Final Report
Pharmaceutical Equivalence Drugs Assessment-I (PEDA-I):
Assess the pharmaceutical equivalence of generic antiretrovirals
distributed in Thailand

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Stephen Kerr, Biostatistician, B. Pharm, MIPH, Ph.D.
Narukjaporin Thammajaruk, B. Pharm, M. Pharm
Suwapit Prasertthanawut, B. Pharm

Institute and Laboratory:
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Pharmaceutical Technology Service Center,
Faculty of Pharmaceutical Sciences, Chulalongkorn University
National Health Security Office (NHSO), Thailand

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First of all, we would like to express our gratitude to the Chulalongkorn University which funded this study in code of GRB_BBS_64_58_30_18 through the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

We would also like to express our sincere thankfulness to all primary hospitals and their pharmacists who helped in process of PEDA study and to staff of Faculty of Pharmaceutical Sciences, Chulalongkorn University for pharmacology analysis; and finally, the HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT) staffs, who made a success of this study.
บทความภาษาไทย

วัตถุประสงค์: ประเทศไทยมีแนวโน้มการจ่ายยาจากการรักษาผู้ป่วยติดเชื้อไวรัสเอชไอวีในทุกระดับสังคม เพื่อลดการกระจายเชื้อ และการดำเนินโรคในโรคติดต่อดีเด่นขึ้น เมื่อพิจารณาจากสถานการณ์ อยู่ในรูปแบบลำดับที่สูงที่สุด ไม่ยอมรับจะละเลยเนื่องจากมีความจำเป็นในแต่ละด้าน ประสิทธิ์และความคุมทุน แต่ในอดีตมีผลจัดทุนได้มีรายงานถูกต้องในการที่เกี่ยวกับการที่มีคุณภาพตากล่าวมาตรฐานที่เกี่ยวกับเรื่องในประเทศไทยหรือกําลังพัฒนา จะมีผลเสียต่อผู้ป่วยและระบบสุขภาพ ดังนั้นการประกันคุณภาพยาที่ไม่ดี ท้าทายในการเป็นนั้นที่จําเป็นเพื่อให้เกิดคุณลักษณะด้านประสิทธิภาพ และความปลอดภัยของยาต่างๆ โครงการวิจัยนี้เป็นการศึกษาวิจัยเพื่อประกอบคุณภาพยาโดยสุ่มตัวผู้รักษาไวรัสเอชไอวีในรูปแบบลำดับตามแหล่งต่างๆ ในประเทศไทย รวมถึงประเทศเคาน์เตอร์

วิธีการ: โครงการนี้ได้สุ่มตัวอย่างยาสามชนิด Tenofovir 300 mg, Efavirenz 600 mg และ Lopinavir/ritonavir 200/50mg จากโรงพยาบาลชุมชน 10 แห่งตามภาคต่างๆ ในประเทศไทยที่มีการจ่ายยาด้านคุณภาพสิทธิ์สเปเชียล ที่มีการจ่ายยาต้านไวรัส 2 และ 3 และร้านขายยาเอกชน slight 3 แห่ง (ในประเทศใหญ่ 2 แห่งและเวียดนาม 1 แห่ง) ที่มีผู้ใช้ยาจากคงเหลือกําลังข้ามตัว จุดกลางการพัฒนาที่อยู่ในสู่ในเวียดนาม คุณภาพยา ได้แก่การตรวจสอบคุณภาพและบันทึกของสารออกฤทธิ์ในเม็ดยา ความเสี่ยงของมิจฉาชีพยา และการชะลอยา โดยประเมินเพื่อกำกับการสัญญาต่างๆ ที่ต้องการมีการต่างๆ ที่ต้องการมี

ผลการศึกษา: โครงการสุ่มตัวอย่างยาต้านไวรัส 42 ชุด จากทั้งหมด 15 แห่ง ในเดือนกรกฎาคม-มิถุนายน พ.ศ.2558 ซึ่งยาที่นี้เป็นยาสามชนิดที่ผลิตในประเทศไทย 23 ชุด ประเทศอินเดีย 17 ชุด ประเทศอินเดีย 1 ชุด และประเทศเวียดนาม 1 ชุด ในการตรวจยาพบว่า ยาส่วนใหญ่จะมีคุณภาพดีมากกว่ายาที่ส่งจากประเทศอินเดีย แต่อย่างไรก็ตามทางเวียดนามมีการรับ chooser ที่ส่งไปสามารถกระทำได้โดยไม่มีปัญหาการส่งยาจากประเทศ

สรุป: การศึกษาวิจัยนี้พบว่า ด้วยระดับการต้านไวรัสเอชไอวีที่สูงมีคุณภาพที่ได้มาตรฐาน แต่การที่ยึดตามสามารถต่างชื่อได้จากผู้รับยาจากอินเดียไม่ทำให้ผู้ติดเชื้อเอชไอวีรู้จักการติดตามการใช้ยาที่เหมาะสม ซึ่งอาจส่งผลต่อการต้านไวรัสenty และการต้านต่อไป
Pharmaceutical Equivalence of Distributed Generic Antiretroviral (ARV) in Asian settings: the cross-sectional surveillance study – PEDA study

Abstract

Objectives: Ensuring that medicines meet quality standards is mandatory for ensuring safety and efficacy. There have been occasional reports of substandard generic medicines, especially in resource-limiting settings where policies to control quality may be less rigorous. As HIV treatment in Thailand depends mostly on affordable generic antiretrovirals (ARV), we performed quality assurance testing of several generic ARV available from different sources in Thailand and a source from Vietnam.

Methods: We sampled Tenofovir 300 mg, Efavirenz 600 mg and Lopinavir/ritonavir 200/50mg from 10 primary hospitals randomly selected from those participating in the National AIDS Program, 2 non-government organization ARV clinics, and 3 private drug stores. Quality of ARV was analyzed by blinded investigators at the Faculty of Pharmaceutical Science, Chulalongkorn University. The analysis included an identification test for drug molecules, a chemical composition assay to quantitate the active ingredients, a uniformity of mass test and a dissolution test to assess in-vitro drug release. Comparisons were made against the standards described in the WHO international pharmacopeia.

Results: A total of 42 batches of ARV from 15 sources were sampled from January – March 2015. Among those generics, 23, 17, 1 and 1 were Thai-made, Indian-made and Chinese-made and Vietnamese-made respectively. All sampled products, regardless of manufacturers or sources, met the International Pharmacopeia standards for composition assay, mass uniformity and dissolution. Although local regulations restrict ARV supply to hospitals and clinics, samples of ARV could be bought from private drug stores even without formal prescription.

Conclusion: Sampled generic ARVs distributed within Thailand and 1 Vietnamese pharmacy showed consistent quality. However some products were illegally supplied without prescription, highlighting the importance of dispensing ARV for treatment or prevention in facilities where continuity along the HIV treatment and care cascade is available.
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Introduction

In 2014, there were an estimated of 450,000 people living with HIV in Thailand, with 8000 total new infections. Since there is no definitive cure, HIV is a chronic disease requiring life-long treatment. In October 2014, new Thai National HIV/AIDS guidelines were launched which recommend initiating treatment "regardless of CD4 count". Early ARV initiation has public health benefits by minimizing sexual transmission of HIV, and also benefits the individual by preventing the development of serious AIDS and non-AIDS-related events. While there is an attempt to scale up ARV for HIV infected individuals, drug accessibility remains a global challenge, especially where financial resources are constrained. In Thailand, 100% of financial resources for HIV treatment are domestic; the country depends mostly on generic ARV products.

Generic drugs, according to U.S. Food and Drug Administration (FDA), are the same as their branded counterparts in dosage, strength, safety, route of administration, indication and action; in fact, they are supposed to be therapeutically equivalent. By FDA regulations, a generic drug must contain an identical amount of the active ingredient(s) as in the branded product. The active ingredient is any component in a tablet that produces the pharmacological effect for an expected medical purpose. The Thai FDA has guidelines for approval of generic drugs which requires evidence of product interchangeability equivalence, namely bioequivalence studies, comparative in vitro dissolution/release studies, comparative clinical studies, and comparative pharmacodynamics studies. The World Health Organization (WHO) has defined two specific terms that relate to quality aspects of medicines: substandard and counterfeit medicines. Substandard medicines are legal products that do not meet quality standards and specifications; they may occur as a result of human error, negligence, or resource restriction. In contrast, counterfeit or fake drugs are intentionally and fraudulently disguised regarding drug components, active ingredients, packaging and labeling, and are made illegally by non-licensed companies.

Incidents regarding poor-quality generic drugs have been regularly reported, particularly among life-saving anti-infective drugs within resource-limiting regions where there are less rigorous restrictions on procurement and sale, and less public awareness. According to the U.S. Pharmacopeial Convention (USP) reports during 2003-2013, the proportion of substandard medicines in Asia was 2.9%; lower than that described in Africa and South America. However, Asia was reported to have the
highest proportion of counterfeit medicines with a total number of 70 samples (out of 81 counterfeit products), representing 86% of sampled counterfeit products. Prevalence of sampled substandard medicine in Asia was 2.9% and Thailand was one of the least consistent in reporting data to a medicines quality database. Problems associated with poor-quality drugs include increased morbidity and mortality, unnecessary adverse effects, suboptimal treatment leading to drug resistance, and also loss of confidence in health systems and waste of financial resources.

Therefore, it is very important for generic ARVs to be consistently monitored. Our study sampled generic ARV available from different sources in Thailand and assessed the quality by analyzing the pharmaceutical equivalence of the products.

Method:

Sampling from sources

In order to represent ARVs distributed in Thailand, we obtained ARVs from primary hospitals participating in the National Universal Coverage program under the auspices of the National Health Security Office (NHSO), non-government organization (NGO) ARV clinics, and private drug stores. From a total of 603 primary hospitals that distributed ARVs through the NHSO (assessed data August 2011), two hospitals in each of the 5 regions of the country (North, South, East, West, and Central) were randomly selected. For NGO sources, we collected ARV from the Thai Red Cross AIDS Research Center and the HIV-Netherlands-Australia-Thailand Research Collaboration (HIVNAT) pharmacies. For private sources, we bought ARV from 2 private pharmacies in Bangkok and 1 private pharmacy in Vietnam.

Selection of ARVs

We selected two preferred first line ARVs (Tenofovir (TDF) 300mg and Efavirenz (EFV) 600mg) and one preferred second line ARV (Lopinavir/ritonavir (LPV/r) 200/50mg) recommended in the Thai National HIV/AIDS guidelines for this study. Each ARV sample contained an adequate amount of tablets for Pharmaceutical analysis (at least 90 tablets), and had a shelf life extending beyond the analysis date.

Drug profile:

- **Tenofovir (TDF)** belongs to Nucleoside Reverse Transcriptase Inhibitor class (NRTI). In Thailand, there is in a single tablet formulation, or combines with emtricitabine as Truvada or with emtricitabine (FTC) and efavirenz (EFV) as Atripla. There are three branded products (Viread, Truvada and Atripla) and two generics (Tenofovir, and Ricovir-EM). According to international pharmacopoeia, Tenofovir tablets contain tenofovir disoproxilfumarate not
less than 90.0% and not more than 110.0% of the amount of tenofovirdisoproxilfumarate, stated on the label.

- **Efavirenz (EFV)** belongs to Non-nucleoside Reverse Transcriptase Inhibitor class (NNRTI). In Thailand, it is available in both capsule and tablet formulations. There are five branded products (Stocrin 50 mg, 200 mg, 600 mg and combination as Atripla) and two generics (Efavirenz 200 mg, 600 mg). According to international pharmacopoeia, Efavirenz tablets contain not less than 90.0% and not more than 110.0% of the amount efavirenz, stated on the label.

- **Lopinavir/ritonavir (LPV/r)** belongs to Protease Inhibitors class (PIs). In Thailand, there is in tablet, capsule and solution formulation. There are three branded product (Aluvia LPV/r 100mg/25mg and Kaletra LPV/r 133mg/33mg and oral solution 80 mg/20 mg) and two generic product (LPV/r 200mg/50mg and oral solution 80 mg/20 mg). According to international pharmacopoeia, Lopinavir and ritonavir tablets contain lopinavir and ritonavir not less than 90.0% and not more than 110.0% of the amounts of lopinavir and ritonavir, stated on the label.

