PAB/CRPMC and Site Pharmacists Network Sessions 2018:

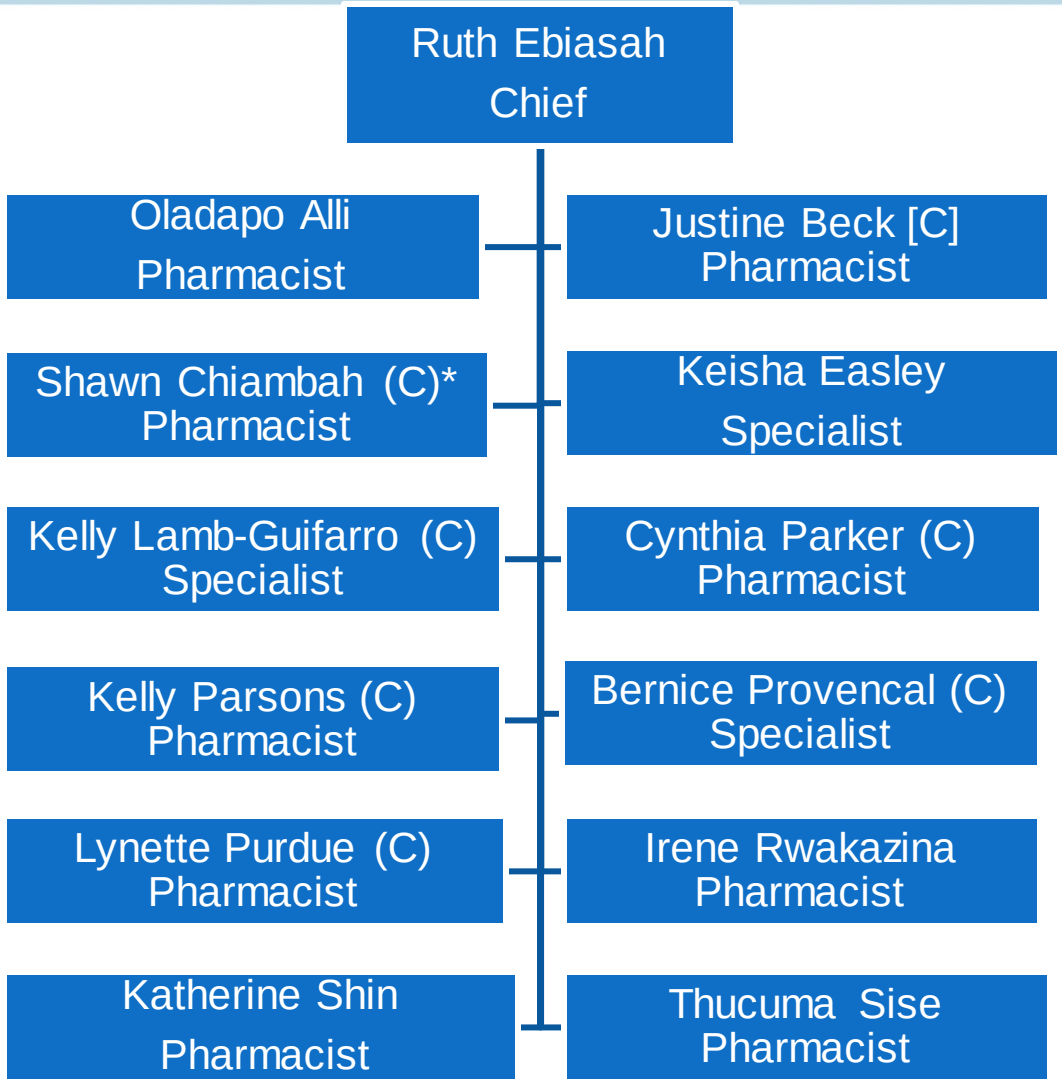
Inspection Readiness and Quality Management

Pharmaceutical Affairs Branch (PAB)

Ruth Ebiasah, Pharm.D., M.S., R.Ph.

PAB Branch Chief

Pharmaceutical Affairs Branch



C = Contractor

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Ruth Ebiasah, Pharm.D., M.S., R.Ph.

- **DAIDS PAB Branch Chief**
- **Worked in DAIDS PAB from 2009-2013, then September 2016-present**
- **Fun Facts:**
  - I represent the Bison and Buckeye (alma maters are Howard University and The Ohio State University)
  - Love to read crime and mystery thrillers
  - Am a Trekkie at heart and Twilight Zone fanatic
  - No time for hobbies! I have three boys!!

Oladapo Alli, Pharm.D., R.Ph.

