Closure Protocol for the APIM Kilo Lab (B901)

Prepared by:	Mr J.R. Williams, Manager APIM B901	
Signature:		Date: 26 Mar 09

Reviewed by:	Mr A. Tait, GO RDPE	
Signature:		Date: 26 MARCH 09

Reviewed by:	I D Cousins, EHS	
Signature:		Date: 30 MARCH 09

Approved by:	Mr N.J Hill, GQO-Validation Support	
Signature:		Date: 26 MAR 2009

Approved by:	Dr T. Ward, Senior Director APIM	
Signature:	Tony Ward.	Date: 26. MAR 2009

Approved by:	Mr T. Humphreys, Associate Director GO/FS	
Signature:		Date: 26 MAR 2009

TABLE OF CONTENTS

1. Principle

This protocol establishes the overarching plan for the cessation of manufacturing activities in Active Pharmaceutical Ingredients Manufacturing (APIM) Kilo Laboratory (KL). This document, together with associated checklists (ref. B901/CD/CHKLISTS V01) will both define the desired "idle" state and confirm its attainment.

This closure protocol only becomes live once final processing activities in KL cease and all future work is scheduled in other APIM facilities.

Outline approaches are given for the management of Good Manufacturing Practice (GMP) and Environmental, Health and Safety (EHS) issues to control and document activities leading to closure and handover to Global Operations/Facilities Solutions (GO/FS).

2. Scope

This Protocol applies to all APIM KL areas including people, process equipment, plant rooms, storage areas, ancillary equipment and external utilities and waste areas.

3. Responsibility

The responsibility for the execution of this plan rests with the APIM management team in conjunction with Global Operations (GO) Engineering, EHS & Quality Assurance (QA) support. Team members are: -

- Mr John R Williams, KL Manager
- Mr Andy Tait, GO Research & Development Process & Equipment, (RDPE)
- Mr Troy Humphreys, GO Facilities Solutions (GO/FS)
- Mr Brian Crocker, Environmental, Health and Safety (EHS)
- Mr Jon Fowler, EHS
- Mr Ian Cousins, EHS
- Mr Nick J Hill, Global Quality Operations – Validation (GQO-V)

4. Colleague Management

Colleague management of APIM colleagues post cessation of manufacturing will be decided once statutory consultation has been finalised.

5. Document Structure

This Protocol with integral report shall be supplemented by approved checklists that detail and confirm the actions taken to close the APIM KL and associated systems.

The Protocol/report together with any residual risk forms, completed checklists and any attachments (including a list of ongoing maintenance requirements) will constitute the handover package to GO/FS.

6. EHS Management

6.1 The decontamination and decommissioning of the APIM KL equipment and facility is an EHS rather than a GMP issue. This is the responsibility of APIM management with support and guidance from EHS & GO Engineering.

6.2 The planned KL closure checklists will be approved by EHS and supported by EHS Decommissioning Hazard Study [1].

6.3 It is especially important to assess and control non routine activities during times of change and as such the generic range of EHS systems will be retained until handover e.g.

- Risk assessments.
- Change control.
- Fire risk assessment.
- DSEAR
- Safe systems of working
- Lone working considerations
- Accident and incident reporting and investigation.

6.4 All EHS documentation associated with closure will be archived with the closure documents and handover on exit to GO/FS.

6.5 A residual risk register will be developed for the entire facility to itemise all services left filled or live at time of exit and handover to GO/FS. This will include details of any lubricants not drained and a status of Fire /life safety equipment. A detailed list of all isolated electrical and Utility systems will be attached as a separate item.

6.6 The building security arrangements will be reviewed and documented. All general access on card readers will be cleared and a new list created to include only legitimate safety/security/fire and engineering/utility staff. It will be agreed who the contractor access cards shall be transferred to. *[Current assumption is that readers are retained]*. All other access will be covered under permit to work controlled by Pilot Plant (PP) Safe System of Work (SSoW) permit office.

6.7 All closure activities will be supervised by KL Manager or his designated PP facilities leads and will be performed by either process technicians familiar with the area or engineering staff under SSoW. Risk Assessments and Method Statements may be required for non-routine engineering activities.

6.8 The impact on the Waste Water Treatment Facility (WWTF) from any decontamination activities will be assessed by the normal routine sampling of all aqueous waste tanks TA02 & TA03 for inhibition testing prior to discharge.

6.9 Any chemical decontaminations requiring something other than water will be performed with common organic solvents such as acetone or methanol and these waste liquors will be discharged to solvent waste tank ST01 and sent to the Solvent Handling Facility (SHF) for appropriate disposal (e.g., incineration).

6.10 Once all decontaminations of equipment are complete, the waste aqueous tanks TA02 and TA03 and spent solvent tank ST01 will be emptied to the WWTF and the SHF and washed out. Any final discharges will be checked if required before discharge to the WWTF.

7. GMP Management

7.1 This is the responsibility of the APIM management closure team with appropriate consultation with World-Wide Pharmaceutical Sciences (WWPS) QA-API.

7.2 The need for final closure calibrations has been assessed – see reference [2].

7.3 All original hard copies of batch records & the equipment log books will be stored in APIM document store in B530 and thereafter archived as per policy/procedure.

7.4 All equipment specifications and drawings P&IDs will be held in the APIM Technical Library until such time as they are archived.

7.5 All KL procedures and SOIs will be made obsolete, but preserved in GDMS.

7.6 Calibration records will be held and archived by RDPE.

7.7 Maintenance /service records will be archived by RDPE.

7.8 Following the last manufacturing batch, electronic information from the KL PCS will be archived to the B902 Process Control System (PCS) Historian and retained.

7.9 Copies of all audit documents will be retained by the WWPS QA-API group.

7.10 All outstanding Corrective and Preventive Actions (CAPAs) and Quality Investigations (QIs) will be closed and held by WWPS QA-API. The rationale justifying closure will be added to the CAPA or QI.

7.11 Any references to the KL will be removed from the Site Master File as appropriate.

8. Plant Area Checklists

Checklists will be issued for each system once these have been identified and grouped together. The checklists will be developed to reflect and define the final end state for each area/system. Each checklist will be approved for execution and between them will deliver a minimum of the following:-

- Define the equipment cleanliness acceptance standard and confirm that this has been met
- Define the acceptance standards for the cleanliness of process areas, define how the areas are to be cleaned and confirm that this has been achieved
- Confirm that associated Change Controls are closed
- Confirm that associated QIs and relevant actions are closed
- Confirm that process instruments have been removed from the active calibration schedule
- Identify which (if any) instruments are to remain on an active calibration schedule
- Confirm that planned preventive maintenance schedules have been suspended
- Define requirements for ongoing maintenance and/or condition monitoring
- Define which lubricants, hydraulic fluids and seal pots etc are to be drained and which are to be left charged and confirm the end state of each
- Define how services to the associated area are to be left and confirm final status of each
- Incorporate an agreed format for the isolation status of electrical and other utilities
- Feed into the Residual Risk Register (including boundaries, any known ground contamination and areas requiring Personal Protective Equipment (PPE))
- Confirm that documents have been completed and removed for destruction/archive
- Confirm that inventories have been removed for disposal etc
- Define how drains are to be left (e.g. plugged/spaded/trapped etc) and confirm their final status – including requirements for ongoing maintenance
- Confirm that portable equipment (including pallets and drums) has been removed or specify where stored
- Define an agreed end state for lifting devices and personnel/goods lifts and confirm status at point of handover
- Define the required end state of building heating and ventilation systems and confirm at point of handover
- Define the agreed status of lighting systems, access lighting and confirm status at handover
- Define the agreed status of the breathing air system and confirm status at handover
- Define the agreed status of fire protection systems (including spill/fire call points, sprinklers, CO_2 system) and confirm status at handover.
- Define the final security arrangements and confirm active
- Confirm that all M3 inventory transactions have been closed out.