**Collection of ARVs**

For hospital sources, Local Pharmacists (who voluntarily collaborated with this study) were asked to randomly collect 1-3 bottles of each designated ARV from dispensing shelves. In addition, they completed a drug record form for each ARV sample, recording information including product name, dose, batch number, storage condition, manufactured date and expiry date. Pharmacists then shipped sampled ARVs along with completed drug record forms to the study team. Transportation to the analysis site was done using the Thai Express Mail Service and temperature was monitored during shipment.

For NGO ARV clinics and private sources, ARVs were bought by study coordinators. LPV/r (200/50mg) tablets were unavailable at 2 NGO clinics and 1 private pharmacy. Required documents including temperature assessment were not available for ARV purchased from the private pharmacies.
**Pharmaceutical Analysis of ARVs**

Evaluation of ARVs quality was conducted according to standard procedures for pharmaceutical analysis described under specific product monographs, namely, Lopinavir and Ritonavir tablets, Efavirenz tablets, and Tenofovir tablets, published in the International Pharmacopeia (4th edition) by WHO. To assess the quality of medicines in this study, four different parameters including identity test, assay, uniformity of mass, and dissolution were selected for ARVs analysis. Counterfeit medicines are commonly associated with the absence of the active substance. Therefore, the Identity test was conducted to confirm the presence and identity of the active substance in the tested formulation. The content and strength of drug were determined by a quantitative assay of the amount of active substance in dosage form. Uniformity of mass was tested to confirm homogeneity of the amount of active substances among tablets manufactured in the same batch. Dissolution of ARVs, with the exception of Efavirenz tablets due to the lack of an official analytical method in pharmacopeia, was conducted to test the performance of the ARV tablet that the drug substance will release with an acceptable rate which greatly affects the bioavailability of the medicine. Drug analysis was performed by the Pharmaceutical Technology Service Center, Faculty of Pharmaceutical Science, Chulalongkorn University. Evaluation of ARV quality was based on acceptance criteria of each specification described in the drug monograph. Sources and storage conditions were blinded from the analysts.
Table 1.A Lopinavir (200 mg)/Ritonavir (50 mg) drug sources and characteristics

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Abbreviations: Lopinavir, LPV; Ritonavir, RTV; the Government Pharmaceutical Organization, GPO; Thailand, THA; India, IND.
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**Abbreviations:** Tenofovir, TDF; the Government Pharmaceutical Organization, GPO; Thailand, THA; India, IND; Vietnam, VN.
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<th>Expiry date</th>
<th>Identi-ification</th>
<th>% of label amount</th>
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<th>Dissolution n, %</th>
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**Abbreviations:** Efavirenz, EFV; the Government Pharmaceutical Organization, GPO; Thailand, THA; China, CHN; India, IND.
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<th>Uniformity, %</th>
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<td>Max</td>
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<td>(1.76)%</td>
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<td>98.9</td>
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Abbreviations: Lopinavir, LPV; Ritonavir, RTV; Tenofovir, TDF; Efavirenz, EFV; Label amount, L.A.; Standard deviation, SD
Forty-two batches of ARV (TDF, EFV, LPV/r) from 15 sources (10 primary hospitals, 2 NGO clinics and 3 private drug stores) were collected between January – March 2015. Temperature during shipment of ARV samples from sites to the analysis facility did not substantially exceed 30 °C, except for 5 shipments from primary hospitals where the temperature was over 30 °C for ≤ 2 hours. All ARV samples came in the original package and no broken pills were observed. Of 15 TDF samples collected, 10 samples (from all hospitals) were made locally in Thailand (not WHO prequalified); the rest were generics made in India (3 WHO prequalified, and Vietnam (1 not WHO prequalified)). Fifteen samples of EFV were collected. Two samples (1 each from a primary hospital and 1 from an NGO clinic) were Thai-made generics (not WHO prequalified), 1 sample was a generic made in China (WHO prequalified) and the rest were Indian-made generics (WHO prequalified). LPV/r obtained from the 10 hospital sources was a Thai-made generic formulation (not WHO prequalified). We also sampled 1 Thai-made (not WHO prequalified) and 1 Indian-made (WHO prequalified) LPV/r generic tablets from 2 private sources. (Assess the WHO prequalification database at http://apps.who.int/medicines/who-prequalification) [Table 1.A.B.C]
For ARV obtained from hospital sources, ARV Storage conditions were assessed from self-administered questionnaires completed by a hospital pharmacist. Nine out of 10 hospitals had air conditioned storage facilities with temperature less than 30 °C. Seven out of 10 hospitals had humidity monitoring. Humidity was less than 60 % relative humidity (RH) at most of the hospitals where monitoring was undertaken. There was 1 site with humidity of 67 %RH. One hospital site had neither humidity nor temperature monitoring, because drugs were stored at the ARV clinic, not in pharmacy facility. NGO ARV clinics also had temperature and humidity controlled to be less than 30 °C and 60 %RH respectively. We could not assess storage conditions at private pharmacies. Of note, while a doctor's prescription is required for ARV dispensed at hospitals and the NGO ARV clinics, no formal prescription was needed in the private pharmacies where our ARV samples were procured.

Identification test and Chemical composition assay
The drug identities are demonstrated by the same retention time as corresponding International pharmacopeia reference standards using the relevant drug content assay. Each sample met the International pharmacopeia standard for drug content [Figure 3]. Mean drug content values, as described in [Table 2], were close to 100% of the labelled amount; 99.9%/101.9% for LPV/r, 100% for TDF, and 96.9% for EFV. The standard deviations of all drug content assay values were relatively close; 1.76/0.93 for LPV/r, 2.10 for TDF, and 1.11 for EFV.

Uniformity of mass
Uniformity of mass was used to assess uniformity of production batch for all the samples. The results ranged from -2.53% to 2.08% for LPV/r, -4.54% to 4.47% for TDF and -2.85% to 2.25% for EFV. All results were within the accepted values which range from -5% to 5%. The % deviation under uniformity of mass is calculated from the difference between the weight of individual unit and the average weight of the sample. The acceptance range is based on the criteria in the International pharmacopeia.

Test for dissolution
For dissolution tests, the cumulative amount of drug (percentage of labelled amount) that dissolves over a period of time in a dissolution medium is measured. As shown in Table 2, LPV/r and TDF samples comply with the international pharmacopeia dissolution test limit of ≥ 80% of the labeled amount.
There was no significant association between sources of ARV, WHO prequalification status, manufactured sites and storage conditions and the results of this pharmaceutical equivalence analysis.

Discussion:
The primary goal of this research study was to perform independent surveillance on the quality of commonly used generic ARV available for patients in Thailand. Although this could not represent whole ARV distributing in the region, the findings showed satisfactory quality of all ARV samples from different sources and types based on drug content, uniformity of mass and dissolution even though some batches (including those manufactured in Thailand) are not WHO prequalified. TDF test results varied most widely when compared to EFV and LPV/r, however all parameters were within the International Pharmacopeia standards. These wider ranges might reflect more variability in manufacturing sites of TDF, while LPV/r samples were retrieved from a smaller number of manufacturers. Although our findings are supported by previous studies, two samples of ARV from Thailand were found to be substandard in a USP convention database report in 2008 (http://www.usp.org/worldwide/medQualityDatabase). Therefore, continuous monitoring is required to ensure that products used in National Treatment Programs meet the quality standards necessary to ensure an effective and safe response to HIV. In addition, counterfeit medicines, particularly anti-malarials have frequently been found when reviewing the quality of medicines in Southeast Asian countries, and WHO estimates the use of counterfeit drugs causes approximately 1 million deaths per year.

Although ARVs are life-saving medications, they can cause adverse events if taken incorrectly and reduce a patient’s options for future treatment if they continue to be dosed in the presence of genotypic resistance. HIV care is life-long and requires multidisciplinary support, and monitoring of viral load and other safety parameters. Our finding that generic ARV could be purchased from two private pharmacies without a formal prescription, despite their supply being restricted only to hospitals and registered clinics, highlights the important public health issue of getting patients into the proper healthcare system cascade. Self-treatment with ARV, either for treatment or prevention, without proper follow up from healthcare professionals skilled in managing HIV might lead to adverse events, adherence problems, and consequently drug resistance. While we promote ARV accessibility by generic...
importation/licensing, regulation is necessary to ensure that ARV are dispensed with a proper monitoring and follow-up system in place.

There are some limitations of our study. First, the small number of ARV samples assayed limits the power to detect any abnormalities. However, we maximized our resources by randomly selecting a majority of primary hospitals where they supposedly have the least quality control systems. Second, almost all LPV/r sampled were Thai-made generics; this reflects the situation in the past that Thailand had issues compulsory licenses for antiretroviral drugs including Abbott’s Kaletra®, to cope with the enormous expenditure necessary to provide life-long treatment with ARV for approximately 1% of the population. Nevertheless, although Thai ARV are not WHO pre-qualified, a study has shown comparable pharmacokinetics between Thai generic and Indian generics, and the Thai FDA has rigorous standards for bioequivalence. Finally, although we were unable to include all pharmaceutical analysis methods, namely impurities and breaking forces, we covered the three most important components relating to bioavailability and efficacy: active ingredient, uniformity and dissolution. Some strengths of our study are also noteworthy. The sampling and collection of ARV were processed in systematic and fashion. In addition, our ARV sources and storage conditions were blinded from analysts so they did not pose any bias during analysis. Lastly, while occasional surveillance of drug quality in Thailand already takes place, the surveillance might not focus on ARV. Our study is independent and focuses on commonly used ARV in the Thai National Treatment Program.

Suggestion and study further:
In conclusion, many sectors in Thailand have worked together to scale up ARV treatment; this study ensures the quality of the sampled drug being utilized, emphasizes further continuous monitoring, and at the same time, points out that ARV dispensing should occur in facility-based settings where regular follow-up and care are delivered.

Study Outcome:
Besides ensuring the quality of sampled generic ARV, the study helps in setting up system for independent quality monitoring of drugs. It could be scaled up in term of drug classes and sites, covering Asean Economic Community which will formally start at the end of 2015.
The study team has written the manuscript named "Pharmaceutical Equivalence of Distributed Generic Antiretroviral (ARV) in Asian settings: the cross-sectional surveillance study - PEDA study". It was submitted to journal and in the process of review.

Publication:
See Appendix

Bibliography:


25. Thai Health (Thai Health Promotion Foundation). Drug system report. Thai Health (Thai Health Promotion Foundation), Thai Health (Thai Health Promotion Foundation), 2011.


Appendix
- Supplement tables
- Publication
- Study team biosketch
### Supplementary Table

Supplementary Table 1. Descriptive statistics of Lopinavir (200 mg)/Ritonavir (50 mg) drug content, uniformity of mass and dissolution tests, by WHO pre-qualification status, Sampling site, and country of manufacture.

<table>
<thead>
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<th>Uniformity of mass, % (WHO Spec. ±5%)</th>
<th>Dissolution, % (WHO Spec. ≥ 80% L.A.)</th>
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**Abbreviations:** Non-Governmental Organizations, NGO
Supplementary Table 1.B Descriptive statistics of Tenofovir drug (300 mg) content, uniformity of mass and dissolution tests, by WHO pre-qualification status, Sampling site, and country of manufacture

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Abbreviations: Non-Governmental Organizations, NGO
Supplementary Table 1.C Descriptive statistics of Efavirenz drug (600 mg) content, uniformity of mass and dissolution tests, by WHO pre-qualification status, Sampling site, and country of manufacture

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<td></td>
<td>(WHO Spec, 90.0-110.0%)</td>
<td>(WHO Spec, ±5%)</td>
<td>(WHO Spec, ≥80% L.A.)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Min</td>
<td>Max</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>WHO pre-qualification status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13</td>
<td>94.9</td>
<td>98.9</td>
<td>97.1 (1.04)</td>
</tr>
<tr>
<td>No</td>
<td>2</td>
<td>95.4</td>
<td>95.6</td>
<td>95.5 (0.14)</td>
</tr>
<tr>
<td>Sampling sites</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hospital</td>
<td>10</td>
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<td>97.8</td>
<td>97.1 (0.78)</td>
</tr>
<tr>
<td>NGO Clinic</td>
<td>2</td>
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<td>95.6</td>
<td>95.3 (0.49)</td>
</tr>
<tr>
<td>Private</td>
<td>3</td>
<td>95.6</td>
<td>98.9</td>
<td>97.1 (1.67)</td>
</tr>
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<td>Manufacturer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Countries</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td>2</td>
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<td>95.6</td>
<td>95.5 (0.14)</td>
</tr>
<tr>
<td>India</td>
<td>12</td>
<td>94.9</td>
<td>98.9</td>
<td>97.2 (0.99)</td>
</tr>
<tr>
<td>China</td>
<td>1</td>
<td>-</td>
<td></td>
<td>Chulalongkorn 95.6 (0)</td>
</tr>
</tbody>
</table>

Abbreviations: Non-Governmental Organizations, NGO
FIGURES

Figure 1 Geographic location of sampling sites in Thailand and Vietnam

1 Source: http://www.mapcruzin.com/free-thailand-maps.htm
Figure 2 Sampled drugs, ordered by site id

(A) LPV/RTV
(B) TDF
(C) EFV
NOTE: WHO specification of drug quality, 90-110%

Figure 3: percent of label amount of each sampled ARV, by sampling site
RESEARCH ARTICLE

Pharmaceutical Equivalence of Distributed Generic Antiretroviral (ARV) in Asian Settings: The Cross-Sectional Surveillance Study - PEDA Study

Vorapot Sapsirisavat1,‡, Vorasit Vongsutilers2,*, Narukjaporn Thammajaruk1, Kanitta Pussadee1, Prakit Riyaten1, Stephen Kerr1,3, Anchalee Avihingsanon1,§, Praphan Phanuphak1,§, Kiat Ruxrungtham1,‡, PEDA study team1

1 HIV-NAT, Thai Red Cross AIDS Research Centre, 104 Ratchadamri Road, Pathumwan, Bangkok, 10330, Thailand. 2 Faculty of Pharmaceutical Sciences, Chulalongkorn University, Rama 4 Road, Pathumwan, Bangkok, 10330, Thailand. 3 Department of Global Health, Academic Medical Center, University of Amsterdam, Amsterdam Institute of Global Health and Development, Trinity Building C, Pietersbergweg 17, 1105 BM, Amsterdam Zuiderzeestraat, The Netherlands. 4 Department of Medicine, Faculty of Medicine, Chulalongkorn University, 254 Phayathai Road, Pathumwan, Bangkok, Thailand.

