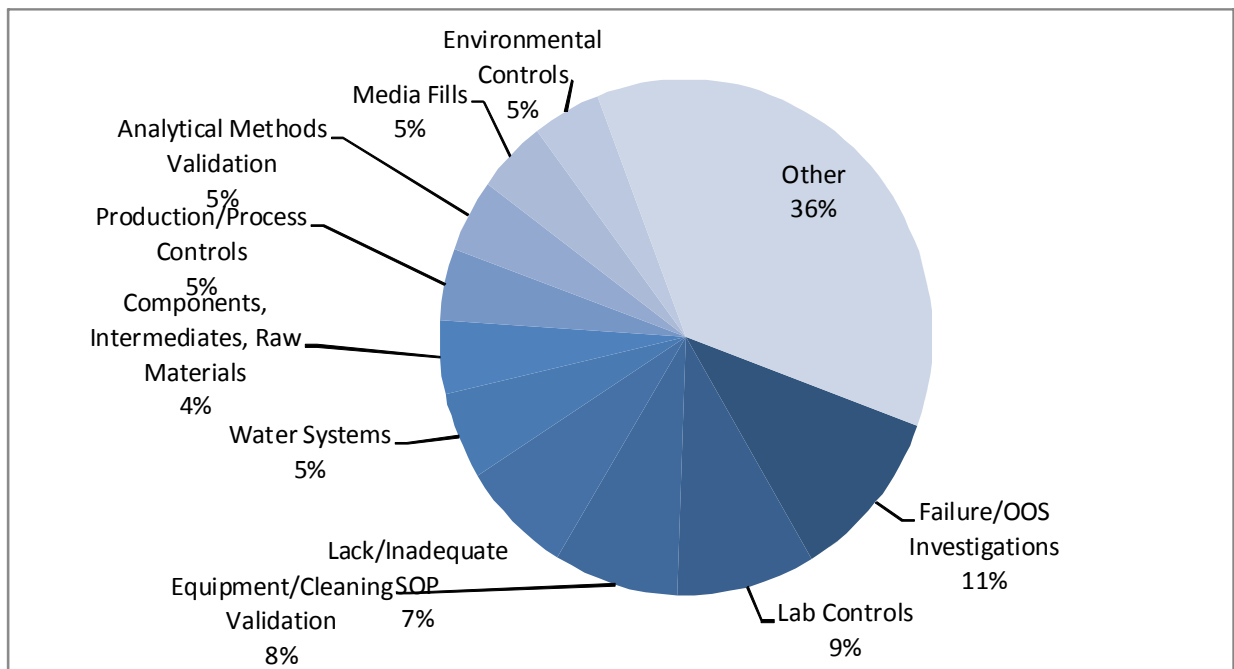
Assign one person to be the company's contact for receiving the audit report and answering any follow up questions that the auditors may have after leaving the site. A person should also be delegated the responsibility for coordinating any correction actions and compiling the audit report.

A post audit review should be conducted to identify areas of weakness identified not only by the auditors, but by personnel during the audit (and not detected by the auditors). It is better to correct these weaknesses now rather than wait for the auditor to identify them next time around.

Internal audits

Self-inspections, or internal audits, should be conducted to ensure compliance with the code of GMP. It is worthwhile focusing on the areas receiving the majority of GMP deficiencies, as reported by regulatory authorities.

The FDA reported failure / OOS investigations as the most common GMP deficiency for 2004³ as detailed in the chart below.



If you are seeking GMP compliance for the first time, it is useful to engage a GMP consultant.

³ www.fda.gov/cder/about/smallbiz/Presentations/6.ppt

Establish an SOP

A key to success during any audit is preparation. You may like to consider establishing a company procedure for the management of GMP audits – from the opening to closing meeting. This should also include the steps to follow for an 'unscheduled' audit.

Your procedure should define roles and responsibilities of all personnel likely to be involved in an audit including:

- security & reception (remember first impressions count!)
- escorts
- scribes (note takers)
- subject matter experts
- runners.

The procedure should also include the company policy on electronic data, entry into controlled areas, hygiene, sample collection and the use of cameras, videos and sound recording.

Secrets for success

The secrets to success at any audit include:

- being well prepared
- having good audit management
- providing a good first impression
- ensuring that personnel who front the auditors have the require technical ability, confidence and presentation skills
- establishing an SOP and training personnel

The message that you want to convey during an audit is that you have everything under control and that you know what you are doing.

About PharmOut

PharmOut is a boutique consultancy to the Pharmaceutical, Medical Device and Veterinary drug industries. We specialise in GMP compliance, validation and continuous improvement consulting and training.

Some of our customers include include Abbott Australasia (Healthcare), AC Immune SA, Acrux Limited, Agronico Research Pty Ltd, Amcor Limited, APHS Pty Ltd, AstraZeneca, Ausonex Pty Ltd, Austin Nuclear Medicine and Centre for PET, Australasian Lubricant Manufacturing Co., Avexa Limited, BD - Australia / New Zealand, Bernafon Pty Ltd, BioMerieux Australia Pty Ltd, CathRx Ltd, ClearStep Australia Pty Ltd, CSL Bioplasma, CSL Parkville, Emerson Process Management, Ensign Laboratories, Enterix Pty Ltd, Faulding FH & Co Limited, Fonterra Co-operative Group, GCL Ltd, Go Medical, GSK, Hospira Pty Ltd, House With No Steps, IDT - Institute of Drug Technology, IG Science Pty Ltd, Intellidesign, Invetech Pty Ltd, Mayne Pharma Ltd, MDI - Medical Developments International, Pall Australia, Peplin Operations Pty Ltd, Pharmatel Fresenius Kabi Pty Limited, Probe Analytical - Intertek Caleb Brett, PT. Sanbe Farma, RoyalBrisbane Women's Hospital, Siemens Ltd, Supercare Pty Ltd.

How PharmOut can help

International regulatory assistance

We can assist you to obtain approval from the following international regulatory authorities – FDA, MHRA, TGA.

Audit readiness / GAP Assessments

We have experienced consultants able to perform GMP Audit Readiness / GMP GAP assessments for your facility against GMP requirements. We are also able to offer assistance in correcting any deficiencies found.

APVMA GMP code

We have consultants experienced with Veterinary Drug GMP compliance.

Training

We offer GAMP/ GLP/ GMP training services and can specifically tailor these to meet your business needs.



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