Area/system	Description and limit of consideration	Comments	Check list No.
Reactors KL 1,2,3,4,5,6,28 & 30	Decontaminate reactor and glassware to CVT clean. Drain glycol from condensers to drum and flush with water. Drain HTF from jacket. Isolate services.	KL 28 & 30 transferred to gram lab B530. KL 1 to 6 decontaminated , glycol drained **but HTF still in jackets and lines**	1
Gas scrubbers. KL 16,17 & KL 26 (mobile scrubber)	Drain scrubbing medium, acid wash to de-scale and water wash to drain to neutral pH.	Scrubbers cleaned	2
Vacuum pumps, VPO1,2,3,4 /lines. Including waste oil/solvent line to waste tank	Back flush vac lines with water and solvent to waste solvent tank. Remove soiled filters and clean strainers	VPO1 & 2 cleaned, filters replaced, glass knockout pots decontaminated as far as possible. VPO3 & 4 drained of glycol and water. Decons not possible	3
G16 fume cupboards (16 in total) and drains to waste tanks.	Decontaminate		4
G13 fume cupboard and drains.	Decontaminate		4
KL 32 laminar flow booth and drains.	Decontaminate		4
KL 27 & KL 31 vacuum ovens.	Decontaminate. Drain jackets, remove filters and clean vacuum lines.		5
KL 29 FD and tool temp unit	Drain tool temp unit & FD jacket. Ensure FD is visually clean.	Tool temp drained down, except glycol pipe drops. KL 29 transferred to PP. B902	5
KL 13,20 & MNFO4	Decontaminate and clean	KL 13 to loan to gram lab & KL 20 to PP. Document transfer	5
G13 & G14, chemical storage areas	Return all chemicals to IM. Reconcile on M3. Dispose of all consumable potentially contaminated process containers, (buckets and bins). Empty all solvent cans to waste. Remove all old process hoses & fittings. Incinerate those not suitable for transfer to B902 pilot plant.	All chemicals cleared out back to IM. G14 used to store clean process hoses and empty, clean solvent cans.	6

Area/system	Description and limit of consideration	Comments	Check list No.
B295 Solvent storage/dispensing areas	Return all chemicals to IM. Reconcile on M3.	Area remaining operational for gram lab and IM	6
Pit and solvent/water waste tanks. ST01. TA02& TA03.	Empty and clean to remove any solids. Blow transfer line to SHF with Nitrogen.	The responsibility for keeping the pit free from rain water is joint between IM and B902.	7
HTF compressor	Grenco to drain oil, cooling water and ammonia. Turn off ammonia alarms.	System to be left full of Nitrogen in place of ammonia	8
HTF lines and tank	.System left full to prevent corrosion	Tank, lines, reactor jackets and solvent tank HE left filled with oil.	8
Glycol tank and lines	Drain glycol from tank and lines. Drum up for return to utilities or disposal.	Lines and tank drained & decontaminated as far as possible with water washing	8
AHU1 and extract fans	Remove soiled filters and dispose. AHU filters to be removed and not replaced		9
AHU2 (LFB) and extract	Remove soiled filters and dispose. Clean out any visible dust from booth side of system.		9
Reactor relief catch tanks	Wash line through to drain with water. Isolate nitrogen supply.	Tank and lines flushed through with water.	10
Mobile stirrer separators. KL10, 21 & 35	Decontaminate, clean & transfer to Gram Lab (KL35) and PP (KL10 & 21).	Equipment transferred to B530 and 902.	11
Mobile receivers. KL 33 & 34	Decontaminate and store in G11.	Equipment cleaned.Stored in G11	11
PCS	Isolate KL from PP main frame. Remove any hardware needed.		12
CO2 , Firetrace, sprinklers, VESDA, detectors, fire panels, pump house, pit fire water pump and Fire extinguishers	2 spare pilot cylinders for CO2 system to be held by fire dept.		13

9. Miscellaneous Other Services and Items

Aspects not requiring decontamination or disconnection but requiring documenting in attachments.

Area/System	Description and Limit of Consideration	Comments/ Responsible Person	Attachment No
Security /access	Identify and document access changes.	Security access list cancelled, kilo specific cards activated	N/A
Statutory insurance items for pressure and lifting equipment.	Identify and document status of items and control measures to prevent use.	SIC informed and final status agreed	N/A
Safety equipment. Eye wash and safety showers.	Decide final operational state and document on attachments.	2 showers disconnected (ones by scrubbers and HTF skid).. all internal ones drained	N/A
Utility supplies of Electricity (including UPS system), mains water, Purified Water, Cooling Water, Compressed Air, Breathing Air, Nitrogen, Steam, Condensate Return and Heat Tracing.	For each utility itemise final status.	Purified water system isolated and drained. Some Dowcal left in HE unit . Steam, nitrogen , breathing air , C/W breathing air , condensate and water isolated to facility . Some physical breaks in pipes made and systems drained. Drawings updated	See isolation log info.
BEMS system	Identify final state for system and alarm reporting.	Andy Tait is to follow up	N/A
Air Conditioning Units	Document exit status for all units.	Units drained of gas.	N/A
Plant room extract fans	Document exit status for all units.	Fans turned off	N/A
Kitchen area G2	Remove equipment and isolate services?	Water drained, some equipment left unplugged	N/A
Office areas	Remove computers, printers, fax machine, PC's, lone worker alarms, radios etc	Arranged.	N/A
Glassware/equipment store	Ensure all glassware stored is clean, discard as appropriate. Items other than general QVF glassware spares should be itemised in attachments, e.g. Prosonic spools, CE units and CR unit.	Glassware store pruned of stock and tidied up.	N/A

Area/System	Description and Limit of Consideration	Comments/ Responsible Person	Attachment No.
Steps and ladders	Return to engineers or offer to PP.	Some steps left in G16 , engineers ladders removed.	N/A
Computer and phone cabinets in communications room	Liaise with IT and Nortel on these items.	Responsible parties informed nothing done, future access via GO permit office	N/A
Pest/vermin control	Establish what is required, implement and document.	Under control of GO	N/A
EHS, Compliance & GMP	Transfer log books and documents to B530 document store, ensure that procedures can be resurrected on GDMS. Itemise any outstanding quality or EHS investigations and close.	All items done	N/A
Calibration reports	Confirm that all calibration reports remain in system.	RDPE (Ian Hall informed)	N/A
Scales	Transfer to PP if required. Document transfer. Inform contract department.	KL 22 & 24 transferred to PP 902. Maintenance contract maintained.	N/A
Engineering tasks	Itemise any outstanding engineering jobs not completed and not already covered on checklists.	None	N/A
Consumables	Transfer to PP all stationery, PPE, Tyvex suits consumables etc.	Complete	N/A
Critical engineering spares	Confirm whether critical spares still require storage in engineering stores. If so get definitive list for attachment to Protocol.	Critical spares have been retained within the KL	N/A
Lightening protection	Ensure contract is maintained.	Tim Oliver contacted to ensure contract remains in place	N/A
Service contracts	Identify contract to be cancelled	Contracts being cancelled	N/A
Insurance	Determine changes and insurance needs for new 'closed' facility status.	**GO to organise**	N/A
Routine running of equipment	Identify and document any equipment that needs routine maintenance or running and put in place.	**None identified**	N/A

10. Relocated Equipment List

List all equipment relocated to other areas such as APIM pilot plant or gram lab and ensure change controls are issued where required. All changes of location where required should be amended in Technical Library and Global Operations and the companies Statutory Inspection Controller notified.

Equipment Identity	Transferred To	Notification Sent To	Sign/Date
KL 28 & 30 plus Huber units	Gram lab B530. 2.112	RDIS for Hubers. RDPE /SIC	
KL 35	Gram lab B530. 2.112	GO, RDPE/SIC	
KL 13	Gram lab B530. 2.112	GO, RDPE/SIC	
KL 55 CE unit	Gram lab B530. 2.112	GO, RDPE/SIC	
KL 10, KL 21	B902 Pilot plant	GO, RDPE/SIC	
KL 22 & 24 scales	B902 Pilot plant	RDIS/GO	
KL 72 & 73 pumps	B902 Pilot plant	GO	29 May 09
KL 56 CE unit	B902 Pilot plant	GO	
KL 43 Lasentec	B902 Pilot plant	GO	
KL 40 & 41 solvent cans	B902 Pilot plant	GO/SIC	
KL 36 Cuno	B902 Pilot plant	GO, RDPE/SIC	
KL 29 FD	B902 Pilot plant	GO, RDPE/SIC	
KL 20 MF	B902 Pilot plant	GO, RDPE/SIC	

11. Acronyms

Acronym	Description
AHU	Air Handling Unit
APIM	Active Pharmaceutical Ingredients Manufacturing
CAPA	Corrective and Preventative Action
C/C or CC	APIM change control system
CE	Continuous Extractor
COSHH	Control of Substances Hazardous to Heath
CR	Continuous Reactor
CVT	Cleaning Verification Test.
FD	Filter Dryer (KL 32)
GDMS	Global Document Management System
GMP	Good Manufacturing Practice
GO/FS	Global Operations Facilities Solutions
HTF	Heat Transfer Fluid (Syltherm LT)
LFB	Laminar Flow Booth (KL 32)
KL	Kilo Laboratory (B901)
PCS	Process Control System
PP	Pilot Plant (B902)
PPE	Personal Protective Equipment
QI	Quality Investigation
RDPE	Research and Development Processes & Equipment.
SIC	Statutory Inspection controller
SSoW	Safe Systems of Work
SHF	Solvent Handling Facility (Tank Farm)
SOI	Standard Operating Instruction
WWPS QA	World-Wide Pharmaceutical Sciences Quality Assurance
WWTF	Waste Water Treatment Facility