‡ These authors contributed equally to this work.
§ These authors are first authors on this work.
† Membership of the PEDA study team is listed in the Acknowledgments.

Abstract

Objectives
Ensuring that medicines meet quality standards is mandatory for ensuring safety and efficacy. There have been occasional reports of substandard generic medicines, especially in resource-limited settings where policies to control quality may be less rigorous. As HIV treatment in Thailand depends mostly on affordable generic antiretrovirals (ARV), we performed quality assurance testing of several generic ARV available from different sources in Thailand and a source from Vietnam.

Methods
We sampled Tenofovir 300mg, Efavirenz 600mg and Lopinavir/ritonavir 200/50mg from 10 primary hospitals randomly selected from those participating in the National AIDS Program, 2 non-government organization ARV clinics, and 3 private drug stores. Quality of ARV was analyzed by blinded investigators at the Faculty of Pharmaceutical Science, Chulalongkorn University. The analysis included an identification test for drug molecules, a chemical composition assay to quantitate the active ingredients, a uniformity of mass test and a dissolution test to assess in-vitro drug release. Comparisons were made against the standards described in the WHO International pharmacopoeia.

Results
A total of 42 batches of ARV from 15 sources were sampled from January–March 2015. Among those generics, 23, 17, 1, and 1 were Thai-made, Indian-made, Vietnamese-made and Chinese-made, respectively. All sampled products, regardless of manufacturers or
responsibility for the decision to submit the manuscript for publication.

Competing Interests: KR has received the Senior Research Scholar Award from the Thailand Research Fund, and the Research Professor Fund from Chulalongkorn University, Bangkok, Thailand. KR also received honoraria or consultation fees from Merck, Roche, Jensen-Cilag, Tibotec, Mylan and GPO (Governmental pharmaceutical organization, Thailand) as well as participated in a company sponsored speaker’s bureau from Abbott, Gilead, Bristol-Myers Squibb, Merck, Roche, Jensen-Cilag, GlaxoSmithKline, and GPO (Governmental pharmaceutical organization). The rest of the authors declare no conflict of interest. This does not alter the authors' adherence to PLOS ONE policies on sharing data and materials.

Introduction

In 2014, there were an estimated of 450,000 people living with HIV in Thailand, with 8000 total new infections[1]. Since there is no definitive cure, HIV is a chronic disease requiring lifelong treatment. In October 2014, new Thai National HIV/AIDS guidelines were launched which recommend initiating treatment “regardless of CD4 count”[2]. Early ARV initiation has public health benefits by minimizing sexual transmission of HIV[3], and also benefits the individual by preventing the development of serious AIDS and non-AIDS-related events[4]. While there is an attempt to scale up ARV for HIV infected individuals, drug accessibility remains a global challenge, especially where financial resources are constrained[5]. In Thailand, 100% of financial resources for HIV treatment are domestic[1]; the country depends mostly on generic ARV products.

Generic drugs, according to U.S. food and drug administration (FDA), are the same as their branded counterparts in dosage, strength, safety, route of administration, indication and action; in fact, they are supposed to be therapeutically equivalent. By FDA regulations, a generic drug must contain an identical amount of the active ingredient(s) as in the branded product[6]. The active ingredient is any component in a tablet that produces the pharmacological effect for an expected medical purpose[7]. However, an active ingredient is just one component of the quality requirements, and is not in itself sufficient to ensure therapeutic equivalence. The Thai FDA has guidelines for approval of generic drugs which requires evidence of product interchangeability equivalence; namely bioequivalence studies, comparative in vitro dissolution/release studies, comparative clinical studies, and comparative pharmacodynamics studies[8]. The World Health Organization (WHO) has a recommended survey protocol that defines specific items that relate to quality aspects of medicines, and substandard and counterfeit medicines. Substandard medicines are legal products that do not meet quality standards and specifications; they may occur as a result of human error, negligence, or resource restriction. In contrast, counterfeit or fake drugs are intentionally and fraudulently disguised regarding drug components, active ingredients, packaging and labeling, and are made illegally by non-licensed companies[9].

Incidents regarding poor-quality generic drugs have been regularly reported, particularly among life-saving anti-infective drugs within resource-limiting regions where there are less rigorous restrictions on procurement and sale, and less public awareness[10–12]. According to the U.S. Pharmacopeial Convention (USP) reports during 2003-2013, the proportion of substandard medicines in Asia was 2.9%; lower than that described in Africa and South America. However, Asia was reported to have the highest proportion of counterfeit medicines with a
total number of 70 samples (out of 81 counterfeit products), representing 86% of sampled counterfeit products. Prevalence of sampled substandard medicine in Asia was 2.9% and Thailand was one of the least consistent in reporting data to a medicines quality database[13]. Problems associated with poor-quality drugs include increased morbidity and mortality, unnecessary adverse effects, suboptimal treatment leading to drug resistance, and also loss of confidence in health systems and waste of financial resources[14]. Therefore, it is very important for generic ARVs to be consistently monitored. Our study sampled generic ARV available from different sources in Thailand and assessed the quality by analyzing the pharmaceutical equivalence of the products.

**Materials and Methods**

The methodology has been reported in accordance with existing literature on medicines' quality surveys[9,15].

**Sampling from sources**

In order to represent ARVs distributed in Thailand, we obtained ARVs from primary hospitals participating in the National Universal Coverage program under the auspices of the National Health Security Office (NHSO), non-government organization (NGO) ARV clinics, and private drug stores. Six hundred and three primary hospitals that distributed ARVs through the NHSO (assessed data August 2011) were grouped by geographical location (North, South, East, West, and Central), and 2 hospitals from each region were randomly selected. For NGO sources, we collected ARV from the Thai Red Cross AIDS Research Center and the HIV-Netherlands-Australia-Thailand Research Collaboration (HIVNAT) pharmacies. For private sources, we bought ARV from 2 private pharmacies in Bangkok and 1 private pharmacy in Vietnam. [Fig 1] Convenience sampling was used to select these ARV in locations where the HIV prevalence is high.

**Selection of ARVs**

We selected two preferred first line ARVs (Tenofovir (TDF) 300mg and Efavirenz (EFV) 600mg) and one preferred second line ARV (Lopinavir/ritonavir (LPV/r) 200/50mg) recommended in the Thai National HIV/AIDS guidelines for this study[21]. Each ARV sample contained an adequate amount of tablets for Pharmaceutical analysis (at least 90 tablets), and had a shelf life extending beyond the analysis date.[Fig 2]

**Collection of ARVs**

For hospital sources, Local Pharmacists (who voluntarily collaborated with this study) were asked to randomly collect 1–3 bottles of each designated ARV from dispensing shelves. In addition, they collected a drug record form for each ARV sample, recording information including product name, dose, batch number, storage condition, manufactured date and expiry date. Pharmacists then shipped sampled ARVs along with completed drug record forms to the study team. Transportation to the analysis site was done using the Thai Express Mail Service and temperature was monitored during shipment.

For NGO ARV clinics and private sources, ARVs were bought by study coordinators. They acted as mystery shoppers and did not declare the objective of study to the seller. LPV/r (200/50mg) tablets were unavailable at 2 NGO clinics and 1 private pharmacy. Required documents including temperature assessment were not available for ARV purchased from the private pharmacies.
Fig 1. Geographic location of sampling sites in Thailand and Vietnam.
doi:10.1371/journal.pone.0157039.g001
Pharmaceutical Analysis of ARVs

Evaluation of ARVs quality was conducted according to standard procedures for pharmaceutical analysis described under specific product monographs, namely, Lopinavir and Ritonavir tablets, Efavirenz tablets, and Tenofovir tablets, published in the International Pharmacopeia (4th edition) by WHO. To assess the quality of medicines in this study, four different parameters including identity test, quantitative assay, uniformity of mass, and dissolution were selected for ARVs analysis. Counterfeit and substandard medicines are partly associated with the absence or insufficient quantities of the active substance. Therefore, the Identity test was conducted to confirm the presence and identity of the active substance in the tested formulation. The content and strength of drug were determined by a quantitative assay of the amount of active substance in dosage form. Uniformity of mass was tested to confirm homogeneity of the amount of active substances among tablets manufactured in the same batch. Dissolution of ARVs, with the exception of Efavirenz tablets due to the lack of an official analytical method in pharmacopeia, was conducted to test the performance of the ARV tablet that the drug substance will release with an acceptable rate which greatly affects the bioavailability of the
Drug analysis was performed by the Pharmaceutical Technology Service Center, Faculty of Pharmaceutical Science, Chulalongkorn University. Pharmaceutical Technology Service Center is an accredited laboratory complying with the ISO/IEC 17025:2005 and the requirements of the Bureau of Laboratory Quality Standards in the field of drug testing. Evaluation of ARV quality was based on acceptance criteria of each specification described in the drug monograph, and descriptive summary statistics were calculated using Stata 14 (Statacorp, College Station, TX, USA). Sources and storage conditions were blinded from the analysts [16].

This research study was approved by the Institutional Review Board, Faculty of Medicine, Chulalongkorn University since October 2013. Informed consent process is not required by the ethics committee/IRB because the study was conducted and analyzed for the medicine tablets that were collected. This study was not conducted in patients.

This research study was not conducted in collaboration with Thailand Drug Regulation Authority (Thai FDA) because one objective of this study was to create an independent medicine quality surveillance system. However, a summary of the study results will be disseminated to relevant agencies and organizations with an interesting drug safety and quality.

Results

Forty-two batches of ARV (TDF, EFV, LPV/r) from 15 sources (10 primary hospitals, 2 NGO clinics and 3 private drug stores) were collected between January-March 2015. Temperature during shipment of ARV samples from sites to the analysis facility did not substantially exceed 30 °C, except for 5 shipments from primary hospitals where the temperature was over 30 °C for ≤2 hours. All ARV samples came in the original package and no broken pills were observed. Of 15 TDF samples collected, 10 samples (from all hospitals) were made locally in Thailand (not WHO prequalified); the rest were generics made in India (3 WHO prequalified, 1 not) and Vietnam (1 not WHO prequalified). Fifteen samples of EFV were collected. Two samples (1 each from a primary hospital and 1 from an NGO clinic) were Thai-made generics (not WHO prequalified), 1 sample was a generic made in China (WHO prequalified) and the rest were Indian-made generics (WHO prequalified). LPV/r obtained from the 10 hospital sources was a Thai-made generic formulation (not WHO prequalified). We also sampled 1 Thai-made (not WHO prequalified) and 1 Indian-made (WHO prequalified) LPV/r generic tablets from 2 private sources (Assess the WHO prequalification database at http://apps.who.int/medicines/ [15,16] [Tables 1, 2 and 3].