- **Working at DAIDS PAB since 2014**
- **CTU Portfolio:**
  - Columbia Partnership for Prevention and Control of HIV/AIDS CTU
  - Thailand HIV/AIDS and Infectious Diseases (Thai) CTU
  - United States Military HIV Research Program (MHRP) CTU
  - Stellenbosch University CTU
  - Weill Cornell Medical College-New Jersey Medical School CTU
- **Protocol Portfolio:** A5332, A5353, A5354, A5343, A5356, A5360, HVTN 115, HVTN 098, HVTN 125, HVTN 124, IMPAACT 2001, 2006; Geovax (under development), RV398
- **Fun Fact:** Enjoys traveling the world

Justine Beck, Pharm.D., R.Ph., BCPS

- **Working at DAIDS since 2017**
- **CTU Portfolio:**
  - Integrated University of Puerto Rico CTU
  - Miami Treatment and Prevention CTU
  - University of Rochester HIV/AIDS CTU
  - Terry Beirn CPCRA CTU, Vanderbilt CTU
- **Protocol Portfolio:** A5300B/I2003B (PHOENIx), A5324, A5362, A5371, A5374, A5372s, IMPAACT 2005, IMPAACT 2014, IMPAACT 2020, HVTN 128
- **Fun Fact:** Enjoys cooking and baking.

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Kelly Parsons, Pharm.D., R.Ph., BCPS

- **Working at DAIDS since 2017**
- **CTU Portfolio:**
  - Pitt-Ohio State CTU
  - Alabama CTU
  - Matero Reference Clinic CRS
  - UAB HIVTR-CCR5 Non-Network CRS
- **Protocol Portfolio:** A5365, A5367, A5375, A5376, IMPAACT 2009, IMPAACT 2019, IMPAACT 2021, P1110
- **Fun Fact:** Loves to play tennis

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Lynette Purdue, Pharm.D., R.Ph.

- **Working at DAIDS PAB since 1992**
- **CTU Portfolio:**
  - Johns Hopkins University Kampala HIV CTU
  - The Johns Hopkins Baltimore-Washington-India (BWI) CTU
  - The Johns Hopkins University-Blantyre CTU
  - Vanderbilt CTU
  - Terry Beirn CPCRA CTU
  - HIV Centers for Underrepresented Populations in Research (HIV Cure) CTU
  - Harvard/Boston/Providence (Harvard/B/P) CTU
- **Protocol Portfolio:** IMPAACT 1081, 1092, 1112, 1115, 2007, 2008, 2010, 2013, 2015; HVTN 116, HPTN 077, RV397, RV398
- **Fun Fact:** Lynette painted the picture in the background of her photograph!

Irene Rwakazina, Pharm.D., R.Ph., CCRP

- **Working at DAIDS PAB since 2016**
- **CTU Portfolio:**
  - Soweto Clinical Trials Unit for NIAID Networks CTU
  - UZ-UCSF CTU
  - University of North Carolina Global HIV Prevention and Treatment CTU
  - Impacta Peru CTU
  - Case CTU
- **Protocol Portfolio:** A5363, A5366, IMPAACT 2017, HVTN 107, HVTN 108, HVTN 111, HVTN 114, HVTN 120, HVTN 126, HVTN 702
- **Fun Fact:** Loves dancing, especially Latin dances: salsa, bachata, merengue.

Katherine Shin, Pharm.D., R.Ph.

- **Working at DAIDS PAB since 2004**
- **CTU Portfolio:**
  - University of Cape Town CTU
  - WITS HIV Research Group CTU
  - CAPRISA Clinical Trials Unit for AIDS/ Tuberculosis Prevention and Treatment
  - Emory CDC CTU
  - Philadelphia HIV Therapeutics and Prevention CTU
  - Chinese CTU for HIV Research CTU
  - UCLA AIDS Prevention and Treatment CTU
  - San Francisco Bay CTU
- **Protocol Portfolio:** A5264, A5279, A5357, A5359, P1078, P1090, HVTN 100, HVTN 122, HVTN 703/HPTN 081, HVTN704/HPTN 085, HPTN 076, HPTN 083, HPTN 084, HIVTR CCR5,
- **Fun Fact:** Used to be a site pharmacist for DAIDS studies at U. Maryland and U. of Pennsylvania and loves to travel

Thucuma Sise, Pharm.D., R.Ph., BCPS

- **Working at DAIDS PAB since 2011**
- **CTU Portfolio:**
  - Seattle-Lausanne CTU
  - The Fiocruz Therapeutic and Prevention HIV/AIDS CTU
  - The UCSD CD4 Collaborative CTU
  - Botswana-Harvard School of Public Health AIDS Initiative Partnership CTU
  - Chicago CTU
  - GHESKIO HIV CTU
- **Protocol Portfolio:** P1101, P1108, P1093, P1076, P1066, IMPAACT 2014, A5336, A5300, A5274, A5325, A5327
- **Fun Fact:** Loves to cook and travel!

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Keisha Easley, MSA, CPhT

- **Working at DAIDS PAB since 2009**
- **CTU Portfolio:**
  - Columbia Partnership for Prevention and Control of HIV/AIDS CTU
  - Thailand HIV/AIDS and Infectious Diseases (Thai) CTU
  - United States Military HIV Research Program (MHRP) CTU
  - Stellenbosch University CTU
  - Weill Cornell Medical College-New Jersey Medical School CTU
  - Soweto Clinical Trials Unit for NIAID Networks CTU
  - UZ-UCSF CTU
  - University of North Carolina Global HIV Prevention and Treatment CTU
  - Impacta Peru CTU
  - Case CTU
  - Pitt-Ohio State CTU
  - Alabama CTU
  - Matero Reference Clinic CRS
  - UAB HIVTR-CCR5 Non-Network CRS
- **Protocol Portfolio:** PAB REPRIEVE Project Manager; PAB Site Development Coordinator for AMP and PHOENIX
- **Fun Fact:** Loves to organize for fun!