12. Residual Risk Register

No	Risk Description	Check list ref	Sign/Date
1	ESIMS action item 4122 suspended. To review condenser glycol relief valves	**1**	
2	CAPA 9408 closed. Need to review reactor agitator coatings.	**1**	
3	Reactor jackets and lines left full of Syltherm LT , HTF fluid.	**1**	
4	Scrubber lines from reactors clean but may have residual risk of contamination.	**2**	
5	VPO1 & 2 vac lines cleaned but some residual risk of chemical contamination.	**3**	
6	KL 27 & 31 Oven vac lines potentially contaminated from oven to pumps.	**3**	
7	Vac lines in LFB KL 32 not cleaned, risk of possible chemical contamination.	**5**	
8	Tool temp heater/cooler still contains residual Dowcal (glycol) in pipe drops to unit. Main tank and pipe work emptied and cleaned.	**5**	
9	Pit bund area not cleaned of solid wastes, (mainly algae and air born dust washed from roads). Some oil. All 3 waste tanks have a thin film of solid waste around walls, so residual risk of contamination is present in all tanks.	**7**	29 May 09.
10	Some residual risk of glycol (Dowcal) in lines and tank, despite water flushing/drain down.	**8**	
11	HTF tank, lines, reactor jackets and solvent waste tank HE still full. System static and at ambient temp under N2. Flow and return headers to upper plant room isolated on tank to keep pipes full of HTF.	**8**	
12	AHU 1 & 2 & associated extract fans. Risk of chemical contamination in ductwork and filter housings	**9**	
13	HTF still present in vent condenser, pump and lines on waste solvent tank ST01.	**7**	
14	Entry into the under-crop of building 901 will require confined space entry certification		

13. Report Approval

13.1 Conclusion

The KL closure protocol has been completed and the results documented. All residual risks have been recorded in the Residual Risk Register: Section 12 and on Residual Risk Forms in Appendix of this document. All checklists have been completed.

Comments:

No Comments 29 May 09

Completed by:	Date: 29 May 09.

13.2 Approval

The requirements of the Kilo lab protocol have been met and the facility is in a state whereby it can now be handed over to GO/FS. Attention is drawn to the Residual Risk Register (Section 12) the details of which are contained in appendix .

APPROVAL

Title	Name	Signature	Date
KL Manager/Building Owner	J WILLIAMS		29 May 09
EHS			03 JUNE 2009
Quality Assurance	N J Hill		29 MAY 2009
GO FS Manager	T D HUMPHREYS		8th June 2009

14. References

[1] Hazard Study 7
[2] Assessment on the Need for Final Process Measurement Instrument Calibrations – Kilo Laboratory, dated 9th Feb 2009.

15. List of Appendices

Appendix No	Description	# Pages Within Appendix
1	Residual Risk Forms	4 (4 SHEETS) 29 MAY 09
2	Closure Checklists	16 (8 SHEETS) 29 MAY 09

16. List of Attachments

Attachment #	Description	# Pages Associated With Attachment
1	Hazard Study 7	15 (8 SHEETS) JK 29 MAY 09
2	Hazard Study 7 Consolidated Action List	5 (3 SHEETS) JK 29 MAY 09
3	Final Calibrations Memorandum	~~3~~ 8 (5 SHEETS) JK 29 MAY 09
4	P&IDs for Utility Modifications	7 (7 SHEETS) JK 29 MAY 09
5	Isolation Log	~~2~~ 3 SHEETS JK 29 MAY 09
6	Cleaning Sheets	6 (6 SHEETS) JK 29 MAY 09
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17. Revision History

Version No.	Reason for Revision	Supersedes Document Dated
1.0	Original	N/A

Appendix 1

Residual Risk Forms

PGRD Pharmaceutical Sciences Sandwich	Residual Risk Form (B901)	Document ID: B901/CD/RESRISK V 01

For use where further elaboration is needed on residual risks

Residual Risk No.	1		
Checklist Number	1	**Asset/Tag # if available**	ESIMS 4122. Condenser glycol relief valves
Risk Description (attach additional documentation if required):			
An ESIMS No 4122 was suspended once announcement of closure of kilo lab was made. The action item was to review whether an additional pressure relief was needed to protect glass condenser coils on reactors KL 1, 2, 3, 4, 5, 6, 28 & 30 in case the glycol return valves on fume cupboard 'bull nose' was accidentally shut and pressure build up was possible as glycol warmed up in coils.			
Signed: J Williams		**Print Name:** J WILLIAMS **Date:** 28 May 09	
Recommended Precautions:			
Signed: (EHS)		**Print Name:** I. ROBINS **Date:** 5 JUNE 2009	
GO/FS Approval			
The residual risk is understood and accepted for handover:			
Signed: (GO/FS)		**Print Name:** TD HUMPHREYS **Date:** 8th JUNE 2009	

Pfizer	PGRD Pharmaceutical Sciences Sandwich	Residual Risk Form (B901)	Document ID: B901/CD/RESRISK V 01

For use where further elaboration is needed on residual risks

Residual Risk No.	2		
Checklist Number	1	**Asset/Tag # if available**	KL 1, 2, 3, 4,5, & 6
Risk Description (attach additional documentation if required):			
A CAPA No 9408 was closed out once announcement of closure of kilo lab was made. The action was to review whether reactor agitator coatings were fit for purpose on reactors KL 1, 2, 3, 4, 5, & 6, following previous failures of coating. A spare Hastelloy agitator is available in B901 plant room for fitting to KL 6 which currently is fitted with a coated agitator which failed just before closure announcement and was not replaced.			
Signed:		**Print Name:** J WILLIAMS **Date:** 28 May 09	
Recommended Precautions:			
Signed: **(EHS)**		**Print Name:** IAIN COUSINS **Date:** 8 JUNE 2009	
GO/FS Approval			
The residual risk is understood and accepted for handover:			
Signed: **(GO/FS)**		**Print Name:** TD HUMPHREYS **Date:** 9th JUNE 2009	

Pfizer	PGRD Pharmaceutical Sciences Sandwich	Residual Risk Form (B901)	Document ID: B901/CD/RESRISK V 01

For use where further elaboration is needed on residual risks

Residual Risk No.	3 & 11		
Checklist Number	1 & 8	**Asset/Tag # if available**	KL 1, 2, 3, 4,5, & 6 and HTF system
Risk Description (attach additional documentation if required):			
HTF system has been left filled with HTF fluid (Syltherm LT). This decision was taken to reduce the risk of corrosion in system should it ever be decided to re-open the facility. The HTF compressor has been electrically isolated and drained of ammonia and oil and this replaced with a Nitrogen back fill. Th e bulk HTF has been warmed to ambient temperature and the main flow and return header valves (3 in total) on the back of the HTF tank that supply the upper plant room F & R pipes & the solvent waste tank STO1 vent condenser/HE have been isolated to maintain a full pipe system for reactor jackets and HE. Each reactor jacket is protected from over pressurisation by a relief valve back to oil tank. The HTF in the tank is being kept under a nitrogen blanket to ensure no ingress of moisture. Grenco will maintain the N2 charge on the compressors under contract			
Signed: JWilliams	**Print Name:** J Williams **Date:** 28 May 09		
Recommended Precautions:			
Signed: **(EHS)**	**Print Name:** I D COLLINS **Date:** 8 JUNE 2009		
GO/FS Approval			
The residual risk is understood and accepted for handover:			
Signed: **(GO/FS)**	**Print Name:** TD HUMPHREYS **Date:** 9th JUNE 2009		

PGRD Pharmaceutical Sciences Sandwich	Residual Risk Form (B901)	Document ID: B901/CD/RESRISK V 01

For use where further elaboration is needed on residual risks

Residual Risk No.	**8 & 10**		
Checklist Number	**5 & 8**	**Asset/Tag # if available**	**Glycol system**
Risk Description (attach additional documentation if required):			
The kilo lab glycol system, (part of HTF/Ammonia compressor system) has been drained of Dowcal (glycol) and the tank and pipes flushed through the system with water, which was then drained and disposed of. Reactor condensers and lines have been disconnected and the glycol drained out in all G16 fume cupboards. The plate HE unit that interfaces with the cold HTF has been drained as has the pipe work to ovens. Header pipes in plant room F & R are empty and flushed with water. **Some residual Dowcal is left in pipe drops to tool temp unit and the purified water system HE unit as these were not possible to drain without dismantling these units completely, so some residual risk of contamination is possible.**			
Signed: J Williams	**Print Name:** J WILLIAMS **Date:** 28 May 09		
Recommended Precautions:			
Signed: (EHS) Iain Cousins	**Print Name:** I.O COUSINS **Date:** 8 JUNE 2009		
GO/FS Approval			
The residual risk is understood and accepted for handover:			
Signed: (GO/FS)	**Print Name:** TD HUMPHREYS **Date:** 9th JUNE 2009		

Appendix 2

Closure Checklists

Pfizer **PGRD** **Pharmaceutical Sciences** **Sandwich**	**Closure Checklists No's 1-13 for the APIM Kilo Lab (B901)**	**Document ID:** **B901/CD/CHKLISTS V 01**

Closure Checklist No's 1 -13 for the APIM Kilo Lab (B901)

Prepared By:	**Mr J.R. Williams, Manager APIM B901**	
Signature:		**Date:** 26 Mar 09

Reviewed By:	**Mr A. Tait, GO RDPE**	
Signature:		**Date:** 26 MARCH 09

Approved By:	**Mr I.D. Cousins, EHS**	
Signature:		**Date:** 23 APRIL 09

Approved By:	**Mr N.J. Hill, Global Quality Operations – Validation Support**	
Signature:		**Date:** 26 MAR 2009

Approved By:	**Dr T. Ward, Senior Director APIM**	
Signature:		**Date:** 26. MAR 2009.