For ARV obtained from hospital sources, ARV Storage conditions were assessed from self-administered questionnaires completed by a hospital pharmacist. Nine out of 10 hospitals had air conditioned storage facilities with temperature less than 30°C. Seven out of 10 hospitals had humidity monitoring. Humidity was less than 60% relative humidity (RH) at most of the hospitals where monitoring was undertaken. There was 1 site with humidity of 67%RH. One hospital site had neither humidity nor temperature monitoring, because drugs were stored at the ARV clinic, not in pharmacy facility. NGO ARV clinics also had temperature and humidity controlled to be less than 30°C and 60%RH respectively. We could not assess storage conditions at private pharmacies. Of note, while a doctor’s prescription is required for ARV dispensed at hospitals and the NGO ARV clinics, no formal prescription was needed in the private pharmacies where our ARV samples were procured.

Identification test and Chemical composition assay

The drug identities are demonstrated by the same retention time as corresponding International Pharmacopeia reference standards using the relevant drug content assay. Each sample met the International Pharmacopeia standard for drug content [Fig 3]. Mean drug content values, as described in [Table 4], were close to 100% of the labelled amount; 99.9%/101.9% for
Table 1. Lopinavir (200 mg)/Ritonavir (50 mg) drug sources and characteristics.

<table>
<thead>
<tr>
<th>Site</th>
<th>Lot No.</th>
<th>Manufacturer</th>
<th>Country</th>
<th>Trade name</th>
<th>WHO Prequal.</th>
<th>Expiry date</th>
<th>Identification</th>
<th>% of label amount</th>
<th>Uniformity of mass, %</th>
<th>Dissolution, % (LPV/RTV)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Min</td>
<td>Max</td>
</tr>
<tr>
<td>001</td>
<td>W570041</td>
<td>GPO</td>
<td>THA</td>
<td>Lopinavir/ Ritonavir</td>
<td>NO</td>
<td>21 Jan 16</td>
<td>Positive</td>
<td>102.1/100.8</td>
<td>-1.20</td>
<td>1.64</td>
</tr>
<tr>
<td>002</td>
<td>W560404</td>
<td>GPO</td>
<td>THA</td>
<td>Lopinavir/ Ritonavir</td>
<td>NO</td>
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<td>Positive</td>
<td>103.2/102.4</td>
<td>-1.28</td>
<td>1.48</td>
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<td>003</td>
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<td>GPO</td>
<td>THA</td>
<td>Lopinavir/ Ritonavir</td>
<td>NO</td>
<td>17 Mar 15</td>
<td>Positive</td>
<td>102.1/103.6</td>
<td>-1.11</td>
<td>1.25</td>
</tr>
<tr>
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<td>THA</td>
<td>Lopinavir/ Ritonavir</td>
<td>NO</td>
<td>17 Mar 15</td>
<td>Positive</td>
<td>101.9/103.3</td>
<td>-2.22</td>
<td>2.08</td>
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<td>THA</td>
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<td>NO</td>
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<td>Positive</td>
<td>99.4/101.8</td>
<td>-2.16</td>
<td>1.07</td>
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<td>W560432</td>
<td>GPO</td>
<td>THA</td>
<td>Lopinavir/ Ritonavir</td>
<td>NO</td>
<td>23 Jul 15</td>
<td>Positive</td>
<td>99.0/103.0</td>
<td>-2.10</td>
<td>1.87</td>
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<td>GPO</td>
<td>THA</td>
<td>Lopinavir/ Ritonavir</td>
<td>NO</td>
<td>20 Jul 16</td>
<td>Positive</td>
<td>98.6/101.5</td>
<td>-1.74</td>
<td>2.05</td>
</tr>
<tr>
<td>008</td>
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<td>GPO</td>
<td>THA</td>
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<td>NO</td>
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<td>Positive</td>
<td>99.4/101.4</td>
<td>-2.09</td>
<td>1.76</td>
</tr>
<tr>
<td>009</td>
<td>W570285</td>
<td>GPO</td>
<td>THA</td>
<td>Lopinavir/ Ritonavir</td>
<td>NO</td>
<td>15 May 16</td>
<td>Positive</td>
<td>98.4/101.0</td>
<td>-2.53</td>
<td>1.94</td>
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<tr>
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<td>GPO</td>
<td>THA</td>
<td>Lopinavir/ Ritonavir</td>
<td>NO</td>
<td>22 Oct 15</td>
<td>Positive</td>
<td>97.8/101.5</td>
<td>-1.47</td>
<td>1.79</td>
</tr>
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<td>GPO</td>
<td>THA</td>
<td>Lopinavir/ Ritonavir</td>
<td>NO</td>
<td>17 Mar 16</td>
<td>Positive</td>
<td>98.2/101.2</td>
<td>-1.33</td>
<td>1.52</td>
</tr>
<tr>
<td>012</td>
<td>B000458</td>
<td>Mylan</td>
<td>IND</td>
<td>Lopinavir/ Ritonavir</td>
<td>YES</td>
<td>30 Jun 16</td>
<td>Positive</td>
<td>99.7/101.4</td>
<td>-1.69</td>
<td>1.31</td>
</tr>
</tbody>
</table>

Abbreviations: Lopinavir, LPV; Ritonavir, RTV; the Government Pharmaceutical Organization, GPO; Thailand, THA; India, IND.

LPV/rt, 100% for TDF, and 96.9% for EFV. The standard deviations of all drug content assay values were relatively close; 1.760.93 for LPV/rt, 2.10 for TDF, and 1.11 for EFV.

Uniformity of mass

Uniformity of mass was used to assess uniformity of production batch for all the samples. The results ranged from -2.53% to 2.08% for LPV/rt, -4.54% to 4.47% for TDF and -2.85% to 2.25% for EFV. All results were within the accepted values which range from -5% to 5%. The % deviation under uniformity of mass is calculated from the difference between the weight of individual unit and the average weight of the sample. The acceptance range is based on the criteria in the International pharmacopeia.

Test for dissolution

For dissolution tests, the cumulative amount of drug (percentage of labelled amount) that dissolves over a period of time in a dissolution medium is measured. As shown in Table 4, LPV/rt and TDF samples comply with the international pharmacopeia dissolution test limit of ≥ 80% of the labeled amount.

There was no significant association between sources of ARV, WHO prequalification status, manufactured sites and storage conditions and the results of this pharmaceutical equivalence analysis.
### Table 3. Tenofovir (300 mg) drug sources and characteristics.

<table>
<thead>
<tr>
<th>Site</th>
<th>Lot No.</th>
<th>Manufacturer</th>
<th>Country</th>
<th>Trade name</th>
<th>WHO Prequal.</th>
<th>Expiry date</th>
<th>Identification</th>
<th>% of label amount</th>
<th>Uniformity of mass, %</th>
<th>Dissolution, %</th>
</tr>
</thead>
<tbody>
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<td>013</td>
<td>A570270</td>
<td>GPO</td>
<td>THA</td>
<td>Tenofovir GPO 300</td>
<td>NO</td>
<td>12 Feb 16</td>
<td>Positive</td>
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<td>-0.81</td>
<td>1.46</td>
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<td>A562265</td>
<td>GPO</td>
<td>THA</td>
<td>Tenofovir GPO 300</td>
<td>NO</td>
<td>27 Jun 16</td>
<td>Positive</td>
<td>100.0</td>
<td>-1.64</td>
<td>1.08</td>
</tr>
<tr>
<td>015</td>
<td>A570270</td>
<td>GPO</td>
<td>THA</td>
<td>Tenofovir GPO 300</td>
<td>NO</td>
<td>12 Feb 16</td>
<td>Positive</td>
<td>101.6</td>
<td>-1.44</td>
<td>1.26</td>
</tr>
<tr>
<td>016</td>
<td>A570554</td>
<td>GPO</td>
<td>THA</td>
<td>Tenofovir GPO 300</td>
<td>NO</td>
<td>18 Mar 16</td>
<td>Positive</td>
<td>99.6</td>
<td>-1.16</td>
<td>1.17</td>
</tr>
<tr>
<td>017</td>
<td>A570375</td>
<td>GPO</td>
<td>THA</td>
<td>Tenofovir GPO 300</td>
<td>NO</td>
<td>20 Feb 16</td>
<td>Positive</td>
<td>102.4</td>
<td>-1.34</td>
<td>0.70</td>
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<tr>
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<td>GPO</td>
<td>THA</td>
<td>Tenofovir GPO 300</td>
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<td>17 Feb 16</td>
<td>Positive</td>
<td>103.4</td>
<td>-1.45</td>
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<td>THA</td>
<td>Tenofovir GPO 300</td>
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<td>20 Mar 16</td>
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<td>-1.42</td>
<td>1.19</td>
</tr>
<tr>
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<td>GPO</td>
<td>THA</td>
<td>Tenofovir GPO 300</td>
<td>NO</td>
<td>13 Feb 16</td>
<td>Positive</td>
<td>98.6</td>
<td>-1.08</td>
<td>1.21</td>
</tr>
<tr>
<td>021</td>
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<td>GPO</td>
<td>THA</td>
<td>Tenofovir GPO 300</td>
<td>NO</td>
<td>19 Mar 16</td>
<td>Positive</td>
<td>98.4</td>
<td>-0.79</td>
<td>1.19</td>
</tr>
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<td>022</td>
<td>A570742</td>
<td>GPO</td>
<td>THA</td>
<td>Tenofovir GPO 300</td>
<td>NO</td>
<td>22 Apr 16</td>
<td>Positive</td>
<td>97.0</td>
<td>-0.82</td>
<td>1.16</td>
</tr>
<tr>
<td>023</td>
<td>8027079</td>
<td>Mylan</td>
<td>IND</td>
<td>RICOVIR</td>
<td>YES</td>
<td>31 Jul 17</td>
<td>Positive</td>
<td>102.5</td>
<td>-4.54</td>
<td>4.47</td>
</tr>
<tr>
<td>024</td>
<td>020414</td>
<td>STADA</td>
<td>VN</td>
<td>Tenofovir STADA</td>
<td>NO</td>
<td>02 Feb 16</td>
<td>Positive</td>
<td>100.6</td>
<td>-2.49</td>
<td>2.05</td>
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<td>IND</td>
<td>TEVIR</td>
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<td>RICOVIR</td>
<td>YES</td>
<td>31 Jul 17</td>
<td>Positive</td>
<td>98.4</td>
<td>-2.61</td>
<td>3.55</td>
</tr>
<tr>
<td>027</td>
<td>E131707</td>
<td>Hetero</td>
<td>IND</td>
<td>TENOF</td>
<td>YES</td>
<td>31 Jul 15</td>
<td>Positive</td>
<td>97.5</td>
<td>-2.10</td>
<td>2.14</td>
</tr>
</tbody>
</table>

**Abbreviations:** Tenofovir, TDF; the Government Pharmaceutical Organization, GPO; Thailand, THA; India, IND; Vietnam, VN.