Bernice (Be) Provencal, MBA/HI, CPhT

- **Working at DAIDS PAB since 2016**
- **CTU Portfolio:**
  - University of Cape Town CTU
  - WITS HIV Research Group CTU
  - CAPRISA Clinical Trials Unit for AIDS/ Tuberculosis Prevention and Treatment
  - Emory CDC CTU
  - Philadelphia HIV Therapeutics and Prevention CTU
  - Chinese CTU for HIV Research CTU
  - UCLA AIDS Prevention and Treatment CTU
  - San Francisco Bay CTU
  - Soweto Clinical Trials Unit for NIAID Networks CTU
  - UZ-UCSF CTU
  - University of North Carolina Global HIV Prevention and Treatment CTU
  - Impacta Peru CTU
  - Case CTU
- **Protocol Portfolio:** PAB Site Development Coordinator for HPTN 083 and HPTN 084
- **Fun Fact:** Can speak fluent German

New PAB Members

Pharmacy Specialist

Kelly Lamb-Guifarro

Pharmacists

Cynthia Parker

Shawn Chiambah

(Start Date- June 25th)

Presentation Overview

- Temperature Excursion Reporting Form (TERF)
- Incident Report Form (IRF)
- Inspection Readiness Overview
- Quality Management
- Q & A

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Temperature Excursion Reporting Form

Temperature Excursion Reporting Form- Page 1

Division of AIDS (DAIDS)
Pharmaceutical Affairs Branch (PAB)

Temperature Excursion Reporting Form

This form serves to notify the Pharmaceutical Affairs Branch (PAB) at the Division of AIDS (DAIDS) of a temperature excursion that occurred in the Clinical Research Site Pharmacy. The Pharmacist of Record (PoR) or Associate Pharmacist (AP) must use this Temperature Excursion Reporting Form to communicate the details of the temperature excursion as soon as s/he becomes aware of the temperature excursion.

Instructions to the Pharmacist: Please complete form and sign, scan, & submit the completed form via email to the CRPMC (crpmctempex@thermofisher.onmicrosoft.com). Electronic signature of the completed form is permitted. Instructions for the final disposition of affected study product will be provided after review of the information provided. *An additional Incident Report Form may be required upon PAB request.*

Quarantine all affected study products immediately at the appropriate storage temperature while awaiting determination of suitability for continued use. Clearly label products as "quarantined" and separate from unaffected products

CRS Name(s):								CRS Number(s):	Pharmacy Org ID#	
Pharmacist Name and Title (PoR/AP):				Email Address:					Phone Number:	
Protocol Number	Product Name/ Strength/Package Size	Lot Number/ NSC Number	Exp. Date/ Retest Date/ Mfg. Date [dd-mmm-yy]	Quantity	Appropriate Temperature Storage Range (specify C or F)	Excursion Temperature (specify C or F)	Duration of Exposure (specify min, hrs., days)	Date(s) of Excursion [dd-mmm-yy]	FINAL DISPOSITION (FOR CRPMC USE ONLY)	[dd-mmm-yy]
								From: _____ To: _____	☐ Suitable for use ☐ Not Suitable for use	Date _____
								From: _____ To: _____	☐ Suitable for use ☐ Not Suitable for use	Date _____
								From: _____ To: _____	☐ Suitable for use ☐ Not Suitable for use	Date _____
								From: _____ To: _____	☐ Suitable for use ☐ Not Suitable for use	Date _____
								From: _____ To: _____	☐ Suitable for use ☐ Not Suitable for use	Date _____