Approved By:	**Mr T. Humphreys, Director GO**	
Signature:		**Date:** 26 Mar 2009

Index

This document is supplemental to closure protocol B901/CD V01

Appendix 2 Sheet 7 of 18

Checklist No 1 – Reactors

Reactor Ref. #	Equipment clean to CVT by solvent boil out?	List outstanding Change Controls & QIs etc	Instruments removed from active schedules?	Planned Maintenance schedules suspended?	List any ongoing maintenance issues	Confirm jacket drained of HTF	Confirm glycol drained from condenser and lines disconnected & flushed	List any electrical or instrument isolations	Are reactors dry and solvent free?
KL 1	Yes. LIMS ref 33548	None open	Yes	Requested	None	No	Yes	Pump, heater, agitator isolated on MCC	Yes
KL 2	Yes. LIMS ref 33549	None open	Yes	Requested	None	No	Yes	Pump, heater, agitator isolated on MCC	Yes
KL 3	Yes. LIMS ref 33550	None open	Yes	Requested	None	No	Yes	Pump, heater, agitator isolated on MCC	Yes
KL 4	Yes. LIMS ref 33551	None open	Yes	Requested	None	No	Yes	Pump, heater, agitator isolated on MCC	Yes
KL 5	Yes. LIMS ref 33552	None open	Yes	Requested	None	No	Yes	Pump, heater, agitator isolated on MCC	Yes
KL 6	Yes. LIMS ref 33553	None open	Yes	Requested	Hole in vessel agitator coating	No	Yes	Pump, heater, agitator isolated on MCC	Yes
KL 28	Equipment transferred to Gram lab B530. C/C to be raised prior to use					N/A	Yes	None	N/A
KL 30	Equipment transferred to Gram lab B530. C/C to be raised prior to use					N/A	Yes	None	N/a

Residual Risk Register: No 1. ESIMS action item 4122 suspended. Action to review pressure relief valves on condensers.
No 2. CAPA 9408 closed. Review of agitator coatings required.
No 3. Reactor jackets and lines left filled with HTF, Syltherm LT to prevent corrosion

All tasks carried out and checklist completed Sign ..... Print WILLIAMS Date 28 May 09

Checklist No 2 – Gas Scrubbers

Equip. Ref. #	Equipment drained and acid de-scaled?	List outstanding Change Controls & QI's etc	Instruments removed from active schedules?	Planned Maintenance schedules suspended?	List any ongoing maintenance issues	Confirm condenser drained of Cooling Water	Confirm electrical trace heating on lagged water pipes	List any electrical or instrument isolations	List any alarm isolations
KL 16	Yes	None	Yes	Requested	None	Yes	Still operational	Circulating pump isolated at MCC	PCS system off
KL 17	Yes	None	Yes	Requested	None	N/A	Still operational	Circulating pump isolated at MCC	PCS system off
KL 26	Yes	None	N/A	N/A	None	N/A	N/A	N/A	N/A

Residual Risk Register: No 4. Scrubber lines from reactors KL 1 to KL 6 have been acid, water and solvent washed, residual risk of chemical contamination

All tasks carried out and checklist completed Sign.....Print..... Date.....

Appendix 2 Sheet 3 of 8

Checklist No 3 – Vacuum Pumps

Equip. Ref. #	Vac pump drained of waste oil/ solvent?	Filters and strainers removed and cleaned. Were new filters fitted?	List outstanding Change Controls & QIs etc	Instruments removed from active schedules?	Planned Maintenance schedules suspended?	List any ongoing maintenance issues	List any electrical or instrument isolations	List any alarm isolations	List any mechanical isolations
VP 01	Yes	Pump decontaminate, no new filters fitted	None	Yes	Yes	None	Isolated at MCC	PCS shutdown	Vac valves to G16 closed. Solvent drains shut/spaded off to waste solvent tank
VP 02	Yes	Pump decontaminate, no new filters fitted	None	Yes	Yes	None	Isolated at MCC	PCS shutdown	Vac valves to G16 closed. Solvent drains shut/spaded off to waste solvent tank
VP 03	Waste Solvent /oil drained	N/A	None	Yes	Yes	None	Local isolation in vac pump room G9A	PCS shutdown	C/W, N2 & glycol isolated & drained
VP 04	Waste Solvent /oil drained	N/A	None	Yes	Yes	None	Local isolation in vac pump room G9B	PCS shutdown	C/W, N2 & glycol isolated & drained

Residual Risk Register: No 5. All glass vac lines in G16 reactor hall from VPO1 & VPO2 ,flushed with water, acid and solvents, some residual contamination possible.

No 6. Oven vac lines potentially contaminated between line filter housing and vac pumps.

All tasks carried out and checklist completed Sign..... Print..... Date.....

Checklist No 4 – Fume Cupboards and Flow Booth

Fume Cupboard Ref. #	Portable equip. removed and area cleaned?	List outstanding Change Controls & QIs, COSHH issues etc	Instruments removed from active schedules	Planned Maintenance schedules suspended – including COSHH testing?	List any ongoing maintenance issues	Confirm solvent drain to ST01 flushed and spaded off	Confirm aqueous drain to TA02 and TA03 are cleaned. Is the FC drain plugged?	List any electrical or instrument isolations not covered by the reactor checklist
GN2104 FC 378	Yes	None	Yes	Requested	None	Yes	Yes	PCS electrics in bull nose isolated
GN2100 FC 379	Yes	None	Yes	Requested	None	Yes	Yes	PCS electrics in bull nose isolated
GN2102 FC 380	Yes	None	Yes	Requested	None	Yes	Yes	PCS electrics in bull nose isolated
GN2201 FC 381	Yes	None	Yes	Requested	None	Yes	Yes	None
GN2200 FC 382	Yes	None	Yes	Requested	None	Yes	Yes	None
GN2103 FC 383	Yes	None	Yes	Requested	None	Yes	Yes	PCS electrics in bull nose isolated
GN2101 FC 384	Yes	None	Yes	Requested	None	Yes	Yes	PCS electrics in bull nose isolated
GN2105 FC 385	Yes	None	Yes	Requested	None	Yes	Yes	PCS electrics in bull nose isolated
GN2814 FC386	Yes	None	Yes	Requested	None	Yes	Yes	PCS electrics in bull nose isolated

Residual Risk Register: **Note , all fume cupboard sashes deliberately left open so fume cupboards and reactor hall all one open are for fire detection purposes following isolation of former CO2 system detectors**

All tasks carried out and checklist completed **Sign**..... **Print**.....WILLIAM..... **Date**.....28May09.....

APPENDIX 2 SHEET 4 of 8

Checklist No 4 – Fume Cupboards and Flow Booth – Continued

Fume Cupboard Ref. #	Portable equip. removed and area cleaned?	List outstanding Change Controls & QIs, COSHH issues etc	Instruments removed from active schedules	Planned Maintenance schedules suspended – including COSHH testing?	List any ongoing maintenance issues	Confirm solvent drain to ST01 flushed and spaded off	Confirm aqueous drain to TA02 and TA03 are cleaned. Is the drain plugged?	List any electrical or instrument isolations not covered by the reactor checklist
GN2301 FC 392	Yes	None	Yes	Requested	None	N/A	Yes	None
GN2300 FC 391	Yes	None	Yes	Requested	None	N/A	Yes	None
GN2303 FC 390	KL9 still in FC	None	Yes	Requested	None	Yes	Yes	None
GN2400 FC 389	Yes	None	Yes	Requested	None	Yes	Yes	None
GN2302 FC 388	Yes	None	Yes	Requested	None	Yes	Yes	PCS electrics in bull nose isolated
GN2800 FC 387	Yes	None	Yes	Requested	None	Yes, spaded under work top	Rubber plug in sink drain	None
GN3001 FC 394 in G13	Yes	None	Yes	Requested	None	N/A	Rubber plug in sink drain	None
KL 32 LFB	Yes	None	Yes	Requested	None	Line valve on drain is shut	Plug in floor drain.	PCS electrics in bull nose isolated

Residual Risk Register: **Note , all fume cupboard sashes deliberately left open so fume cupboards and reactor hall all one open are for fire detection purposes following isolation of former CO2 system detectors**

All tasks carried out and checklist completed Sign..... Print..... Date..28 May 09.....