doi:10.1371/journal.pone.0157039.002

### Table 3. Efavirenz (600 mg) drug sources and characteristics.

<table>
<thead>
<tr>
<th>Site</th>
<th>Lot No.</th>
<th>Manufacturer</th>
<th>Country</th>
<th>Trade name</th>
<th>WHO Prequal.</th>
<th>Expiry date</th>
<th>Identification</th>
<th>% of label amount</th>
<th>Uniformity of mass, %</th>
<th>Dissolution, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>028</td>
<td>EM22186</td>
<td>Mylan</td>
<td>IND</td>
<td>Efavirenz</td>
<td>YES</td>
<td>31 May 17</td>
<td>Positive</td>
<td>96.3</td>
<td>-2.22</td>
<td>1.25</td>
</tr>
<tr>
<td>029</td>
<td>EM35108</td>
<td>Emece</td>
<td>IND</td>
<td>Efavirenz</td>
<td>YES</td>
<td>30 Apr 15</td>
<td>Positive</td>
<td>96.8</td>
<td>-1.83</td>
<td>2.21</td>
</tr>
<tr>
<td>030</td>
<td>3027189</td>
<td>Mylan</td>
<td>IND</td>
<td>Efavirenz</td>
<td>YES</td>
<td>31 May 17</td>
<td>Positive</td>
<td>95.9</td>
<td>-1.66</td>
<td>1.62</td>
</tr>
<tr>
<td>031</td>
<td>3027187</td>
<td>Mylan</td>
<td>IND</td>
<td>Efavirenz</td>
<td>YES</td>
<td>31 May 17</td>
<td>Positive</td>
<td>97.6</td>
<td>-2.65</td>
<td>1.67</td>
</tr>
<tr>
<td>032</td>
<td>3027185</td>
<td>Mylan</td>
<td>IND</td>
<td>Efavirenz</td>
<td>YES</td>
<td>31 May 17</td>
<td>Positive</td>
<td>97.3</td>
<td>-2.21</td>
<td>1.64</td>
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<tr>
<td>033</td>
<td>3027466</td>
<td>Mylan</td>
<td>IND</td>
<td>Efavirenz</td>
<td>YES</td>
<td>31 May 17</td>
<td>Positive</td>
<td>97.8</td>
<td>-1.06</td>
<td>0.80</td>
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<tr>
<td>034</td>
<td>3031217</td>
<td>Mylan</td>
<td>IND</td>
<td>Efavirenz</td>
<td>YES</td>
<td>30 Sep 17</td>
<td>Positive</td>
<td>97.6</td>
<td>-1.11</td>
<td>1.14</td>
</tr>
<tr>
<td>035</td>
<td>A570330</td>
<td>GPO</td>
<td>THA</td>
<td>Efavirenz</td>
<td>NO</td>
<td>10 Sep 15</td>
<td>Positive</td>
<td>95.4</td>
<td>-1.56</td>
<td>1.28</td>
</tr>
<tr>
<td>036</td>
<td>3031198</td>
<td>Mylan</td>
<td>IND</td>
<td>Efavirenz</td>
<td>YES</td>
<td>31 Aug 17</td>
<td>Positive</td>
<td>97.8</td>
<td>-1.51</td>
<td>1.83</td>
</tr>
<tr>
<td>037</td>
<td>3031240</td>
<td>Mylan</td>
<td>IND</td>
<td>Efavirenz</td>
<td>YES</td>
<td>30 Sep 17</td>
<td>Positive</td>
<td>97.7</td>
<td>-1.76</td>
<td>1.91</td>
</tr>
<tr>
<td>038</td>
<td>3059355</td>
<td>Mylan</td>
<td>IND</td>
<td>Efavirenz</td>
<td>YES</td>
<td>30 Apr 17</td>
<td>Positive</td>
<td>95.8</td>
<td>-2.25</td>
<td>2.08</td>
</tr>
<tr>
<td>039</td>
<td>EF213003A</td>
<td>Hetero</td>
<td>IND</td>
<td>ESTIVA-600</td>
<td>YES</td>
<td>30 Nov 16</td>
<td>Positive</td>
<td>99.9</td>
<td>-0.98</td>
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<tr>
<td>040</td>
<td>A570845</td>
<td>GPO</td>
<td>THA</td>
<td>Efavirenz</td>
<td>NO</td>
<td>22 Oct 15</td>
<td>Positive</td>
<td>95.6</td>
<td>-2.08</td>
<td>2.25</td>
</tr>
<tr>
<td>041</td>
<td>V1723</td>
<td>Zhejiang Huaizhi Pharm.</td>
<td>CHI</td>
<td>STOCRIN</td>
<td>YES</td>
<td>05 Mar 16</td>
<td>Positive</td>
<td>95.6</td>
<td>-1.01</td>
<td>0.75</td>
</tr>
<tr>
<td>042</td>
<td>E140642</td>
<td>Hetero</td>
<td>IND</td>
<td>ESTIVA-600</td>
<td>YES</td>
<td>28 Feb 17</td>
<td>Positive</td>
<td>94.9</td>
<td>-2.59</td>
<td>1.02</td>
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</table>

**Abbreviations:** Efavirenz, EFV; the Government Pharmaceutical Organization, GPO; Thailand, THA; China, CHI; India, IND.

doi:10.1371/journal.pone.0157039.003
NOTE: WHO specification of drug quality, 90-110%

Fig 3. Percent of label amount of each sampled ARV, by sampling site.

Discussion

The primary goal of this research study was to perform independent surveillance on the quality of commonly used generic ARV available for patients in Thailand. Although this could not represent whole ARV distributing in the region, the findings showed satisfactory quality of all.

Table 4. Descriptive statistics of drug content, uniformity of mass and dissolution tests.

<table>
<thead>
<tr>
<th>ARV</th>
<th>N</th>
<th>% of label amount (L.A.)</th>
<th>Uniformity of mass, %</th>
<th>Dissolution, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>WHO Specification</td>
<td>Min</td>
<td>Max</td>
</tr>
<tr>
<td>LPV</td>
<td>12</td>
<td>90.0-110.0%</td>
<td>97.8</td>
<td>103.2</td>
</tr>
<tr>
<td>RTV</td>
<td>15</td>
<td>90.0-110.0%</td>
<td>97.0</td>
<td>103.4</td>
</tr>
<tr>
<td>TDF</td>
<td>15</td>
<td>90.0-110.0%</td>
<td>94.9</td>
<td>96.9</td>
</tr>
<tr>
<td>EFV</td>
<td>15</td>
<td>90.0-110.0%</td>
<td>94.9</td>
<td>96.9</td>
</tr>
</tbody>
</table>

Abbreviations: Lopinavir, LPV; Ritonavir, RTV; Tenofovir, TDF; Efavirenz, EFV; Label amount, L.A.; Standard deviation, SD
ARV samples from different sources and types based on drug content, uniformity of mass and dissolution even though some batches (including those manufactured in Thailand) are not WHO prequalified. TDF test results varied most widely when compared to EFV and LPV/r, however all parameters were within the International Pharmacopeia standards. These wider ranges might reflect more variability in manufacturing sites of TDF, while LPV/r samples were retrieved from a smaller number of manufacturers. Although our findings are supported by previous studies [19-21], two samples of ARV from Thailand were found to be substandard in a USP convention database report in 2008 (http://www.usp.org/worldwide/medQualityDatabase) [22]. Therefore, continuous monitoring is required to ensure that products used in National Treatment Programs meet the quality standards necessary to ensure an effective and safe response to HIV. In addition, counterfeit medicines, particularly anti-malarials have frequently been found when reviewing the quality of medicines in Southeast Asian countries [11,12], and WHO estimates the use of counterfeit drugs causes approximately 1 million deaths per year [23].

Although ARVs are life-saving medications, they can cause adverse events if taken incorrectly and reduce a patient’s options for future treatment if they continue to be dosed in the presence of genotypic resistance. HIV care is life-long and requires multidisciplinary support, and monitoring of viral load and other safety parameters. Our finding that generic ARV could be purchased from two private pharmacies without a formal prescription, despite their supply being restricted only to hospitals and registered clinics, highlights the important public health issue of getting patients into the proper healthcare system cascade. Self-treatment with ARV, either for treatment or prevention, without proper follow up from healthcare professionals skilled in managing HIV might lead to adverse events, adherence problems, and consequently drug resistance [24-26]. While we promote ARV accessibility by generic importation/licensing, regulation is necessary to ensure that ARV are dispensed with a proper monitoring and follow-up system in place.

There are some limitations of our study. First, the small number of ARV samples assayed limits the power to detect any abnormalities. However, we maximized our resources by sampling ARV from primary hospitals which in theory, have the least rigorous quality control systems in place. The fact that hospital ARV samples were selected by local pharmacists, could potentially result in a “positive” selection bias. Second, since there is no mechanism to check the availability of ARV in facilities outside the NHSOs system, convenience sampling was used for ARV from private pharmacies and NGO’s in locations where we suspected ARV would be available. This approach could miss stores in other areas who might have substandard products. Third, almost all LPV/r tablet sampled were Thai-made generics; this reflects the situation in the past when Thailand issued compulsory licenses for antiretroviral drugs including Abbott’s Kaletra®, to cope with the enormous expenditure incurred by procurement of brand name ARV. Nevertheless, although Thai ARV are not WHO pre-qualified, a study has shown comparable pharmacokinetics between Thai generic and Indian generics [27], and the Thai FDA has rigorous standards for bioequivalence [8]. Finally, we were unable to include all pharmaceutical analysis methods, namely impurities and related substances, thus not allowing to us to exclude the presence of possible contaminants and resulting potential for toxicity. However, we covered the three most important components relating to bioavailability and efficacy: active ingredient, uniformity and dissolution. Some strengths of our study are also noteworthy. The collection of ARV were processed in systematic fashion. In addition, our ARV sources and storage conditions were blinded from analysts so they did not pose any bias during analysis. Lastly, while occasional surveillance of drug quality in Thailand already takes place [28], the surveillance might not focus on ARV. Our study is independent and focuses on commonly used ARV in the Thai National Treatment Program.
In conclusion, many sectors in Thailand have worked together to scale up ARV treatment; this study ensures the quality of the sampled drug being utilized, emphasizes further continuous monitoring, and at the same time, points out that ARV dispensing should occur in facility-based settings where regular follow-up and care are delivered.

**Supporting Information**

**S1 Table.** Descriptive statistics of Lopinavir (200 mg)/Ritonavir (50 mg) drug content, uniformity of mass and dissolution tests, by WHO pre-qualification status, Sampling site, and country of manufacture.

**S2 Table.** Descriptive statistics of Tenofovir drug (300 mg) content, uniformity of mass and dissolution tests, by WHO pre-qualification status, Sampling site, and country of manufacture.

**S3 Table.** Descriptive statistics of Efavirenz drug (600 mg) content, uniformity of mass and dissolution tests, by WHO pre-qualification status, Sampling site, and country of manufacture.

**Acknowledgments**

PEDA study team

Suop Chantapoom, Chanatta Wisetsing, Rittichai Suwannarat, Noppisa Wimolluk, Labpika Chiangthien, Pattaraphon Nilchaay, Nopporn Somjit, Toungporn Pratumrat, Natnaree Sirisopa, Parinya Suheerasak

**Author Contributions**

Conceived and designed the experiments: VS VV NT SK AA PP KR. Performed the experiments: VV. Analyzed the data: VS PR SK. Wrote the paper: VS VV NT SK AA PP KR. Coordinated the study: KP.

**References**

6. Food and Drug Administration: Drugs@FDA Glossary of Terms, last updated 02/02/2012. US FDA.


20. convention USP Medicines Quality Database. Available at: http://www.usp.org/worldwide/medicinesQualityDatabase/


NAME: Ruxrungtham, Kiat

eRA COMMONS USER NAME (agency login): 

POSITION TITLE: CTU Co-Investigator/CRS Leader/Study PI/Investigator of Record

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>Completion Date</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Faculty of Medicine, Chiangmai University, Chiang Mai</td>
<td>MD</td>
<td>03/1979</td>
<td>Medicine</td>
</tr>
<tr>
<td>Department of Medicine, Faculty of Medicine</td>
<td>MS</td>
<td>05/1989</td>
<td>Allergy and Clinical Immunology</td>
</tr>
<tr>
<td>Chulalongkorn University, Bangkok</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

A. Personal Statement

I am primarily responsible for all of the research activities including fulfilling all of the study-specific objectives and requirements; taking primary responsibility for GCP compliance; carrying out appropriate communication with local government and regulatory agencies and ensuring that the completion of local IRB and OHRP requirements are done in a timely manner or within the designated timeframe for the study protocol; chairing the monthly meetings and taking the final responsibility for all of the specific tasks delegated to the research staff; carrying out protocol training for its site personnel; supervising all local staffs; attending all related meetings and taking conference calls; performing as the Study Physician if needed; and prescribing study drugs.

