



HIV Drug Interactions and Antiretroviral (ARV) Therapeutic Drug Monitoring (TDM) Registry: Attaining Compliance With Clinical Laboratory Improvement Act (CLIA) and the Health Insurance Portability and Accountability Act (HIPAA)

J. Slish, L. Catanzaro, L. Esch, F. Lliguicota, R. DiFrancesco, G. Morse

Laboratory for Antiviral Research School of Pharmacy and Pharmaceutical Sciences, University at Buffalo, The State University of New York

Abstract

HIV Drug Interactions and Antiretroviral (ARV) Therapeutic Drug Monitoring (TDM) Registry: Attaining Compliance With Clinical Laboratory Improvement Act (CLIA) and the Health Insurance Portability and Accountability Act (HIPAA).

J. Slish, L. Catanzaro, L. Esch, F. Lliguicota, R. DiFrancesco, G. Morse. Laboratory for Antiviral Research, University at Buffalo (UB) School of Pharmacy and Pharmaceutical Sciences, New York, USA.

Key Words: Therapeutic Drug Monitoring, Antiretrovirals, Drug Interactions, CLIA, and HIPAA

Background: The HIV Drug Interactions and TDM Registry is a clinical research initiative designed to examine adherence, drug interactions and antiretroviral (ARV) plasma concentrations in HIV-infected subjects. The Clinical Laboratory Improvement Act (CLIA) and Health Insurance Portability and Accountability Act (HIPAA) mandate that such operations follow a standard set of guidelines.

Methods: The UB Laboratory for Antiviral Research (UBLAR) has developed a laboratory program to measure and report ARV concentrations that is compliant with CLIA regulations. The validation of the method was executed in accordance with the FDA guidance for Chromatographic Methods (2001). UBLAR also established a secure, database-driven internet application to provide users a mechanism for data collection and allow submission of plasma samples while maintaining HIPAA compliance. Specimens and the associated data collected do not contain any of the 18 patient identifiers mentioned in the HIPAA regulations. Specimens are uniquely identified by a combination of a random, confidential clinician code and a sample accession number. To comply with HIPAA regulations and ensure patient confidentiality and data protection, UBLAR has implemented policies and procedures that will reduce the probability of data corruption on both personal and networked computer systems. A retrospective analysis of the initial 220 subjects was performed to assess the site registration, data entry and lab results components between 2/11/99 and 10/1/2002. Samples were collected at trough or at designated times post-dosing.

Results: From 220 subjects (158 male, 50 female, and 12 unknown), 302 plasma samples and 10 cerebral spinal fluid samples were submitted for analysis by 11 sites. Subject demographics (%) were Caucasian (42), African American (30), Hispanic (8), Asian (1), Native American (2) and other (18). Median plasma concentrations (mg/mL) are as follows: zalcitabine 1.83, didanosine 3.29, zidovudine 3.19, lopinavir 1.48, nelfinavir 2.01, saquinavir 0.836, and ritonavir 0.192 (ritonavir boosting regimen only). Laboratory responses conducted in November 2002 have yielded a two year certification period.

Conclusion: The Registry has been successfully implemented and the site registration, data entry and ARV assay mechanism are well integrated. CLIA and HIPAA compliance have been achieved. Improvements in database and software design have been made to safeguard the integrity of the data.

Objectives

- Establish a confidential website for site registration.
- Develop a CLIA-compliant assay and a HIPAA-compliant registration mechanism
- Implement a limited-center pilot program to test outcomes of the TDM process.
- Develop a reporting process so that sites receive TDM results with a limited pharmacologic assessment.
- Standardize an approach to collect adherence and concurrent medications information.

Methods

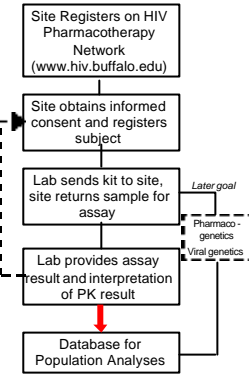
HIPAA Mandated Exclusion Identifiers

- Names
- Geographic info (city, state, zip)
- Elements of dates
- Telephone number
- Fax number
- E-mail address
- Social Security number
- Medical record
- Prescription number
- Health plan beneficiary number
- Account number
- Certificate/license number
- VIN and Serial number
- License plate number
- Device identifiers
- Web URLs
- IP address number
- Biometric identifiers
- Full face photo image
- Comparable photo images
- Unique identifying number

HIPAA Compliant Form

- Specimens and the associated data collected do not contain any of the 18 patient identifiers mentioned in the HIPAA regulations.
- Specimens are uniquely identified by a combination of a random, confidential clinician code and a sample accession number.