Checklist No 5 – Ovens and Mobile Filters

Equip. Ref. #	Equipment visually clean by solvent wash down	List outstanding Change Controls & QIs, COSHH issues etc	Instruments removed from active schedules	Planned Maintenance schedules suspended	List any ongoing maintenance issues	Confirm jackets drained	Confirm water drained from Tool temp unit	List any electrical or instrument isolations	Confirm vac line filters removed, cartridge holder left empty & lines flushed back to oven from filter	Confirm waste solvent lines from vac pump outlet has been drained and valves isolated	Is equip being re-allocated to another APIM facility? Confirm re-location details notified to Tech Library, Go & Statutory Insurance Group
KL 27 Oven	Yes	None	Yes	Requested	None	Yes	N/A	Local lock off on MCC	Yes	Yes	No
KL 31 Oven	Yes	None	Yes	Requested	None	Yes	N/A	Local lock off on MCC	Yes	Yes	No
KL 29 FD	Filter transferred to B902 Pilot Plant. C/C needed before use					Yes	Yes KL 29. & Tool Temp unit	IC No 39558	Not possible	N/A	Yes, but not Tool temp unit
KL 13 MNF	Filter transferred to B530 Gram lab. C/C needed before use					N/A	N/A	N/A	N/A	N/A	Yes
KL 20 MNF	Filter transferred to B902 Pilot Plant. C/C needed before use					N/A	N/A	N/A	N/A	N/A	Yes
MNF04	Yes	None	Yes	Requested	None	N/A	N/A	N/A	N/A	N/A	No

Residual Risk Register: No 7. Vac lines in LFB KL32 not cleaned, as this is not possible without cutting pipes. Risk of chemical contamination in lines.
No 8. KL 29 tool temp heater/cooler still contains some Dowcal (glycol) on local pipe drops. Headers and tank etc drained and flushed.

All tasks carried out and checklist completed Sign..... Print J WILLIAMS 28 May 09 Date 28 May 09

APPENDIX 2 SHEET 5 of 8

Checklist No 6 – Chemical Storage Areas

Chemical Storage Areas	Portable equipment removed and area cleaned of any chemical contamination?	Confirm all chemicals returned to Inventory	List outstanding Change Controls, QIs, COSHH issues etc	Planned maintenance schedules suspended – including annual COSHH testing?	List any ongoing maintenance issues	List any electrical or instrument isolations – including status of heat trace to pipe work & extract fans
B901/G13	Yes	Yes	None	Requested	None	N/A
B901/G14	Yes, except G14 used to store clean hoses and empty/dry solvent cans.	Yes	None	Requested	None	N/A
B295	Area to remain operational post closure for APIM.	No. Area to remain operational post closure for APIM.	None	No. COSHH testing still required.	None	Area left operational.
B295 fenced compound	Area to remain operational post closure for APIM.	No. Area to remain operational post closure for APIM.	N/A	N/A	None	N/A

Residual Risk Register:

All tasks carried out and checklist completed Sign ..... Print ..... Date 28 May 09

Checklist No 7 – Waste Tanks and Pit

Tanks & Tank Pit Area	Tanks emptied & washed to remove solid contamination from walls. Confirm tanks left empty, with lids secured	Confirm pit area has been cleaned of all chemicals by wash down	List outstanding Change Controls etc	Planned maintenance and instrument schedules suspended?	List any ongoing maintenance issues	List any electrical, mechanical or instrument isolations – including status of heat trace to pipe work	Confirm status of vent condenser. Pump electrically isolated & vent condenser & lines drained of HTF	Are alarms isolated?
TA02 Aqueous Waste Tank	Empty, but some residual contamination present as a thin skin on tank walls	N/A	None	Requested	None	Line from pit pump to tanks removed to prevent rain /bund water being pumped into tanks. Main tank fill valves to Kilo shut	N/A	PCS suspended
TA03 Aqueous Waste Tank	Empty, but some residual contamination present as a thin skin on tank walls	N/A	None	Requested	None		N/A	PCS suspended
ST01 Solvent Waste Tank	Empty, but some residual contamination present as a thin skin on tank walls	N/A	None	Requested	Level indicator often ghosts to 100%	Pump isolated at MCC. Spool piece of pipe removed from transfer line to SHF.	Vent condenser pump isolated at MCC. Lines and pump contain HTF	PCS suspended
Pit Bund and Weir Sump	N/A	Pit still contains some oily rain water, but no environmental hazards	None	Requested	None	Line from pit pump to Aq waste tanks blanked off .	N/A	PCS suspended. Fire water pump still live.

Residual Risk Register: No 9. Pit bund area not cleaned of solid wastes, (mainly algae and air born dust washed from roads). All 3 waste tanks contain some residual solid contamination present as a thin skin, it has not been possible to remove this, without engaging specialist tank cleaners or the use of copious solvent.
No 13. Vent condenser, pump and lines contain HTF

All tasks carried out and checklist completed Sign..... .....Print..... Date.....

APPENDIX 2 SHEET 6 of 8

Checklist No 8 – HTF/Glycol Ammonia Chiller

Equipment Description	Confirm bulk of fluid has been drained	Have lines or tanks been decontaminated? List method used & checks performed	List outstanding Change Controls QIs, COSHH issues etc	Planned maintenance schedules suspended?	List any on going maintenance issues	List any electrical or manual isolations or disconnections put in place
HTF Tank	No	Decision taken to leave HTF tank, lines, solvent waste tank HE and reactor jackets full of Syltherm LT fluid to reduce risk of corrosion in pipes etc. The 3 main valves on tank have been shut to keep header F & R lines to upper plant room full. HTF in tank maintained under N2 blanket.	None	Requested	None	HTF skid isolated in MCC room. This has also isolated ammonia alarms.
HTF lines to & from tank	No		None	Requested	None	
HTF lines to reactors	No		None	Requested	None	
HTF lines to vent condenser	No		None	Requested	None	
Glycol Tank	Yes	Yes, drained and water flushed. Dowcal disposed of.	None	Requested	None	
Glycol lines to & from tank	Yes	Yes, drained and water flushed. Dowcal disposed of. Some residual glycol in pipe drops to Tool temp unit and purified water HE unit.	None	Requested	None	
Glycol lines to reactors	Yes	Yes, drained and water flushed. Dowcal disposed of.	None	Requested	None	
HTF compressor	Oil and ammonia drained, nitrogen blanket applied.	Nominally drained only	None	Grenco to maintain some PM	Efficiency of ammonia alarms is questionable	

Residual Risk Register: No 10. Some residual risk of pockets of glycol (Dowcal) in lines and tank . See RRR No 8.
No 11. HTF system still full.

All tasks carried out and checklist completed Sign..... Print WILLIAMS Date 28 May 09

Checklist No 9 – AHU and Extract Systems

Equipment Description	Have potentially contaminated filters been removed?	Have units been decontaminated? List method used & checks performed	List outstanding Change Controls, QIs, COSHH issues etc	Planned maintenance schedules suspended?	List any ongoing maintenance issues	List any electrical or manual isolations or disconnections put in place	Have PCS alarms been isolated or disconnected?
AHU 1 & Extract System	Inlet filters removed. New ones not fitted not fitted	See RRR below	None	Requested	None	MCC isolated	Yes
AHU 2 and Extract System	AHU2 extract and inlet filters removed, new ones not fitted	Extract filter compartments solvent cleaned. See RRR below	None	Requested	None	MCC isolated	Yes

Residual Risk Register: 12. Potential residual risk of contamination in extract system duct work and filters.

All tasks carried out and checklist completed Sign..... .....Print..... Date.....28 May 09.....

APPENDIX 2 SHEET 7 of 8

Checklist No 10 – Reactor Relief Catch Tanks

Equipment Description	Has equipment been decontaminated? List method used & checks performed	List outstanding Change Controls, QIs, COSHH issues etc	Planned maintenance schedules suspended?	List any ongoing maintenance issues	List any electrical or manual isolations or disconnections put in place	Have BEMS and PCS alarms been isolated or disconnected?
Reactor Relief Dump Tank	Tank flushed with water and drained. Tank has never seen chemical contamination from reactors as a result of burst disc rupture	None	Requested	None	Nitrogen supply isolated and copper pipe disconnected in FC 378	PCS shutdown so alarms suspended.
Header Line from Reactors to Dump Tank	Line flushed with water and drained. Line has never seen chemical contamination from reactors as a result of burst disc rupture	None	Requested	None	Nitrogen supply isolated and copper pipe disconnected in FC 378	PCS shutdown so alarms suspended

Residual Risk Register:

All tasks carried out and checklist completed Sign..... Print..... Date 28 May 09

Checklist No 11 – Mobile Separators and Distillate Receivers

Equipment #	Portable equipment removed to storage & cleaned of any chemical contamination?	List outstanding Change Controls, QIs, COSHH issues etc	Planned maintenance schedules suspended?	List any ongoing maintenance issues	Is equipment being re-allocated to another APIM facility?	Confirm re-location details notified to APIM Tech Library, GO & Statutory Insurance Group
Mobile Separator (KL 10)	KL 10 transferred to B902 Pilot Plant. C/C to be raised before use				Yes	GO, SIC , RDPE
Mobile Separator (KL 21)	KL 21 transferred to B902 Pilot Plant. C/C to be raised before use				Yes	GO, SIC , RDPE
Mobile Separator 35	KL 35 transferred to B530 gram lab. C/C to be raised before use				Yes	GO, SIC , RDPE
Mobile Distillate Receivers KL 33 & KL 34	Yes	None	Requested	None	No	N/A

Residual Risk Register:

All tasks carried out and checklist completed **Sign**..... .....**Print**..... **Date**.....28 May 09.....