B. Positions and Honors

Positions and Employment

1995 - Faculty member, Division of Allergy and Clinical Immunology Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok
1996 - Deputy Director, HIV-NAT, Thai Red Cross - AIDS Research Centre, Bangkok
2000 - Director, HIV-NAT Research Laboratory/Chula Clinical Research Lab (ChulaCRL), Bangkok
2007 - Professor of Medicine, Chulalongkorn University, Bangkok
2014 - CTU Co-Investigator/CRS Leader/Study PI/Investigator of Record, HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok

Other Experience and Professional Memberships

1989 - 1990 Guest Researcher, Johns Hopkins Hospital, Baltimore, Maryland, USA (Sponsored by USAID, Supervisor: Thomas C. Quinn, MD)
1991 - 1993 Visiting Researcher, Clinical and Molecular Retrovirology Section, Laboratory of Immunoregulation, NIAID, NIH, Bethesda, MD, USA (Supervisor: H. Clifford Lane)
1997 - Principal investigator, more than 40 phase I, II or III clinical trials both in HIV and HIV-related (co-infection) studies
1997 - Co-investigator, more than 40 phase I, II or III clinical trials both in HIV-related (co-infection) studies
2003 - Member, The Thai AIDS Society (TAS)
2004 - Member, The Allergy, Asthma and Immunology Association, Thailand (AAIAT)
2004 - Advisory member, National laboratory network for HIV/AIDS vaccine trial, treatment and care of the Bureau of AIDS, TB and STDs, CDC, Ministry of Public Health, Thailand
2004 - Co-chair of Track A (Basic Science) Scientific Committee, the XV International AIDS Conference held in Bangkok, Thailand
2005 - 2011 Sub-committee member, AIDS Research Fund on Biomedical research
2006 - Member, Thai National AIDS committee
2006 - Member of the Vaccine Research and Development Sub-Committee, National Vaccine Committee, Ministry of Public Health
2010 - Member, International AIDS Society (IAS)
2010 - Chair, Social Security Office for the HIV/AIDS treatment and care subcommittee
2012 - Chair of the Research sub-committee and the member, The Royal College of Physician, Thailand (RCPT)
2012 - 2013 Co-Chair of the Basic Sciences Track (Track A), 7th IAS Conference on HIV Pathogenesis, Treatment and Prevention (IAS 2013), 30 June - 3 July 2013 in Kuala Lumpur, Malaysia
2012 - 2013 Chair of the scientific Track B (getting to zero death) committee, 11th International Congress on AIDS in Asia and the Pacific in Bangkok in 2013.

Honors
2006 Outstanding Internist Award on Medical Academy, Royal College of Physicians, Thailand
2007 Outstanding Researcher Award, and the Highest Citation Award, Chulalongkorn University, Bangkok, Thailand
2011 Senior Research Scholar Award, The Thailand Research Fund
2011 Outstanding Researcher Award, The National Research Council, Thailand
2015 Senior Research Scholar Award, The Thailand Research Fund
2015 Outstanding Research Award, The Thailand Research Fund

C. Contribution to Science

1. My participation as a site co-investigator in the IeDEA regional network since the beginning in 2006 has led to multiple publications that have informed our understanding of the impact of HIV and treatment outcomes in the Asia-Pacific. In addition to demonstrating the slow uptake of antiretroviral therapy and very low initial CD4 levels in our referral centers, our analyses have evaluated the impact of co-infections, regimen choice, country income level, and sex on treatment outcomes. We organized the first regional study of transmitted and acquired drug resistance and are participating in the IeDEA TB study exploring the molecular epidemiology of drug-resistant Mycobacterium tuberculosis in the context of HIV, using whole genome sequences, across different IeDEA regions.


2. A key priority for my clinical and scientific work has been to improve our local understanding of the HIV epidemic in Thailand. I have published multiple papers on HIV outcomes among adults and children in my country. From work which I am the PI of the NIH funded PREDICT study, we have increased the understanding of when to start antiretroviral therapy in children older than 1 year of age.


I and my center have conducted a number of pharmacokinetic and efficacy researches to address dose optimization for Thai patients such as lopinavir, atazanavir, and efavirenz. The results supported that an approximately 30% lower the dose of these antiretrovirals are efficacious and better tolerated. Our recent randomized controlled non-inferiority study has demonstrated that atazanavir 200 mg was non-inferior to 300 mg when boosted with ritonavir 100 mg once daily in well virologic suppressed patients. These strong evidences will lead to a near future recommendation in the Thai guidelines; and will result to a better tolerable regimen and to a significant cost saving.


I am involved in international randomized studies. The outcome of these studies had shown the drugs' efficacy and safety, which could led to a new treatment option for patients.


Complete List of Published Work in My Bibliography:
http://1.usa.gov/1lrLL0k

D. Research Support

Ongoing Research Support

A5316, NIH
Daar E (PI)
04/29/15-01/01/21
Evaluating pharmacokinetics interactions with vaginal ring contraceptive and ART
This study will look at a method of hormonal birth control, called the NuvaRing, and specific anti-HIV medications, called antiretrovirals (ARVs).
Role: PI

A5288 (MULTI-OCTAVE), NIH
Daar E (PI)
03/04/15-01/01/20
Management Using the Latest Technologies in Resource-limited Settings to Optimize Combination Therapy After Viral Failure
To use novel agents and contemporary management tools, including standard genotyping to select an appropriate third-line regimen, interventions to improve adherence and plasma viral load (VL) monitoring, in order to achieve a à ¥ 65% rate of virologic control at 48 weeks of follow-up
Role: PI

A5332, NIH
Grinspoon S (PI)
01/08/15-01/01/22
REPRIEVEx
This is a randomized trial to prevent vascular events in HIV, tests whether a daily dose of a statin will reduce the risk of cardiovascular disease among HIV-infected individuals (for whom statins are not already recommended according to 2013 US Cholesterol Treatment Guidelines)
Role: PI

A5279, NIH
Campbell T (PI)
10/28/14-01/01/19
Phase III Clinical Trial of Ultra-Short-Course Rifapentine/Isoniazid for the Prevention of Active Tuberculosis in HIV-Infected Individuals with Latent Tuberculosis Infection
To compare the efficacy of a 4-week daily regimen of weight-based RPT/INH to a standard 9-month (36 week) daily INH regimen for TB prevention in HIV-infected individuals
Role: PI
IRC003 and IRC004, NIH
Beigel J (PI)
08/01/11-11/01/20
IRC003 and IRC004
to evaluate the efficacy of the combination antivirals (oseltamivir/amantadine/ribavirin) as compared to oseltamivir alone in the treatment of at-risk subjects with confirmed influenza infection (Primary Efficacy Population).
Role: PI
A5349, NIH
Nahid P and Dorman S (PI)
08/05/15-08/05/18
Rifapentine-containing treatment shortening regimens for pulmonary tuberculosis: A randomized, open-label, controlled phase 3 clinical trial
This study will evaluate the efficacy of a rifapentine-containing regimen to determine whether the single substitution of rifapentine for rifampin makes it possible to reduce to seventeen weeks the duration of treatment for drug-susceptible pulmonary tuberculosis.
Role: PI
Completed Research Support
09-I-0108, NIH
Neaton (PI)
03/01/09-12/31/15
START (Strategic Timing of Anti-Retroviral Treatment)
The purpose of this randomized study is to determine whether immediate initiation of antiretroviral treatment (ART) is superior to deferral of ART until the CD4+ declines below 350 cells/mm3 in terms of morbidity and mortality in HIV-1 infected persons who are antiretroviral naive with a CD4+ count above 500 cells/mm3.
Role: PI
BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

NAME: Sapsirisavat, Vorapot

eRA COMMONS USER NAME (agency login):

POSITION TITLE: Co-investigator/study physician

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (if applicable)</th>
<th>Completion Date</th>
<th>FIELD OF STUDY</th>
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<tr>
<td>Mahidol University, Faculty of Medicine Siriraj Hospital, Bangkok</td>
<td>MD</td>
<td>2012</td>
<td>Medicine</td>
</tr>
<tr>
<td>Peking University, Department of Pediatric and Department of Traditional Chinese Medicine, Beijing</td>
<td>Other training</td>
<td>2009</td>
<td>Pediatric and Chinese Traditional Medicine</td>
</tr>
<tr>
<td>University of Massachusetts Medical School Department of Pediatric, Endocrinology/Diabetes Division, Boston, MA</td>
<td>Other training</td>
<td>2012</td>
<td>Pediatric Endocrinology and Diabetes</td>
</tr>
<tr>
<td>HIV-NAT, Thai Red Cross - AIDS Research Centre, Bangkok</td>
<td>Other training</td>
<td>02/2014</td>
<td>Infectious Diseases Control HIV research among MSM in the developing world</td>
</tr>
<tr>
<td>University of Pittsburgh, Graduate School of Public Health, Pittsburgh, PA</td>
<td>Other training</td>
<td>2014</td>
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</tr>
</tbody>
</table>

A. Personal Statement

I am primarily responsible for all of the research activities including carrying out targeted physical examinations among study volunteers; performing all study related clinical assessments, clinical counseling of medical test results, and implementing appropriate referrals; prescribing study drugs; assessing all drug-related toxicity and adverse events, immediately responding with emergency treatment if needed; alerting the PI regarding any Expedited Adverse Event (EAE); completing all medical records and CRFs related to clinical activities, such as clinical evaluations, physical examinations, and so forth; assisting, if necessary, in recruiting volunteers, community education, conducting consent; taking responsibility for all medical issues; attending all related meetings and taking conference calls; and taking responsibility for GCP compliance.

B. Positions and Honors

Positions and Employment

2007 - 2007 Public Relations Officer, ACTION 2007- Asian Collaborative Training On Infectious, Outbreak Disaster and Refugee Management-Phuket, Bangkok

2007 - 2008 National officer, Standing Committee on Human Right and Peace, IFMSA, Bangkok

2008 - 2009 Regional Coordinator, IFMSA- International Federation of Medical Students'
Associations, Bangkok
2008 - 2009 standing Committee on Human Right and Peace, IFMSA- International Federation of Medical Students' Associations, Bangkok
2012 - 2013 Intern doctor, Damnernsauduak hospital, Ratchaburi
2013 - Clinical Trial Physician, HIV-NAT, Thai Red Cross - AIDS Research Centre, Bangkok
2013 - Rapporteur, MSM and TG on drug use session, APCOM-Asia Pacific Coalition on Male Sexual Health Pre-ICAAP11 Conference, Bangkok
2014 - Co-investigator/study physician, HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok
2014 - Moderator, 17th Bangkok International Symposium, Bangkok

Other Experience and Professional Memberships

Honors

C. Contribution to Science

1. There is evidence of high interindividual variability of the pharmacokinetics of Tenofovir (TFV). The effect of several clinical conditions on the pharmacokinetics of TFV has been observed and may partly explain its variability. We assessed factors influencing the pharmacokinetics of TFV in Thai patients. We found that TFV exposures were independently associated with PI regimens, mild renal impairment, lower body weight, and increasing RTV AUCO-24. Clinicians should be aware of the effect of these factors on TFV exposure when this drug is prescribed.


Complete List of Published Work in My Bibliography:

D. Research Support

Ongoing Research Support
A5316, NIH
Dear E (PI)
Evaluating pharmacokinetics interactions with vaginal ring contraceptive and ART
This study will look at a method of hormonal birth control, called the NuvaRing, and specific anti-HIV medications, called antiretrovirals (ARVs).
Role: Co-Investigator

A5288 (MULTI-OCTAVE), NIH
Dear E (PI)
Management Using the Latest Technologies in Resource-limited Settings to Optimize Combination Therapy After Viral Failure
To use novel agents and contemporary management tools, including standard genotyping to select an appropriate third-line regimen, interventions to improve adherence and plasma viral load (VL) monitoring, in order to achieve a ≥65% rate of virologic control at 48 weeks of follow-up
Role: Co-Investigator
REPRIEVE
This is a randomized trial to prevent vascular events in HIV, tests whether a daily dose of a statin will reduce the risk of cardiovascular disease among HIV-infected individuals (for whom statins are not already recommended according to 2013 US Cholesterol Treatment Guidelines)
Role: Co-Investigator

Phase III Clinical Trial of Ultra-Short-Course Rifapentine/Isoniazid for the Prevention of Active Tuberculosis in HIV-Infected Individuals with Latent Tuberculosis Infection
To compare the efficacy of a 4-week daily regimen of weight-based RPT/INH to a standard 9-month (36 week) daily INH regimen for TB prevention in HIV-infected individuals
Role: Co-Investigator

The goal of this study is to assess the pharmaceutical equivalence of generic antiretrovirals distributed in Thailand both form official and unofficial sources
Role: Co-Investigator

Factors that Attribute to unknown HIV seropositivity and Influence to HIV Testing pattern among High MSM in Bangkok
The goal of this study is to identify psychosocial factors that associated with unknown HIV positive and delayed HIV diagnosis among high risk MSM in Bangkok
Role: PI

Chulalongkorn University

IRC004, NIH/INSIGHT
Beigel J (PI)
IRC004
to evaluate the virologic efficacy of the antiviral Oseltamivir compared to placebo in the treatment of subjects with confirmed influenza (Primary Efficacy Population)
Role: Co-Investigator

IRC003, NIH/INSIGHT
Beigel J (PI)
IRC003
to evaluate the efficacy of the combination antiviral (Oseltamivir/Amantadine/Ribavirin) as compared to oseltamivir alone in the treatment of at-risk subjects with confirmed influenza infection (Primary Efficacy Population)
Role: Co-Investigator

Hepatitis C Co-Infection Study, amFAR TREAT Asia
2013/12/01-2018/12/30
Durier N (PI)
HCV screening study and treatment demonstration project for HIV-positive patients
Role: Co-Investigator