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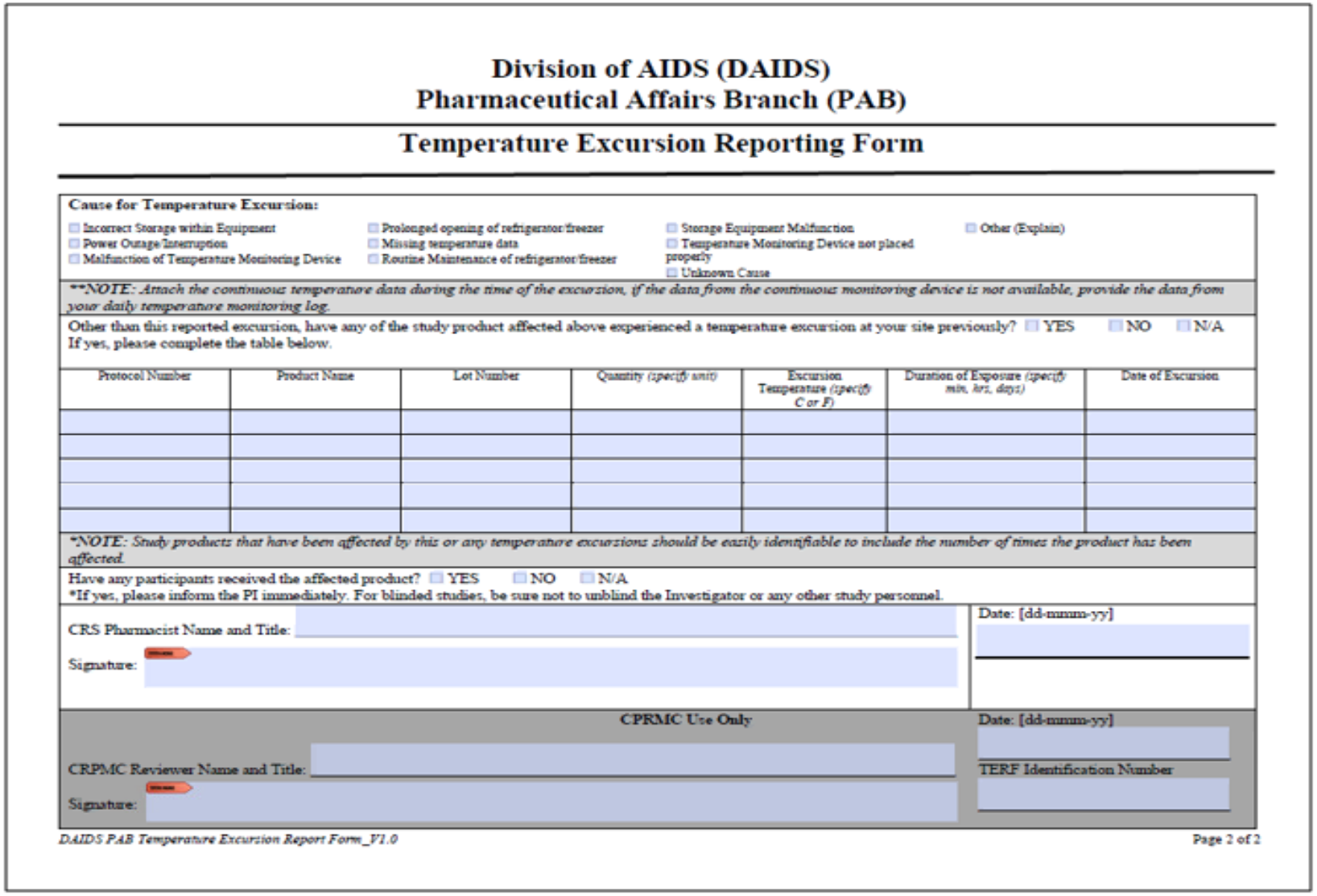
Temperature Excursion Reporting Form- Page 2



Division of AIDS (DAIDS)
Pharmaceutical Affairs Branch (PAB)

Temperature Excursion Reporting Form

Cause for Temperature Excursion:

- ☐ Incorrect Storage within Equipment
- ☐ Power Outage/Interruption
- ☐ Malfunction of Temperature Monitoring Device
- ☐ Prolonged opening of refrigerator/freezer
- ☐ Missing temperature data
- ☐ Routine Maintenance of refrigerator/freezer
- ☐ Storage Equipment Malfunction
- ☐ Temperature Monitoring Device not placed properly
- ☐ Unknown Cause
- ☐ Other (Explain)

***NOTE: Attach the continuous temperature data during the time of the excursion, if the data from the continuous monitoring device is not available, provide the data from your daily temperature monitoring log.*

Other than this reported excursion, have any of the study product affected above experienced a temperature excursion at your site previously? ☐ YES ☐ NO ☐ N/A
If yes, please complete the table below.

Protocol Number	Product Name	Lot Number	Quantity *(specify unit)*	Excursion Temperature *(specify C or F)*	Duration of Exposure *(specify min, hrs, days)*	Date of Excursion

**NOTE: Study products that have been affected by this or any temperature excursions should be easily identifiable to include the number of times the product has been affected.*

Have any participants received the affected product? ☐ YES ☐ NO ☐ N/A
*If yes, please inform the PI immediately. For blinded studies, be sure not to unblind the Investigator or any other study personnel.

CRS Pharmacist Name and Title: _____ Date: [dd-mmm-yy]

Signature: _____

CPRMC Use Only

CRPMC Reviewer Name and Title: _____ Date: [dd-mmm-yy]