APPENDIX 2 SHEET 8 of 8

Checklist No 12 – Process Control System

Equipment #	Description	Power Isolated?	Equipment removed?
MIO4A	IO Server	**Yes**	**No**
MIO4B	IO Server	**Yes**	**No**
KILOA	APACS ACM	**Yes**	**No**
N/A	APACS MBX card and IO cards	**Yes**	**No**
N/A	APACS Marshalling cabinets	**Yes**	**No**
MCOPK01	COP	**Yes**	**Yes**
MLOPK01 – MLOPK09	LOPs	**Yes**	**Yes**
N/A	PC keyboards and monitors	**Yes**	**Yes**
N/A	4 x Netgear hubs	**Yes**	**No**
N/A	Fibre link hub	**Yes**	**No**
N/A	System printer	**Yes**	**Yes**
N/A	UPS System	**Yes**	**No**

The following software applications must be updated to remove the Kilo Lab configuration.

Software Application	Change Control Ref	Application Updated?	Application Tested?	Test Protocol Ref
InTouch Client	These items to be performed by APIM PCS group at a later date.			
Tag Server				
Historian				

Residual Risk Register:

All tasks carried out and checklist completed **Sign**.....**Print** J WILLIAMS **Date** 28 May 09

Checklist No 13– Fire Systems

Fire protection System	Is system isolated from Mars panel/ site fire system?	Are cylinders still in place?	Are cylinders disconnected?	Is sprinkler system still full and/or operational?	Is service contract still in place?	List any outstanding issues on systems	Comments
Fume cupboard CO_2 systems (x9)	Yes, fire detection to rely on main area detectors	No	Yes and removed from building	N/A	No	None	Fume cupboard sashes left open as AHU/extract is off
PCS cabinet Fire trace system	Yes, fire detection to rely on main area detectors and Vesda	No	Yes and removed from building	N/A	No	None	Vesda system still live in MCC room 1.2 and switch room 1.4 as well as main building detectors
Sprinkler system/pump house	No.	N/A	N/A	Operational but system drained of water	Yes	None	
VESDA system in 1.2	Yes, system isolated.	N/A	N/A	N/A	No	None	Decision made with fire department at handover meeting to shut this off and rely on main building alarms.
Building internal fire extinguishers	N/A	Internal fire extinguishers removed	N/A	N/A	No	None	
Building smoke and heat detectors	No	N/A	N/A	N/A	Yes	None	

Residual Risk Register:

All tasks carried out and checklist completed **Sign**..... **Print**.....WILLIAMS..... **Date**...28 May 09.....

Sandwich Laboratories
Pfizer Limited
Sandwich, Kent CT13 9NJ
United Kingdom

Global Research & Development

Date: 9th February 2009

From: Nick Hill

Subject: Assessment on the Need for Final Process Measurement Instrument Calibrations – Kilo Laboratory

INTRODUCTION

In January 2009 it was announced that operations in the Sandwich Kilo Laboratory were to be indefinitely suspended. As a result of this announcement, the need for final calibrations of process measurement instruments has been critically evaluated and the outcome and recommendations captured in this memo.

This forms part of the process of defining the activities necessary to leave the facility in a safe and compliant state, but in a state whereby operations could be resumed in future, should the need arise.

BACKGROUND

Process Measurement Instruments fall into one or a combination of four categories – GMP, EHS, Operational and Reference. Calibration frequency is determined based on the instrument type, performance history, category and use. It is common for reference and operational instruments not to be on a calibration schedule, but to be calibrated on request. However, GMP and EHS related process measurement instruments do feature on calibration schedules and usually require periodic testing in the frequency range 3 to 24 months.

It is normal practice within the commercial manufacturing arena for final calibrations to be conducted upon cessation of production in order to prove that critical and/or regulatory measurements were accurate at the time of making the last batch.

This document does not cover laboratory instruments.

RATIONALE AND APPROACH

To be consistent with science- and risk-based approaches, final calibrations will not be conducted on Safety, Operational and Reference class measurement loops, as inaccuracies in these have been assessed as having little impact on patient safety and environmental protection compliance. This leaves the issue of final calibrations on those process measurement loops that are employed for direct GMP and/or environmental compliance purposes.

Unlike commercial or pilot scale facilities, the Kilo Laboratory has no environmental compliance issues as it is does not feature in site Integrated Pollution Prevention Control (IPPC) licenses This therefore rules out the need to conduct final calibrations on process measurement instrumentation even if in practice it provides environmental protection.

The chemical processes for which the Kilo Laboratory is employed are in very early stage development and although the API isolated and dried there may be used to produce Drug Product that is subsequently employed for small scale human studies, control parameters are not bound by regulatory submissions. There is therefore no risk of operating outside of a manufacturing licence or Marketing Authorisation. Quality systems such as batch documentation, deviation investigations, analytical testing, equipment qualification and change controls – together with high levels of technical supervision, ensure the safety of API used for clinical trials from this scale of manufacture.

In the case of the Kilo Laboratory there are numerous instruments (see appendix 1) that have been classified as GxP, but very few (10) that could be classified as directly measuring aspects that impact product quality. Whilst it is conceivable therefore that final calibrations would be expected for these direct GMP impact instruments (e.g., batch temperature loops) the developmental nature of manufacture and absence of regulatory parameter constraints leads to the conclusion that final calibrations even in this case are not value adding. This is supported by the performance history of the 10 measurement instruments in question (see appendix 2): -

KL1 to KL6 vessel contents temperature transmitters.

KL28 and KL30 reactor contents temperature element/transmitter

KL27 oven jacket water temperature

KL31 oven jacket water temperature

It can be seen from appendix 2 that there were two non-conformances associated with these particular instruments in the period 2003 to 2009. The first non-conformance, associated with KL4 was found to have no impact on product quality and in any case, product made in the period between calibrations was not required for clinical trial use. KL4 was subsequently decommissioned in favour of a new vessel (previously planned). The second non-conformance, associated with KL5 was assessed as acceptable as it remained within a ± 2°C tolerance range.

CONCLUSION

Based on the above analysis, there are no environmental or regulatory compliance issues with respect to the GxP process measurement instruments used in the Kilo Laboratory. In addition to this there is a high degree of technical oversight on Kilo laboratory scale operations and there has been an acceptable history of performance for the process measurement instruments in question over an extended operational period. It is therefore concluded that there is no justification for conducting final calibrations as part of the Kilo Laboratory closure.

APPENDICES

1. B901 Instrument List
2. B901 Non-conformances

SIGNATURES/APPROVAL

Name:	**Signed:**	**Date:**
Nick Hill GQO – Validation Support		10 FEB 2009
Name:	**Signed:**	**Date:**
John Williams B901 Manager		10 Feb 2009

Copies to:

S. Hailey
G. Napier
S. Smith
J. Williams – for the Closure file
T. Ward

Ref: qaadmin on sannas02/VALIDAION_AND_CHANGE CONTROL/B901 – Kilo Lab/KL closure & final calibration needs.doc