FLU002, NIH/INSIGHT 2009/09/01-2020/10/01
Losso MH (PI)
An International Observational Study to Characterize Adults with Influenza
to describe participants in geographically diverse locations with Influenza virus infection (including influenza A subtypes such as H3N2 and 2009 H1N1, or influenza B) and their clinical course over a 14-day period following enrollment
Role: Co-Investigator

FLU003, NIH/INSIGHT 2009/09/01-2020/10/01
Davey Jr., RT (PI)
An international Observational Study to Characterize Adults Who Are Hospitalized with Complications of Influenza
to describe the characteristics and outcomes over a 60-day follow-up period of participants with influenza virus infection (including influenza A subtypes such as H3N2 and 2009 H1N1, or influenza B) who are hospitalized with severe illness and/or complications, in geographically diverse locations.
Role: Co-Investigator

START, NIH/INSIGHT 2009/03/01-2015/12/31
Neaton, JD (PI)
Strategic Timing of Anti-retroviral Treatment
to evaluate the timing of starting HIV treatment
Role: Co-Investigator

HIV-NAT 006, Thai National Health Security office 2002/10/28-2020/11/01
Phanuphak P (PI)
Long-term HIV cohort
A long-term follow-up of HIV-infected patients
Role: Co-Investigator
NAME: Avihingsanon, Anchalee

eRA COMMONS USER NAME (agency login):
POSITION TITLE: Co-investigator/study physician

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

<table>
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<tr>
<th>INSTITUTION AND LOCATION</th>
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<th>COMPLETION DATE MM/YYYY</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Khon Kaen University, Khon Kaen</td>
<td>MD</td>
<td>1992</td>
<td>Medicine</td>
</tr>
<tr>
<td>Amsterdam University, Amsterdam</td>
<td>PHD</td>
<td>2013</td>
<td>HIV and Coinfection</td>
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</tbody>
</table>

A. Personal Statement

I am primarily responsible for all of the research activities including fulfilling all of the study-specific objectives and requirements; carrying out targeted physical examinations among study volunteers; performing all study-related clinical assessments, clinical counseling of medical test results, and implementing appropriate referrals; prescribing study drugs; assessing all drug-related toxicity and adverse events, immediately responding with emergency treatment if needed; alerting the PI regarding any Expedited Adverse Event (EAE); completing all medical records and CRFs related to clinical activities, such as clinical evaluations, physical examinations, and so forth; assisting, if necessary, in recruiting volunteers, community education, conducting consent; carrying out appropriate communication with local government and regulatory agencies and ensures the completion of local IRB and OHRP requirements; chairing the monthly meetings and taking the final responsibility for all of the specific tasks delegated to the research staff; carrying out protocol training for its site personnel; supervising all local staffs; attending all related meetings and taking conference calls; collecting vaginal specimens, taking responsibility for all medical issues; and taking responsibility for GCP compliance.

B. Positions and Honors

Positions and Employment

<table>
<thead>
<tr>
<th>YEAR - YEAR</th>
<th>POSITION AND COMPANY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1992 - 1994</td>
<td>General practitioner, Khon Kaen Hospital, Khon Kaen</td>
</tr>
<tr>
<td>1996 - 1998</td>
<td>Internal Medicine, Samutsakorn Hospital, Samutsakorn</td>
</tr>
<tr>
<td>1999 - 2000</td>
<td>Volunteer, Harvard School of Public Health, Boston, MA</td>
</tr>
<tr>
<td>2000 - 2002</td>
<td>Research Fellow, Division of Infectious Diseases, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA</td>
</tr>
<tr>
<td>2000 - 2002</td>
<td>Project Coordinator for Metabolic and Bone Associated HAART, Beth Israel Hospital, Boston, MA</td>
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<td>2003 -</td>
<td>Clinical trial coordinator, HIV-NAT, Thai Red Cross - AIDS Research Centre, Bangkok</td>
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<td>2003 -</td>
<td>HIV consultant, Thongburi Hospital, Bangkok</td>
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<td>2003 -</td>
<td>Member, Community Advisory Board for HIV/AIDS research at the Thai Red Cross AIDS Research Centre, Bangkok</td>
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<td>HIV expert working group and consultant, Thailand National Health Security Office, Bangkok</td>
</tr>
<tr>
<td>2003 -</td>
<td>HIV consultant, Taksin Hospital, Bangkok</td>
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</tbody>
</table>
2003 - HIV consultant and educator, Wednesday Friend's Club, Bangkok
2011 - Committee member, Thai AIDS Society, Bangkok
2014 - Committee member, Hepatitis Transformation (ACTG)
2014 - Co-investigator/study physician, HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok

Other Experience and Professional Memberships
1997 - member, The Royal College of Physicians of Thailand
1999 - Member, The Infectious Diseases Society of Thailand
2005 - Member, The Thai AIDS Society
2007 - Member, the International AIDS Society (IAS)

Honors
1997 Chief resident of internal medicine, King Chulalongkorn Memorial Hospital
1998 Best Doctor honor, Samutsakorn Provincial Hospital
2006 International scholarship, Conference on Retroviruses and Opportunistic Infections
2006 International scholarship, Australian Society for HIV Medicine
2007 International Scholarship, International AIDS Society
2007 International scholarship, Conference on Retroviruses and Opportunistic Infections
2008 International scholarship, Conference on Retroviruses and Opportunistic Infections
2008 Resource Limited Scholarship, Ninth International Congress on Drug Therapy in HIV Infection
2009 International scholarship, International AIDS Society
2009 International scholarship, European AIDS Conference
2009 International scholarship, Conference on Retroviruses and Opportunistic Infections
2010 International scholarship, Conferences on Retroviruses and Opportunistic Infections
2010 Resource Limited Scholarship, Tenth International Congress on Drug Therapy in HIV Infection
2011 NUFFIC PhD grant award, The Netherlands Embassy
2011 Scholarship award, 1st Global Workshop in HCV
2011 Fellowship Leader Award, AUSAIDS
2012 International scholarship, Conference on Retroviruses and Opportunistic Infections
2012 Resource Limited Scholarship, 10th International Congress on Drug Therapy in HIV Infection
2014 International scholarship, Conference on Retroviruses and Opportunistic Infections
2014 Scholarship, International AIDS Conference
2015 International scholarship, Conference on Retroviruses and Opportunistic Infections
2015 Australia- APEC Women in Research Fellowship award, Asia Pacific Economic Cooperation

C. Contribution to Science
1. We noticed that many of our patients on standard dose of antiretroviral drugs had a lot of side effects. Therefore we checked the drug levels and found out that all of the patients had very high drug levels. Henceforth, the Thai guideline has revised its recommendation as per our findings. Not only did this decrease side effects but also was cost-effective for the country.


2. We now have solid proof that ART should be started early. This finding has changed the BHIVA guidelines.


3. Many of the findings from our TB studies have impacted the HIV treatment guidelines worldwide.


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are available through the national program for all HIV-infected patients. Likewise, HCV treatment and testing are available through the national program for all HIV-infected patients.


Complete List of Published Work in My Bibliography:
http://1.usa.gov/1kDvg74

D. Research Support

Ongoing Research Support

A5316, NIH Daar E (PI) 04/29/15-01/01/21
Evaluating pharmacokinetics interactions with vaginal ring contraceptive and ART
This study will look at a method of hormonal birth control, called the NuvaRing, and specific anti-HIV medications, called antiretrovirals (ARVs).
Role: Co-Investigator

A5288, NIH Daar E (PI) 03/04/15-01/01/20
Management Using the Latest Technologies in Resource-limited Settings to Optimize Combination Therapy After Viral Failure
To use novel agents and contemporary management tools, including standard genotyping to select an appropriate third-line regimen, interventions to improve adherence and plasma viral load (VL) monitoring, in order to achieve a ≥ 65% rate of virologic control at 48 weeks of follow-up
Role: Co-Investigator

A5332, NIH Grinspoon S (PI) 01/08/15-01/01/22
REPRIEVE, a randomized trial to prevent vascular events in HIV, tests whether a daily dose of a statin will reduce the risk of cardiovascular disease among HIV-infected individuals (for whom statins are not already recommended according to 2013 US Cholesterol Treatment Guidelines)
This is a randomized trial to prevent vascular events in HIV, tests whether a daily dose of a statin will reduce the risk of cardiovascular disease among HIV-infected individuals (for whom statins are not already recommended according to 2013 US Cholesterol Treatment Guidelines)
Role: Co-Investigator

A5279, NIH Campbell T (PI) 10/28/14-01/01/19
Phase III Clinical Trial of Ultra short Course Rifapentine/Isoniazid for the Prevention of Active Tuberculosis in HIV-Infected Individuals with Latent Tuberculosis Infection
To compare the efficacy of a 4-week daily regimen of weight-based RPT/INH to a standard 9-month (36 week) daily INH regimen for TB prevention in HIV-infected individuals
Role: Co-Investigator

IRC003 and IRC004, NIH Beigel J and Treanor J (PI) 05/01/12-06/01/20
IRC003 and IRC004
Comparing the Efficacy, Safety, and Tolerability of Combination Antivirals (Amantadine, Ribavirin, Oseltamivir) Versus Oseltamivir for the Treatment of Influenza in Adults at Risk for Complications
Role: Co-Investigator

START, NIAID, NIH Ruxrungtham K (PI) 01/01/10-12/01/16
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Role: Co-Investigator

A5349, NIH Nahid P and Dorman S (PI) 08/05/15-08/05/18
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This study will evaluate the efficacy of a rifapentine-containing regimen to determine whether the single substitution of rifapentine for rifampin makes it possible to reduce to seventeen weeks the duration of treatment for drug-susceptible pulmonary tuberculosis.
Role: Co-Investigator

Completed Research Support
HIV-NAT 116, HIV-NAT Avihingsanon A (PI) 01/01/14-12/01/15
Efficacy and PK of adjusted dose of Lopinavir/ritonavir and rifabutin in active HIV/TB
Role: PI

CHULALONGKORN UNIVERSITY
BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Avihingsanon, Anchalee

ERA COMMONS USER NAME (agency login):

POSITION TITLE: Co-investigator/study physician

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

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Role: Co-Investigator

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Role: Co-Investigator

Completed Research Support

HIV-NAT 116, HIV-NAT Avihingsanon A (PI) 01/01/14-12/01/15
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Role: PI
BIOGRAPHICAL SKETCH

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NAME
Kerr, Stephen

POSITION TITLE
Head of Biostatistics, HIV-NAT, Thai Red Cross AIDS Research Centre

eRA COMMONS USER NAME (credential, e.g., agency login)
STEVEKR

EDUCATION/Training

INSTITUTION AND LOCATION
University of Sydney
University of New South Wales
Brigham and Women’s Hospital
University of Sydney

DEGREE
BPharm
Ph.D.
Postdoctoral
MIPH

MMYY
02/85
02/97
01/99
04/04

FIELD OF STUDY
Pharmacy
Neuropharmacology
NeuroAIDS
Biostatistics

A. Personal Statement

I am Head of Biostatistics and Data Management at the TRC-ARC, and hold a joint appointment in the Biostatistics and Databases Program at the Kirby Institute, Faculty of Medicine at the University of New South Wales. My background in clinical pharmacy, pharmacology, international public health and biostatistics assist in my understanding of the methodologic and clinical issues which are important in pharmacokinetic, prevention and therapeutic studies. I am biostatistician for several NIH funded clinical studies detailed below in this document. I have taught Survival Analysis, Meta-analysis, Critical Appraisal and Rational Drug Use at Chulalongkorn University in Bangkok, and have supervised and mentored PhD students and Junior Investigators in Australia and Thailand. I have also conducted training in Biostatistics for under the Fogarty Training Grants Program and for TREAT ASIA. Under my direction, the Biostatistics Unit at the TRC-ARC has been built up from a team of 2 to a team of 7 biostatisticians, who provide guidance to clinicians on the biostatistical aspects of conducting and analyzing clinical trial and cohort studies in accordance with International regulations and guidelines.