Signature: _____ TERF Identification Number

DAIDS PAB Temperature Excursion Report Form_V1.0 Page 2 of 2

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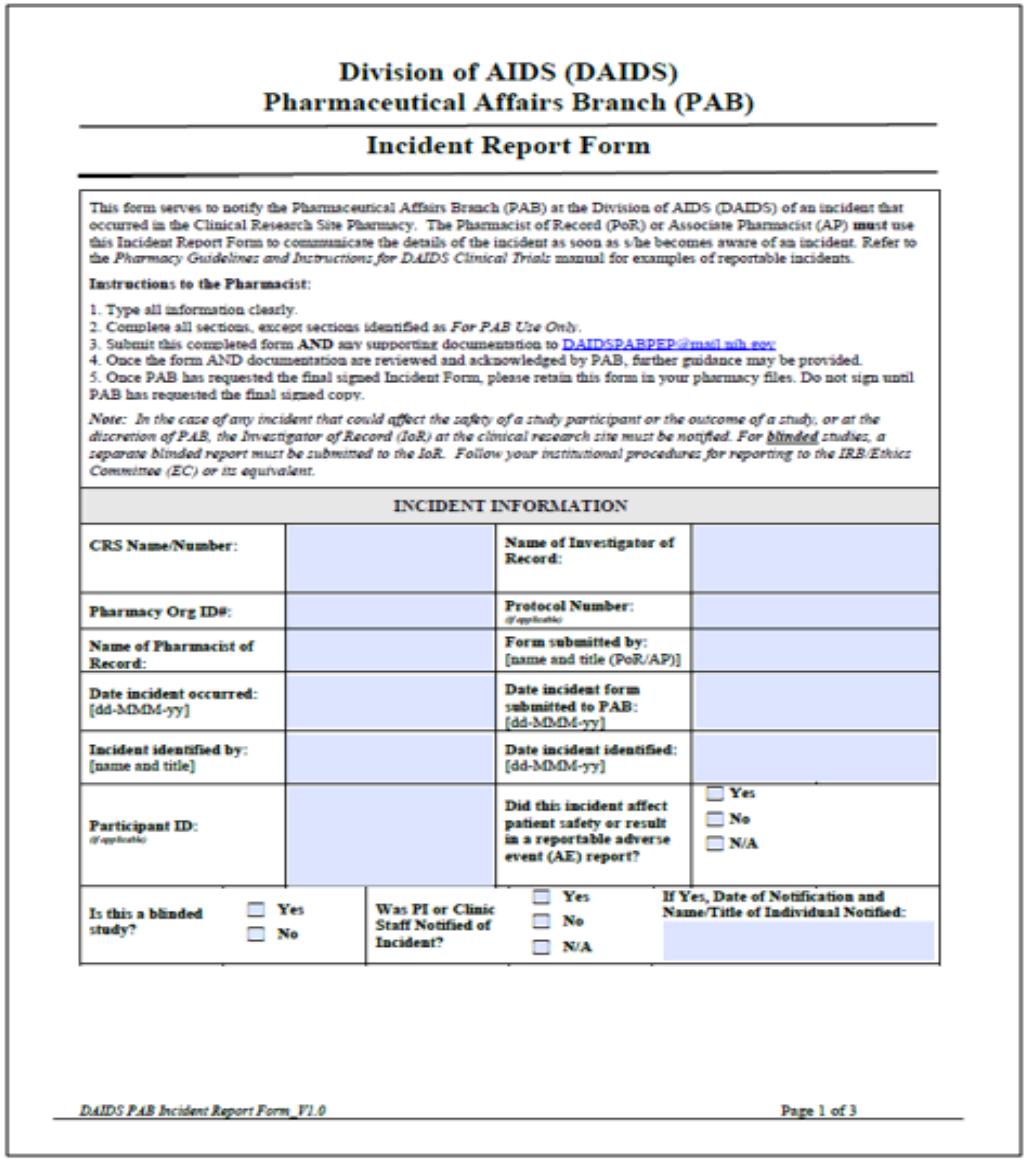
Incident Report Form

Incident Report Form- Page 1



Division of AIDS (DAIDS)
Pharmaceutical Affairs Branch (PAB)

Incident Report Form

This form serves to notify the Pharmaceutical Affairs Branch (PAB) at the Division of AIDS (DAIDS) of an incident that occurred in the Clinical Research Site Pharmacy. The Pharmacist of Record (PoR) or Associate Pharmacist (AP) **must** use this Incident Report Form to communicate the details of the incident as soon as s/he becomes aware of an incident. Refer to the *Pharmacy Guidelines and Instructions for DAIDS Clinical Trials* manual for examples of reportable incidents.

Instructions to the Pharmacist:

1. Type all information clearly.
2. Complete all sections, except sections identified as *For PAB Use Only*.
3. Submit this completed form **AND** any supporting documentation to DAIDSPABPEP@mail.nih.gov
4. Once the form AND documentation are reviewed and acknowledged by PAB, further guidance may be provided.
5. Once PAB has requested the final signed Incident Form, please retain this form in your pharmacy files. Do not sign until PAB has requested the final signed copy.

Note: In the case of any incident that could affect the safety of a study participant or the outcome of a study, or at the discretion of PAB, the Investigator of Record (IoR) at the clinical research site must be notified. For blinded studies, a separate blinded report must be submitted to the IoR. Follow your institutional procedures for reporting to the IRB/Ethics Committee (EC) or its equivalent.