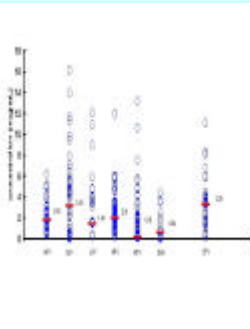
HIV Drug Interactions and Antiretroviral TDM Registry



CLIA Methods

- All laboratory operations are conducted in accordance with the Clinical Laboratory Improvement Act (CLIA) requirements as applied to the Therapeutic Drug Monitoring sections.
- As such, procedures, processes and actions within the laboratory must be executed with the following components in place:
 - Proficiency Testing Program
 - Calibration and Control Procedures
 - Remedial Action Policies
 - Required Personnel Qualifications
 - Documented Personnel Responsibilities
 - Patient Test Management Procedures
 - Comparison of Test Results to Reference Methods
 - Personnel Assessment Program
 - Communications and Complaint Investigation Procedures
- Procedures for All Records and Test Reports
- Test Requisition Requirements
- Test Method/ Equipment/ Instrumentation/ Reagents/ Materials Standard Operating Procedures
- Quality Control and Policy
- Procedure Manual
- Performance Specifications, Equipment Maintenance, and Function Checks

Concentrations versus Antiretroviral



Drug Interactions and TDM Data Report Form

Summary

- CLIA and HIPAA compliance have been achieved for the confidential website registry.
- Currently, twenty-six sites have registered to participate.
- Antiretroviral plasma concentrations were measured for PIs and efavirenz.
- Some early patients had TDM concentrations below assay detection indicating the need to intensify adherence interventions.

Drug Interactions and TDM Data Collection Form

Background:

The HIV Drug Interactions and TDM Registry is a clinical research initiative designed to examine adherence, drug interactions and antiretroviral (ARV) plasma concentrations in HIV-infected subjects. The Registry goals and objectives were presented at the 3rd International Workshop on Clinical Pharmacology of HIV Therapy. This presentation further defines the details required to make the Registry operational within regulatory realms. The UBLAR has established the HIV Pharmacotherapy Network Website (www.hiv.buffalo.edu) as a means of fostering a multicenter exchange of information and the performance of clinical research.

The Clinical Laboratory Improvement Act (CLIA) and Health Insurance Portability and Accountability Act (HIPAA) mandate that such operations follow a standard set of guidelines.

The CLIA standards promote good laboratory practices and assure reliable laboratory results and documentation/records. Regulations under these guidelines define requirements for personnel, procedures, and policies. A laboratory performing assays and reporting results, which are used to treat, diagnose, or manage a patient's care, require certification by CLIA.

HIPAA standards are designed to ensure the privacy of individually identifiable health information by establishing conditions for its use and disclosure by a health plan, healthcare clearinghouse, and certain healthcare providers. Eighteen identifiers have been named which must be excluded from transfer of data outside protected source documentation.

Results Patient Demographics

Race	Caucasian	African American	Hispanic	Asian	Native American	Unreported
Percent (%)	42	30	8	1	2	17
Percent Male	33	20	6	1	2	12
Percent Female	9	10	2	0	0	5

Drug Interactions And TDM Data Report Form

- To comply with HIPAA regulations and ensure patient confidentiality and data protection, UBLAR has implemented policies and procedures that will reduce the probability of data corruption on both personal and networked computer systems.

Individual Antiretroviral Results

Antiretroviral (n)	Concentration Range mg/L (n/N)	Median Concentration mg/L
APV (44)	0.073 -13.17 (1)	1.83
EFV (53)	0.197 -23.60 (4)	3.29
DDV (34)	0.061 -16.13 (3)	3.19
LPV (76)	0.111 -12.66 (24)	1.48
NFV (19)	0.344 -7.32 (2)	2.01
RTV (14)	0.117 -7.54 (4*)	0.192*
SQV (5)	0.140 -4.37 (0)	0.638

Summary of samples collected over prescribed dosing intervals

Conclusions

- The Registry has been successfully implemented and the site registration, data entry and antiretroviral assay mechanisms are well integrated.
- Improvements in database and software design have been made to safeguard the integrity of the data.
- Additional adherence interventions have been incorporated prior to TDM sampling to avoid measuring undetectable specimens.
- A network of clinical sites is evolving that will provide a larger patient database to facilitate population modeling.
- The registry has been utilized to apply for additional funding to support expanded research involving drug interactions and TDM of antiretrovirals.