Appendix 1
Kilo Laboratory Final Calibration Assessment

Tag No.	Plant / Equipment Item	Item Description	Category
PT-01	KL4	Vessel Product Line Pressure Transmitter Indicator	GxP
PY-01-21	KL4	Vessel Product Line Pressure Barrier	GxP
TY-05-24	KL4	Vessel Contents Temperature Barrier	GxP
TE-05	KL4	Vessel Contents Temperature Element	GxP
TT-06	KL4	Vessel Product Line Temperature Transmitter	GxP
TT-05	**KL4**	**Vessel Contents Temperature Transmitter**	**GxP**
PRV-001	VP03	VP03 Nitrogen Supply Pressure Regulating Valve	SHE
PT-001	KL31	Hastalloy Chamber Oven Pressure Transmitter	SHE
TI-22	KL28	Reactor Contents Huber Unit Temperature Display	GxP
TE-002	KL28	Head Temperature Element	GxP
TT-002	KL28	Head Temperature Transmitter	GxP
TE-001	**KL28**	**Reactor Contents Temperature Element**	**GxP**
PSL-002	Utilities	Breathing Air Low Alarm Switch	SHE
LSH-001	CT01	Relief Tank High level Switch	SHE
PAL-002	Utilities	Breathing Air Low Alarm DCS Display	SHE
LT-001	ST01	Solvent Recovery Level Transmitter	SHE
QX-001-CH1	Water	Circulation Loop Return Conductivity Recorder CH1	GxP
TIC-001	KL29	Filter Jacket Controller Temperature Output	GxP
QX-001	Water	Circulation Loop Rreturn Conductivity Transmitter	GxP
TY-001	KL29	Filter Jacket Temperature Barrier	GxP
TI-05	KL4	Vessel Contents Temperature DCS Display	GxP
TI-001	**KL29**	**Filter Jacket Temperature DCS Display**	**GxP**
PI-01	KL4	Vessel Product Line Pressure DCS Display	GxP
TE-001	KL30	Reactor Contents Temperature Element	GxP
TT-001	**KL30**	**Reactor Contents Temperature Transmitter**	**GxP**
PI-27	KL20	Vessel Filter Pressure Gauge	SHE
TE-06	KL1	Vessel Vent Temperature Element	GxP
TT-06	KL1	Vessel Vent Temperature Transmitter	GxP
SE-01	KL1	Vessel Agitator Speed Element	GxP
TE-05	KL1	Vessel Contents Temperature Element	GxP
TT-05	**KL1**	**Vessel Contents Temperature Transmitter**	**GxP**
TE-10	KL1	Vessel Outlet Temperature Element	GxP
TT-10	KL1	Vessel Outlet Valve Temperature Transmitter	GxP
PT-01	KL1	Vessel Pressure Transmitter	GxP
SI-01	KL1	Vessel Agitator SIC DCS Display	GxP
PI-01	KL1	Vessel Pressure DCS Display	GxP
TI-06	KL1	Vessel Vent Temperature DCS Display	GxP
TI-10	KL1	Vessel Outlet Valve Temperature DCS Display	GxP
TE-001	ST01	Solvent Recovery Supply Temperature Element	SHE
TT-001	ST01	Solvent Recovery Supply Temperature Transmitter	SHE
PI-04	NS-01	Laboratory Nitrogen Pressure Indicator	SHE
PT-04	NS-01	Laboratory Nitrogen Pressure Transmitter	SHE
TT-001	VP03	VP03 Inlet Temperature Transmitter	SHE
TT-002	VP03	VP03 Exhaust Temperature Transmitter	SHE
PDIHL-01	KL32	Booth Supply HEPA Differential Pressure Indicator	SHE
PDIHL-02	KL32	Booth Extract Pre-Filter Differential Pressure	SHE
PDIHL-03	KL32	Booth Extract HEPA Differential Pressure	SHE
PDIHL-04	KL32	Booth Supply Fan Differential Pressure	SHE
PDIHL-05	KL32	Booth Extract Fan Differential Pressure	SHE
PDSH-01	KL32	Booth Supply HEPA Differential Pressure	SHE
PDSH-02	KL32	Booth Extract Pre-Filter Differential Pressure	SHE
PDSH-03	KL32	Booth Extract HEPA Differential Pressure	SHE
PDSL-04	KL32	Booth Supply Fan Differential Pressure	SHE
PDSL-05	KL32	Booth Extract Fan Differential Pressure	SHE
TI-002	KL28	Head Temperature Local Indicator	GxP

Appendix 1
Kilo Laboratory Final Calibration Assessment

TY-001	VP03	VP03 Inlet Temperature IS Barrier	SHE
TY-002	VP03	VP03 Exhaust Temperature IS Barrier	SHE
PY-002	VP03	VP03 Exhaust Pressure IS Barrier	SHE
TT-003CH2	Water	Circulation Loop Return Conductivity/Temperature Recorder CH2	GxP
FT-003-Disp	Water	Vent Temperature Display	GxP
TE-001	Water	Tank Temperature Element	GxP
TT-001CH3	Water	Tank Temperature Recorder CH3	GxP
TE-002	Water	Pure Water Cooling Heat Exchange Temperature Element	GxP
TIC-002	Water	Pure Water Cooling Heat Exchange Temperature Indicating Controlle	GxP
TT-003	Water	Circulation Loop Return Conductivity/Temperature Transmitter	GxP
TR-1	Store	Raw Material Humidity Recorder	GxP
TR-2	Store	Raw Material Temperature Recorder	GxP
TR-2	Store	Raw Material Humidity Recorder	GxP
TR-1	Store	Raw Material Temperature Recorder	GxP
TE-01	KL9	Rotary Bath Evaporator Temperature Element	GxP
TI-01	KL9	Rotary Bath Evaporator Temperature Indicator	GxP
TT-01	KL9	Rotary Bath Evaporator Temperature Transmitters	GxP
PI-001	KL29	Filter Dryer Chamber Pressure DCS Display	SHE
TY-01-43	KL9	Rotary Bath Evaporator Temperature Barrier	GxP
PY-01	KL1	Vessel Pressure Barrier	GxP
TY-05-30	KL1	Vessel Contents Temperature Barrier	GxP
TY-06-31	KL1	Vessel Vent Temperature Barrier	GxP
TY-10-32	KL1	Vessel Outlet Valve Temperature Barrier	GxP
TY-06-19	KL3	Vessel Product Line Temperature Barrier	GxP
TIC-001	**KL27**	**Oven Jacket Water Temperature PV Output Controller Display**	**GxP**
PIT-001	KL27	Hastalloy Chamber Oven Pressure Transmitter Local Indicator	SHE
PI-001	KL27	Hastalloy Chamber Oven Pressure DCS Display	SHE
PT-001	KL27	Hastalloy Chamber Oven Pressure Transmitter	SHE
TE-001	VP04	Inlet Temperature Element	SHE
TT-001	VP04	Inlet Temperature Transmitter	SHE
TE-002	VP04	Exhaust Temperature Element	SHE
TT-002	VP04	Exhaust Temperature Transmitter	SHE
TI-001-PV	**KL27**	**Oven Jacket Water Temperature PV DCS Display**	**GxP**
TI-002-SP	KL27	Oven Jacket Water Temperature SP DCS Display	GxP
PY-001	KL27	Oven Pressure IS Barrier	SHE
PI-001	KL31	Hastalloy Chamber Oven Pressure DCS Display	SHE
PIT-001	KL31	Hastalloy Chamber Oven Pressure Transmitter Local Indicator	SHE
PY-01	KL31	Oven Pressure IS Barrier	SHE
TI-001-PV	KL31	Oven Jacket Water Temperature PV DCS Display	GxP
TI-002-SP	KL31	Oven Jacket Water Temperature SP DCS Display	GxP
TIC-001	KL31	Oven Jacket Water Temperature PV Controller Display	GxP
TI-001	VP04	Inlet Temperature DCS Display	SHE
TY-01	VP04	Inlet Temperature IS Barrier	SHE
TI-002	VP04	Exhaust Temperature DCS Display	SHE
TY-002	VP04	Exhaust Temperature IS Barrier	SHE
PI-002	VP04	Exhaust Pressure DCS Display	SHE
PY-002	VP04	Exhaust Pressure IS Barrier	SHE
SE-01	KL4	Vessel Agitator Speed Element	GxP
TE-06	KL4	Vessel Product Line Temperature Element	GxP
PT-002	VP04	Exhaust Pressure Transmitter	SHE
TT-10	KL2	Vessel Outlet Valve Temperature Transmitter	GxP
TT-05	**KL2**	**Vessel Contents Temperature Transmitter**	**GxP**
TE-06	KL5	Vessel Header Temperature Element	GxP
TT-06	KL5	Vessel Header Temperature Transmitter	GxP
TE-06	KL6	Vessel Header Temperature Element	GxP
PT-01	KL2	Vessel Product Line Pressure Transmitter Indicator	GxP
TE-05	KL2	Vessel Contents Temperature Element	GxP
TE-06	KL2	Vessel Product Line Temperature Element	GxP
TT-06	KL2	Vessel Product Line Temperature Transmitter	GxP