INCIDENT INFORMATION

CRS Name/Number:		**Name of Investigator of Record:**	
Pharmacy Org ID#:		**Protocol Number:** *(If applicable)*	
Name of Pharmacist of Record:		**Form submitted by:** [name and title (PoR/AP)]	
Date incident occurred: [dd-MMM-yy]		**Date incident form submitted to PAB:** [dd-MMM-yy]	
Incident identified by: [name and title]		**Date incident identified:** [dd-MMM-yy]	
Participant ID: *(If applicable)*		**Did this incident affect patient safety or result in a reportable adverse event (AE) report?**	☐ Yes ☐ No ☐ N/A

Is this a blinded study?	☐ Yes ☐ No	**Was PI or Clinic Staff Notified of Incident?**	☐ Yes ☐ No ☐ N/A	**If Yes, Date of Notification and Name/Title of Individual Notified:**

DAIDS PAB Incident Report Form_V1.0 **Page 1 of 3**

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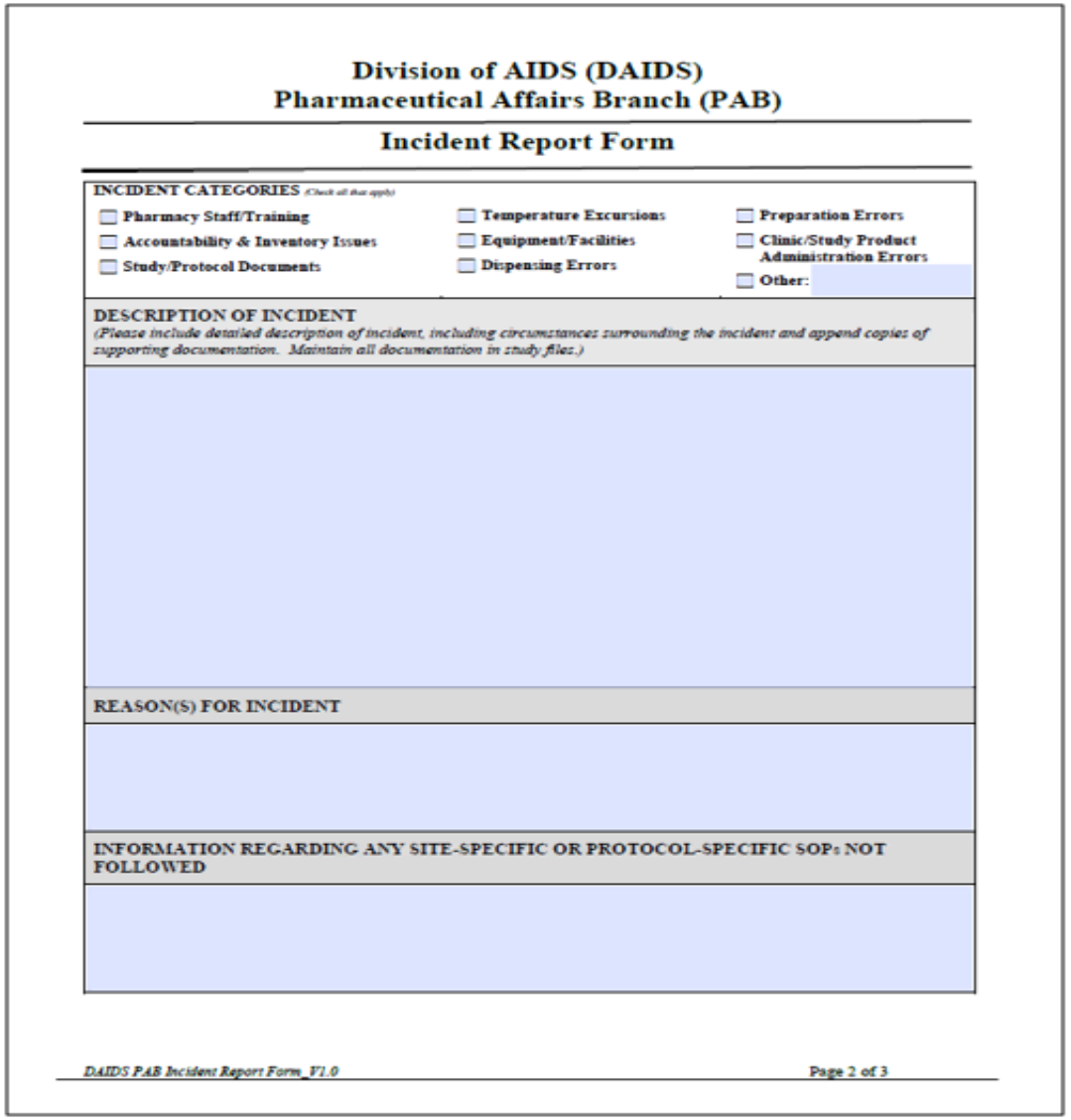
Incident Report Form- Page 2



Division of AIDS (DAIDS)
Pharmaceutical Affairs Branch (PAB)

Incident Report Form

INCIDENT CATEGORIES *(Check all that apply)*

- ☐ Pharmacy Staff/Training
- ☐ Accountability & Inventory Issues
- ☐ Study/Protocol Documents
- ☐ Temperature Excursions
- ☐ Equipment/Facilities
- ☐ Dispensing Errors
- ☐ Preparation Errors
- ☐ Clinic/Study Product Administration Errors
- ☐ Other:

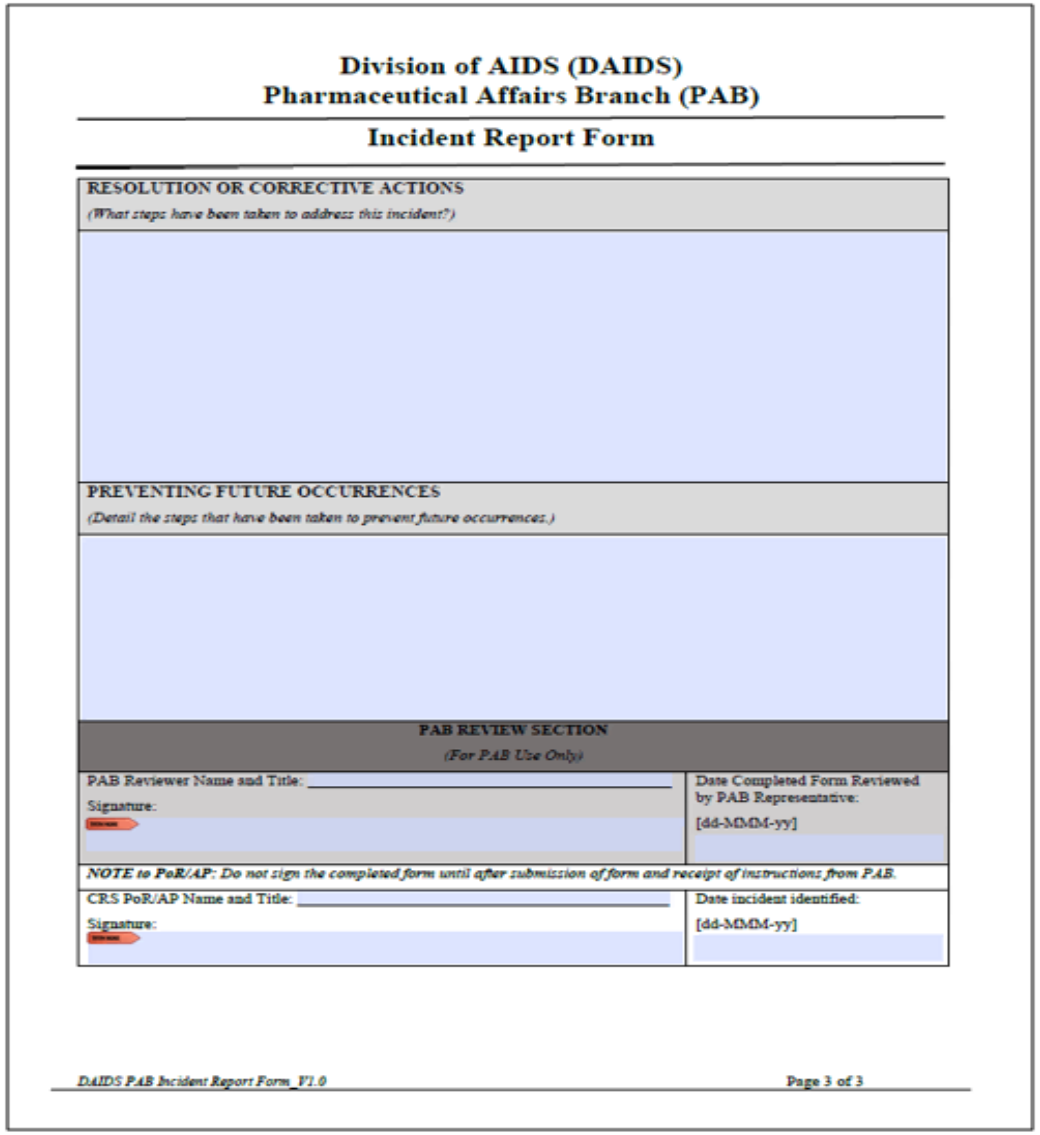
DESCRIPTION OF INCIDENT
(Please include detailed description of incident, including circumstances surrounding the incident and append copies of supporting documentation. Maintain all documentation in study files.)

REASON(S) FOR INCIDENT

INFORMATION REGARDING ANY SITE-SPECIFIC OR PROTOCOL-SPECIFIC SOPs NOT FOLLOWED

DAIDS PAB Incident Report Form_V1.0 Page 2 of 3

Incident Report Form- Page 3



Division of AIDS (DAIDS)
Pharmaceutical Affairs Branch (PAB)

Incident Report Form

RESOLUTION OR CORRECTIVE ACTIONS *(What steps have been taken to address this incident?)*
PREVENTING FUTURE OCCURRENCES *(Detail the steps that have been taken to prevent future occurrences.)*
PAB REVIEW SECTION *(For PAB Use Only)*

PAB Reviewer Name and Title: _____ Signature:	Date Completed Form Reviewed by PAB Representative: [dd-MMM-yy]
***NOTE to PoR/AP:** Do not sign the completed form until after submission of form and receipt of instructions from PAB.*	
CRS PoR/AP Name and Title: _____ Signature:	Date incident identified: [dd-MMM-yy]

DAIDS PAB Incident Report Form_V1.0 Page 3 of 3

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Inspection Readiness Overview

