THE
EXTERNAL
OOS
Intertek Testing Services (Australia) Pty. Ltd.

Trading as:

PROBE Analytical

Melbourne – 29th July 2008
Presentation for:
Parenteral Drug Association Australia Chapter
29th July 2008
Contents

1. Introduction and Company Background
2. Why have an OOS System
3. Preparation for OOS
4. Effective OOS Investigations
5. Laboratory Investigation (LI) & OOS
6. Key Performance Indicator
7. Summary
History of PROBE Analytical

- Originally ICI’s research laboratory

- Intertek is a leading worldwide inspection, testing and certification company that has the experience, expertise, resources and global reach to support its customers through its extensive network of laboratories and offices and over 21,000 people in more than 110 countries.

- Intertek purchased PROBE Analytical in 1999.

- PROBE is an advanced chemical analysis laboratory specialising in Pharmaceutical, Cosmetic, Veterinary testing and a leader in the provision of investigative & problem-solving services.

- PROBE is Intertek’s only TGA accredited laboratory.
PROBE Accreditations

- TGA: GMP
- APVMA
- NATA: ISO/IEC 17025 (various methods)
- ISO:9001
- TGA: Permit to Import Licence
- AQIS (Quarantine approved)
- Drugs/Poisons S4, S7, S8
- NICNAS
54% Pharmaceutical

Stability storage 5°C, 25°C/60% RH, 30°C/65% RH and 40°C/75% RH

Stability testing services

Raw materials, finished products and unknowns (contaminants)
General wet chemistry
- HPLC: UV, RI, Conductivity, FLD, ECD
- LC/MS
- GC: FID, TCD, ECD, MSD
- ICP-OES
- Graphite furnace AA
- NMR
- SEM-EDXA
- FTIR
- Polarimeter
- Brookfield Viscometer
- DTA Thermal analysis
- UV Spectroscopy
Why have an OOS System?

- Customer requirement
- TGA requirement
- Commercial advantage
- Make audits easier
- Tracking for KPI
- Staff training program
- Equipment replacement program
Preparation for OOS

- A GMP Agreement is in place before any work performed

- Use TGA Code of Good Manufacturing Practice for Medical Products as guide for preparing GMP Agreement

- Defines the protocol and responsibilities between PROBE and the client for aspects of testing including OOS Investigations
Preparation for OOS

- OOS results are formally investigated
- Confirmed OOS are reported in writing to client
- OOS investigation is completed within 24 hours
- All documentation is retained for a minimum period of 10 years
Responsibilities

- OOS is PROBE responsibility
- Acceptance or rejection of results is customer responsibility
- Decision to retest is customer responsibility
Effective OOS Investigation

- How the investigation is carried out
  - Laboratory Investigation
  - Out Of Specification Investigation

- How findings are communicated

- How and who makes the decisions

- How retesting is handled
Effective OOS investigation

- OOS affects Lab, QA and Customer
- Requires a good relationship between all parties
- Clearly define roles for OOS investigations
- QA has the final approval for OOS
Laboratory Investigations (LI) & OOS

- Investigations must satisfy both TGA and clients.
- LI used for internal issues
- OOS used for failed results
LI is used for the following:

- Instrument failure
- System suitability failure (internal and external)
- Analyst error
- Expected OOS result

PROBE initiates retesting for LI
Laboratory Investigations (LI) & OOS

- An OOS is used when initial checks pass and result fails

- Customer initiates retesting for OOS (in writing)
Laboratory Investigation Form

PROBE Job Number
Relevant SOP: 165
Customer Details:
Company:
Contact Name:

Sample Details:
PROBE Sample ID:
Customer Sample ID:

Issue Found    Yes / No
Area of Issue
Preparation of Samples
Preparation of Standards
Analysis
Calculations
Other

Details of Issue & any Investigation conducted: (attach extra pages if needed)

Investigation completed by:  References (if any):

Date:
Laboratory Investigation Form

Root Cause of Issue:

Corrective Actions required to prevent reoccurrence of issue:

SIR No: (if applicable)

Is original result invalidated after investigation  Yes / No

Can original raw data still be used:  Yes / No

Does re-analysis of solutions need to be repeated:  Yes / No

Does entire sample / standard preparation and analysis need to be repeated:  Yes/ No

Investigator Signature:  Date:

Supervisor Signature:  Date:
Investigation is a checklist
Paperwork checked
Instrument checked
Calculations checked
Retesting
OOS Form

PROBE No.

OOS No.
As per SOP 165

Customer details
Company:
Contact name:

Sample Details
PROBE Sample ID.
Customer Sample ID.

Reasons for Investigation.

Investigator:
Analyst:
Lab Note book references:

Date:
Close out with in one month of issuing investigation report
OOS Form

1. Specification/Limit
   Correct test method used
   System suitability passed
   Raw data checked
   Calculations checked
   Test method followed correctly
   Lab QC data within acceptance criteria
   Method QC data within acceptance criteria
## OOS Form

<table>
<thead>
<tr>
<th>ACTION</th>
<th>COMMENTS</th>
<th>SIGNATURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub sampling performed correctly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calibration of Instruments and equipment within acceptance criteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample/Standards stored correctly</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potency of reference standard (supplied COA).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Correct Application?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Correct preparation and expiry dates of reagents and reference standards</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Training records – analyst correctly trained</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
OOS Form

2. Instrument/Equipment checked for:
   - Set up
   - Correct operation
   - Unusual noise or performance
   - Calibration

3. Initial Analysts checks acceptable

4. Is result due to sample contamination in laboratory?

5. Does result appear to be caused by
   - Instrument error
   - Analyst error
   - Other laboratory assignable cause
   (if Yes in house re-test required)

6. Can original result be invalidated after this investigation?
7. In-house Laboratory Retest:
   Has client been informed of in-house retest?
   Is in-house retest result acceptable?

8a. OOS Investigation Summary and In-house Retest Summary
    (this section to be completed by analyst)

8b. Detail OOS Root Cause and Corrective Action required (if applicable)
    SIR number (if applicable)

8c. Comments by Supervisor (if applicable)

8d. OOS Investigation Completed:
    Signed (Investigator)
    Signed (Supervisor)
9. Is retest ordered by client (in writing)?
   Is client retest to be conducted on original sample or has another sample been received?
   Any special instructions for client retest (eg. Replicates)?

10a. Client Ordered Retest Summary

10b. Detail root cause and Corrective Action required (if Applicable)
    SIR Number (if applicable)

10c. Comments by Supervisor (if Applicable)

10d. Client Ordered Retesting Completed: (or approval if no retesting was carried out)
    Signed by Analyst:
    Signed by Supervisor:
    Signed by Customer:
    May be signed by PROBE team Leader on behalf of the customer
    (attach email showing their approval of the OOS investigation)
KPI Tracking

- Monitor the number per month
- Assign causes: Equipment, People, Customer or other/unknown causes
- Report monthly to PROBE Team and Management
- Annual QA report
- Generate KPI on PROBE’s performance
- Link to Quality Feedback System
The most important part of external OOS is communication
We thank you for your time and attention during our presentation.
There is a difference

Quality is our business
General Enquiries

Contact Details for all General Enquiries

Stephen Pearson: General Manager

Mark Moffat: Business Development Manager
Ph: +61 (3) 9361 4600       FAX: + 61 (3) 9315 1344

Email: probe@intertek.com

Website: www.intertek-cb.com
and type “PROBE Analytical” in the search box

Address: Building 1, 19 -23 Paramount Road
West Footscray, Victoria, 3012, Australia