Appendix 1
Kilo Laboratory Final Calibration Assessment

TE-05	KL6	Vessel Contents Temperature Element	GxP
TT-05	**KL6**	**Vessel Contents Temperature Transmitter**	**GxP**
PT-01	KL5	Vessel Product Line Pessure Transmitter Indicator	GxP
PT-01	KL6	Vessel Pressure Transmitter	GxP
TE-10	KL2	Vessel Outlet Valve Temperature Element	GxP
TY-10-41	KL2	Vessel Outlet Valve Temperature Barrier	GxP
PY-01-01	KL2	Vessel Product Line Pressure Barrier	GxP
SE-01	KL2	Vessel Agitator Speed Element	GxP
TY-05-04	KL2	Vessel Contents Temperature Barrier	GxP
TY-06-05	KL2	Vessel Product Line Temperature Barrier	GxP
SE-01	KL5	Vessel Agitator Speed Element	GxP
TE-05	KL5	Vessel Contents Temperature Element	GxP
SE-01	KL6	Vessel Agitator Speed Element	GxP
TT-06	KL6	Vessel Header Temperature Transmitter	GxP
TE-10	KL6	Vessel Bottom Valve Temperature Element	GxP
TT-10	KL6	Vessel Bottom Valve Temperature Transmtter	GxP
TT-05	KL5	Vessel Contents Temperature Transmitter	GxP
PY-01-08	KL5	Vessel Product Line Pessure Barrier	GxP
TY-05-11	KL5	Vessel Contents Temperature Barrier	GxP
TY-06-12	KL5	Vessel Header Temperature Barrier	GxP
PT-002	VP03	VP03 Exhaust Pressure Transmitter	SHE
PY-01-33	KL6	Vessel Pressure Barrier	GxP
TY-05-36	KL6	Vessel Contents Temperature Barrier	GxP
TY-06-37	KL6	Vessel Header Temperature Barrier	GxP
TY-10-38	KL6	Vessel Bottom Valve Temperature Barrier	GxP
PT-001	KL29	Filter Dryer Chamber Pressure Transmitter	SHE
TI-001	KL28	Reactor Contents Temperature DCS Display	GxP
PT-01	KL3	Vessel Product Line Pressure Transmitter Indicator	GxP
TE-05	KL3	Vessel Contents Temperature Element	GxP
TT-05	**KL3**	**Vessel Contents Temperature Transmitter**	**GxP**
TE-06	KL3	Vessel Product Line Temperature Element	GxP
TT-06	KL3	Vessel Product Line Temperature Transmitter	GxP
TE-10	KL3	Vessel Outlet Temperature Element	GxP
TT-10	KL3	Vessel Outlet Temperature Transmitter	GxP
SE-01	KL3	Vessel Agitator Speed Element	GxP
SY-01	KL2	Vessel Agitator Speed Barrier	GxP
SY-01-01B	KL5	Vessel Agitator Speed Barrier	GxP
SY-01-26-2	KL1	Vessel Agitator Speed Barrier	GxP
SY-01-26B	KL6	Vessel Agitator Speed Barrier	GxP
TI-05	KL1	Vessel Contents Temperature DCS Display	GxP
LAH-001	CT01	Relief Tank High level DCS Display	SHE
LY-001-17B	CT01	Relief Tank High level Barrier	SHE
LI-001	ST01	Solvent Recovery Level DCS Display	SHE
LY-001-06	ST01	Solvent Recovery Level Barrier	SHE
TI-001	KL30	Reactor Contents Temperature DCS Display	GxP
FAL-01	Scrubbers	Scrubber No.1 Flow DCS Display	SHE
FS-01	Scrubbers	Scrubber No.1 Low Flow Proximity Switch	SHE
FY-01	Scrubbers	Scrubber No.1 Flow Barrier	SHE
FAL-02	Scrubbers	Scrubber No.2 Low Flow Proximity Switch	SHE
FS-02	Scrubbers	Scrubber No.2 Flow DCS Display	SHE
FY-02	Scrubbers	Scrubber No.2 Flow Barrier	SHE
TI-001	ST01	Solvent Recovery Supply Temperature DCS Display	SHE
TY-001	ST01	Solvent Recovery Supply Temperature Barrier	SHE
PY-001-40	KL29	Filter Dryer Chamber Pressure Barrier	SHE
SI-01	KL4	Vessel Agitator DCS Display	GxP
TI-06	KL4	Vessel Product Line Temperature DCS Display	GxP
TY-06-25	KL4	Vessel Product Line Temperature Barrier	GxP
PI-01	KL5	Vessel Pressure DCS Display	GxP
TI-06	KL5	Vessel Header Temperature DCS Display	GxP

Appendix 1
Kilo Laboratory Final Calibration Assessment

TI-10	KL2	Vessel Outlet Valve Temperature DCS Display	GxP
PI-01	KL2	Vessel Product Line Pressure DCS Display	GxP
SI-01	KL2	Vessel Agitator SIC DCS Display	GxP
TI-05	KL2	Vessel Contents Temperature DCS Display	GxP
TI-06	KL2	Vessel Product Line Temperature DCS Display	GxP
SI-01	KL5	Vessel Agitator Speed DCS Display	GxP
SI-01	KL6	Vessel Agitator SIC DCS Display	GxP
PI-01	KL6	Vessel Header Pressure DCS Display	GxP
TI-05	KL6	Vessel Contents Temperature DCS Display	GxP
TI-06	KL6	Vessel Header Temperature DCS Display	GxP
TI-10	KL6	Vessel Bottom Valve Temperature DCS Display	GxP
TI-05	KL5	Vessel Contents Temperature DCS Display	GxP
PI-01	KL3	Vessel Product Line Pressure DCS Display	GxP
TI-05	KL3	Vessel Contents Temperature DCS Display	GxP
TI-06	KL3	Vessel Product Line Temperature DCS Display	GxP
TI-10	KL3	Vessel Outlet Temperature DCS Display	GxP
TY-10-42	KL3	Vessel Outlet Temperature Barrier	GxP
PY-01-15	KL3	Vessel Product Line Pressure Barrier	GxP
SI-01	KL3	Vessel Agitator Speed DCS Display	GxP
SY-01-02A	KL3	Vessel Agitator Speed Barrier	GxP
TY-05-18	KL3	Vessel Contents Temperature Barrier	GxP
LS-001		Effluent Sump Fire Water Level Switch	
LS-003		Effluent Sump Fire Water Level Switch	
AI-01	Water	Pure Water TOC Analyser	GxP

B901 Non-Conformances

BLD	LOOP No	TAG NUMBER	PLANT ITEM	ITEM DESCRIPTION	JOB NUMBER	CATEGORY	DATE RETURNED	COMMENTS
901	L1109	TI-21	KL 30	Temperature Indicator Local	754165	GMP	28-Apr-03	Update I drive with new range
901	L11109	TT-002/TE-002	KL30	Head Temperature Transmitter	20247512	GMP	08-Jan-07	No GMP impact. Change category from GMP to OPS
901	L11151	PIT 01	KL29	Filter Dryer Vessel Pressure Transmitter	20300311	GMP	08-Oct-07	No issues as material is dried
901	L11151	PT-001	KL29	Filter Dryer Chamber Pressure Transmitter	9009202-0	GMP		
901	L11151	PY-001-40	KL29	Filter Dryer Vessel Pressure Barrier	20300311	GMP	08-Oct-07	equipent has not been used since 17/11/06
901	L12523	PDSL04	KL32	Supply Fan Differential Pressure Switch	20295626	SHE	03-Sep-07	Technicians check green band on local gauge
901	L13023	FT003-Disp	Water	Vent Temperature Display	20295627	GMP	05-Jul-07	No GMP impact with water quality during routing testing
901	L13144	PT 02	VP04	Exhaust Pressure Tranmitter	20304067	GMP		
901	L6051	KL2-PT-01	KL2 Vessel	Vessel Product Line Pressure	2018154	GMP	01-Dec-05	
901	L6051	PIT01	KL2 Vessel	Product line Indicator	581465	GMP	05-Jul-01	
901	L6051	PT-001	KL2	Vessel Product Line Pressure Tx	20350251	GMP	07-May-08	No Impact on product quality wilnilst in error. Information only for this instrument quality parameter never set around Pressure/Vac in Process.
901	**L6077**	**N/A**	**KL5**	**Vessel Contents Temperature Transmitter**	**20305553**	**GMP**	**25-Sep-07**	**Vessel temperatures deemed acceptable to tolerance ±2°C**
901	L6077	TT-005/TE-005	KL-5	Vessel Contents Pressure Tx.	40533	GMP	02-Nov-06	
901	L6083	PIT-01	KL3	Vessel Product Line Pressure	20143099	GMP	05-Jul-05	
901	L6099	PIT01	KL4	Pressure Transmitter	759966	GMP	15-May-03	
901	**L6109**	**TT05**	**KL4**	**Vessel Contents Temperature Transmitter**	**20289856**	**GMP**	**25-Jul-07**	**Vessel decommissioned see QCS record 4915**
901	L8447	PI-01	KL-6	Pressure Transmitter	40540	GMP	02-Nov-06	tolerence increased to 2%
901	N/A	PIT-001	KL01	Reactor Pressure Tx	824407	GMP	15-Jan-04	no further action required
901	N/A	PT 001	KL29	Chamber Pressure Transmitter	836628	GMP		no further action required
901	N/A	TIC-001	KL29	Jacket Temperature Controller Disp	836629	GMP		No further action required
901	N/A	TR-1	Chemical Store	Raw Material Humidity Recorder	9007786-0	GMP	01-Jul-08	Equipment has been corrected. Store is not used to store API and all intermediates are sealed in double polybags and protected from moisture uptake by bag closures.
901	N/A	TR2	Store	Raw Material Temperature Recorder	20295622	GMP	02-Oct-07	Please review calibration accuracy to 2°C