Inspection Readiness Overview

Pharmacy Inspection Quick Reference Guide

Pharmacy	Personnel	Process	Product	Protocol
✓Secure and Clean Pharmacy Facilities	✓CVs of Pharmacists	✓Documentation of All Pharmacy Processes	✓Investigational Study Product Temperature Records	✓IRB Approved Protocol and Clarification Memos
✓Limited Access to Pharmacy Areas (pharmacy personnel only)	✓Licensure & Registration of Pharmacists	✓DAIDS PAB Approved Pharmacy Establishment Plan (PEP) and (PEP) Modules	✓Certificates of Analysis	✓Most Recent Version of the IB or Package Inserts
✓Maintenance Records Available for all Equipment	✓Pharmacist Training Records	✓Pharmacy SOPs	✓Investigator Brochures	✓Compliance to Protocol and Study Documents
✓Investigational Study Products Clearly Marked and Stored in the Pharmacy	✓Signature Lists of Pharmacists		✓Complete Prescription Records	✓Protocol Deviation Reports and Documentation
✓Temperature Monitoring Records on File	✓Signature List of Authorized Prescribers		✓Accurate, Signed, and Dated Accountability Records	✓Authenticity, Accuracy, and Completeness of Data

Quality Management

Quality Management (QM)

"The act of overseeing all activities and tasks needed to maintain a desired level of excellence and quality."

Quality Management (QM)

- Part of overall system of oversight
- Includes all activities involved in quality assurance and quality control to ensure consistency in product or service
- Why is it important in clinical trials?
  - Allows planning for effective protocol implementation
  - Assures compliance with sponsor and applicable regulatory requirements
  - Identifies areas in need of corrective action
  - Verifies data accuracy
  - Assures a constant state of readiness for an external audit or monitoring visit

Quality Management System (QMS)

- Used to direct, control and manage quality in clinical trials to support data completeness and data integrity

- Includes the following components:
  - Defined Quality Requirements (AKA "Quality Planning")
  - Quality control (QC)
  - Quality assurance (QA) Processes
  - Corrective and Preventative action (CAPA) Processes
  - Continuous Quality Improvement (CQI) Activities

➢ Examples: IRF and TERF

Definitions

- Quality Control (QC) **= "Real Time Review"**
  - The real time ("day-to-day") observation and documentation of the sites' work processes to ensure that accepted procedures are followed

- Quality Assurance (QA) = **"Retrospective Review"**
  - The periodic, systematic, objective, and comprehensive examination of the total work effort to determine the level of compliance with Good Clinical Practice (GCP) standards

Clinical Quality Management Plan (CQMP)

- DAIDS has instituted a requirement for each CRS to develop, implement and evaluate a Clinical Quality Management Plan (CQMP).

  - The CQMP is a “living document” that will be updated as site procedures are streamlined and new areas of focus are identified

Clinical Quality Management Plan (CQMP)

- A written document specific to a clinical research setting, encompassing both Quality Control and Quality Assurance procedures, and detailing the scope, responsibility, quality indicators, sample size, and frequency of these activities

- On-site Management Tool
  - Describes QC and QA processes to be implemented for internal evaluation and documentation of performance
  - Identifies and resolves problems at earliest stages
  - Verifies compliance
  - Ensures data accuracy and completeness
  - Protects human subjects rights and welfare
  - Ensures Good Clinical Practice standards and regulatory requirements

Clinical Quality Management Plan (CQMP) Elements

- Roles and Responsibilities of Key Personnel
- Key Quality Indicators
- Description of QM Activities
  - QC Activities
  - QA Activities
  - Description of Tools
- QA Audit Frequency and Sample Size
- Documentation of QM Activities
- Description of CQMP Evaluation Process
- QA Reporting Requirements

Site Clinical Quality Management Plan (CQMP) PI Responsibilities

- The Principal Investigator (PI) is ultimately responsible for:
  - Development
  - Implementation
  - Evaluation

  - May delegate QM activities to the CRS Leader and other clinical research personnel qualified by training and experience
    - Pharmacy Component
      - Must be completed by the Pharmacist of Record (PoR)

Clinical Quality Management Plan (CQMP) Pharmacist of Record Responsibilities

- PAB Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks *(Refer to #16 in Section B.)*

  - PoR must be involved in the development and implementation of a Quality Control (QC) and Quality Assurance (QA) plan for his/her respective pharmacy to ensure that safety and standards of good pharmacy practice are upheld.

  - Pharmacy QC/QA plan helps to ensure that the study participant is dispensed the correct study treatment and dose of the proper drug, biologic, vaccine or radiopharmaceutical, as defined by the protocol.

Clinical Quality Management Plan (CQMP) Pharmacy Component Elements

- Study Product Management Record Keeping
- Study Product Management Processes
  - Study Product Preparation Procedures
  - Study Product Administration Procedures
  - Study Product Storage and Temperature Monitoring Processes
- Staff Training/Qualifications
  - Institutional Specific
  - Protocol Specific
  - DAIDS-Specific

Clinical Quality Management Plan (CQMP) Pharmacy-Specific/Protocol Specific Elements

- Tools, Documents, and Forms
  - Internal Sources
  - External Sources

- Summary Reports
  - Trend Analysis
  - Corrective Action Plans
  - Continuous Quality Improvement Activities

Examples

Contact Information

Pharmaceutical Affairs Branch (PAB)
Email: DAIDSPAB@niaid.nih.gov
Phone: (01) (301) 496-8213

Clinical Research Products Management Center (CRPMC)
Email: BIO.CRPMC@ThermoFisher.com
Phone:(01) (301) 294-0741

Questions or Comments?