B. Positions and Honors

Positions and Employment
1985-1989 Clinical Pharmacist, Sydney Children’s Hospital, Randwick, NSW, Australia
1990 Senior Tutor, Department of Pharmacy, University of Sydney, NSW, Australia
1991-1992 Clinical Pharmacist (Oncology/Immunology), St. Vincent’s Hospital, Sydney, NSW, Australia
1992-1994 Consultant Pharmacist, NSW Medicines Information Centre, Sydney, Australia
1993-1998 Research Assistant, Centre for Immunology, St. Vincent’s Hospital, Sydney, NSW, Australia
1999 Postdoctoral Fellow, Brigham and Women’s Hospital/Harvard Medical School, Boston, MA, USA
2000-2004 Decision Support Program Manager, National Prescribing Service, Sydney, NSW, Australia
2000-2004 Adjunct Lecturer, Department of Pharmacy, University of Queensland, Brisbane, QLD
2004- Senior Lecturer, The Kirby Institute, University of New South Wales, Sydney, Australia
2004-2006 Biostatistician, HIV-Netherlands-Australia-Thailand Research Collaboration (HIV-NAT), Thailand
2006- Head of Biostatistics, HIV-NAT, Thai Red Cross AIDS Research Centre, Bangkok, Thailand

Other Experience and Professional Memberships
2001-2004 Member, General Practice Computing Group, Royal Australian College of General Practitioners
2002-2004 Member, Australian Department of Health, Mediconnect Technical Working Group
2002-2004 Member, Australian Department of Health, Mediconnect Evaluation Working Group
2003 The Australian COX-2 Specific Inhibitor (CSI) Prescribing Group
Program Director/Principal Investigator (Last, First, Middle): Chariyalertsak, Suwat, et al.

2003-2004 Member, Australian Council for Safety and Quality in Health Care PDS Working Group
2004 Third Australian National Medicines Symposium Scientific Program Committee
2004-2006 Mentor, Thailand Research Council
2004-2008 Asian Association of Schools of Pharmacy (AASP)
2004-2010 International Society of Pharmacoepidemiology (ISPE)
2007- International Epidemiologic Databases to Evaluate AIDS (leDEA) Cancer Working Group
2009- Biostatistics Reviewer for The Lancet, The Lancet Infectious Diseases
2009- Member, Australasian Society of HIV Medicine (ASHM)
2011- Member, International AIDS Society
2011- Member, American Statistical Association

Honors
1993 Research Scholarship, University of New South Wales, Sydney, Australia
1996 Young Investigator Award, Centre for Immunology, University of New South Wales
1996 Award for Excellence in Research, St Vincent's Hospital/University of New South Wales
1998 Award for Excellence in Research, St Vincent's Hospital/University of New South Wales
1999 CJ Martin Fellowship, National Health and Medical Research Council (NHMRC), Australia

C. Selected Peer-reviewed Publications (Selected from 62 peer-reviewed publications)


The effect of immediate versus deferred antiretroviral initiation on neurodevelopment in children with HIV in Cambodia and Thailand (n=300, 11 sites). Role: Biostatistician

ViiV Healthcare and UNICEF Kerr (PI) 06/2012 - 07/2013
A Randomised trial comparing two interventions to improve adherence to combination antiretroviral therapy (cART) in adolescents and young adults with HIV in Thailand.
This trial compares cognitive restructuring and SMS prompts and a combination of the two strategies to improve adherence in adolescents living with HIV.

Role: PI

**1R01HD073972-01**  
Phanuphak (PI)  
08/2012-07/2017

Human Papillomavirus Infection in Perinatally HIV-infected Adolescents in Asia

This study will evaluate the early natural history of HPV infection and risk factors for HPV acquisition and persistence among HIV-infected and -uninfected adolescents in Asia by monitoring for cervical, vaginal, anal (female and male), oral (female and male), penile, and scrotal HPV infection, and cervical intraepithelial neoplasia.

Role: Biostatistician

**108459-52-ISTA, amfAR, TREAT Asia**  
Phanuphak (PI)  
07/2012-06/2013

Identifying Biomarkers of Anal Intraepithelial Neoplasia in Thai MSM

This study aims to assess the usefulness of biomarkers, including p16 proteins, MCM proteins, high-risk HPV types, and E6 and E7 mRNA/oncoproteins, as adjunct tools to anal Pap smear in identifying HGAIN and to study the impact of HIV infection on the characteristics of anal cytology (by anal Pap smear) and biomarkers.

Role: Biostatistician

**108383-52-IPTA, amfAR, TREAT Asia**  
Ananworanich (PI)  
07/2012-05/2013

Optimizing HIV Treatment for Children in Asia

This is a longitudinal observational cohort study to monitor for treatment failure to second-line ART in Asian children. This study has been implemented in 8 sites, 4 countries.

Role: Biostatistician

Completed Research Support

**CIPRA 1 U19 AI 55741-01A1**  
Ananworanich (PI)  
12/2004-05/2012

The National Institutes of Health

Pediatric Randomized of Early vs Deferred Initiation in Cambodia and Thailand (PREDICT)

An open label, randomized study to compare antiretroviral therapy initiation when CD4+ is between 15-24% to ART initiation when CD4+ falls below 15% in children with HIV infection and moderate immune suppression.

Role: Biostatistician

**R01MH089722**  
Ananworanich (PI)  
05/18/2010-03/31/2011

National Institute of Child & Health Development (NICHD) and National Institute of Mental Health (NIMH)

Neurodevelopment and brain imaging among HIV-infected Children

The effect of immediate versus deferred antiretroviral initiation on neurodevelopment in children with HIV in Cambodia and Thailand (n=300, 11 sites)

Role: Biostatistician

Department of Veterans Affairs, Australia  
Mant (PI)  
2007-2010

Time to all cause mortality analysis for NSAID and COXIB users

This study will assess mortality in patients using NSAID and COXIB.

Role: Biostatistician

**5U01AI069907/107694-46/-107798-47-IGTA**  
Phanuphak (PI)  
07/2009-06/2010

Biomarkers to detect anal intraepithelial neoplasia among Thai men who have sex with men

This study will investigate which biomarkers can reliably and accurately detect anal intraepithelial neoplasia in Thai men who have sex with men.

Role: Biostatistician
**BIOGRAPHICAL SKETCH**

Provide the following information for the Senior key personnel and other significant contributors. 

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

**NAME:** Thammajaruk, Narukjaporn  
**eRA COMMONS USER NAME (agency login):**  
**POSITION TITLE:** Clinical Laboratory Pharmacologist

**EDUCATION/TRAINING**  
(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

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<tr>
<td>Faculty of Pharmaceutical Science, Chulalongkorn University, Bangkok</td>
<td>BS</td>
<td>03/2008</td>
<td>Microbiology</td>
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<td>Faculty of Pharmaceutical Science, Chulalongkorn University, Bangkok</td>
<td>MS</td>
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<td>HIV-NAT, Thai Red Cross - AIDS Research Centre, Bangkok</td>
<td>Other training</td>
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<td>HIV-NAT Laboratory, Thai Red Cross - AIDS Research Centre, Bangkok</td>
<td>Other training</td>
<td>2010</td>
<td>HPLC Operation</td>
</tr>
<tr>
<td>World Courier, Bangkok</td>
<td>Other training</td>
<td>2011</td>
<td>Shipping of infectious substances &amp; biological substances, category B, Kinetex Core-Shell Technology, Columns Ultra-high Performance on ANY LC System</td>
</tr>
<tr>
<td>Kinetex, Bangkok</td>
<td>Other training</td>
<td>2011</td>
<td>basic knowledge in HIV pediatrics, Laboratory Equipment Quality Management for Minimize Risk</td>
</tr>
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<td>2011</td>
<td>ISO/IEC 17025:2005 for Technical requirements</td>
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<td>2011</td>
<td>Lab water; an Innovation Solution</td>
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<td>2012</td>
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<td>Merck Millipore, Bangkok</td>
<td>Other training</td>
<td>2012</td>
<td>Management of Scientific instruments with PIC/S Regulations</td>
</tr>
<tr>
<td>International AIDS Society (IAS), Kuala Lumpur</td>
<td>Other training</td>
<td>2013</td>
<td>7th Conference on HIV Pathogenesis, Treatment and Prevention</td>
</tr>
<tr>
<td>Chulabhorn Research Institute, Bangkok</td>
<td>Other training</td>
<td>2013</td>
<td>Sritiporn Scientific &amp; Technology Conference</td>
</tr>
<tr>
<td>Air Course, Bangkok</td>
<td>Other training</td>
<td>2014</td>
<td>Dangerous Goods Awareness with Concentration on preparing, handling &amp; transporting Infectious Substances</td>
</tr>
</tbody>
</table>
A. Personal Statement

I am currently the clinical laboratory pharmacologist for TRCARC HIV Treatment Clinical Research Site under the Thailand HIV/AIDS and Infectious Disease Clinical Trials Unit (THAI CTU). I am primarily responsible for complying with GCP/GCLP and all SOPs applicable to ACTG responsibilities; performing the duties of a study coordinator for PK/PD project; working with clinical operations, developing the operational strategies for clinical pharmacology studies; providing consultations for implementing pharmacologic studies, operations, and monitoring adherence to the protocol; managing program timelines for clinical pharmacology studies; analyzing data, interpreting results, and other clinical pharmacology-related clinical documentation, including clinical protocols; study reports and other various internal and external documents and communications, as needed; collecting, preparing and processing study specimens for the Clinical Laboratory; assessing the levels of the ART drugs in the study samples; performing, recording, and reporting laboratory results, confirming normal results; reviewing the Quality Control (QC) results daily by using acceptability criteria and L-J chart, Westguard Rules before reporting the patient's results; performing Proficiency Testing (PT); verifying and approving laboratory results; keeping and maintaining records of tests performed, laboratory records; conducting and documenting appropriate quality control and assurance procedures for monitoring an evaluating the quality of the testing process of each method; maintaining communication between laboratory and clinical staff; coordinating with HIV-NAT study nurses, physicians and others for the shipment of biological specimens according to the IATA guidelines; conducting, managing and performing laboratory equipment/instrument maintenance system; maintaining high standards of laboratory house keeping, ensuring laboratory supplies and stocks are managed; using appropriate Personal Protective Equipment (PPE); demonstrating compliance with infection control policies and procedures; and performing work in a manner that reduces risk of transmission of infection to patients, self, and co-workers. I have around 4 years experience as a clinical laboratory pharmacologist for the HIV-NAT lab and can develop and validate assays for various drugs.

B. Positions and Honors

Positions and Employment
2010 - Clinical Laboratory Pharmacologist, HIV-NAT, Thai Red Cross - AIDS Research Centre, Bangkok

Other Experience and Professional Memberships
2008 - Member, Pharmacy Council of Thailand
2013 - Member, International AIDS Society (IAS)

Honors
2014 HIV Research Trust Scholarship, Wellcome Trust

C. Contribution to Science

1. The findings from these studies will help the sexual health/reproductive pharmacokinetics field


2. The findings from these studies will help the pharmacokinetics field:

3. The finding from this study will contribute to the pharmacogenomics field for TDF:

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/1rA91AGUETmQD/bibliography/47600351/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

Tenoforv Renal Toxicity and Glomerular Filtration Rate (GFR) Validation, Office of the National Research Council of Thailand
Phanupak P (PI)
Incidence and Predictor of TDF Associated Nephrotoxicity and Pharmacokinetic of TDF in HIV-1 Infected Thai Patients: A Sub-study of HIV-NAT 006 Long Term Cohort
To assess and validate equation eGFR in HIV-infected subjects and -uninfected Thai patients
Role: OP

A5279, NIH
Campbell T (PI)
Phase III Clinical Trial of Ultra-Short-Course Rifapentine/Isoniazid for the Prevention of Active Tuberculosis in HIV-Infected Individuals with Latent Tuberculosis Infection
To compare the efficacy of a 4-week daily regimen of weight-based RPT/INH to a standard 9-month (36 week) daily INH regimen for TB prevention in HIV-infected individuals
Role: OP

A5332, NIH
Grinspoon S (PI)
REPRIEVE
This is a randomized trial to prevent vascular events in HIV, tests whether a daily dose of a statin will reduce the risk of cardiovascular disease among HIV-infected individuals (for whom statins are not already recommended according to 2013 US Cholesterol Treatment Guidelines)
Management Using the Latest Technologies in Resource-limited Settings to Optimize Combination Therapy After Viral Failure

To use novel agents and contemporary management tools, including standard genotyping to select an appropriate third-line regimen, interventions to improve adherence and plasma viral load (VL) monitoring, in order to achieve a ≥ 65% rate of virologic control at 48 weeks of follow-up.

Evaluating pharmacokinetics interactions with vaginal ring contraceptive and ART

This study will look at a method of hormonal birth control, called the NuvaRing, and specific anti-HIV medications, called antiretrovirals (ARVs).

Hormonal contraception in HIV-positive women

This is a prospective cohort study with 200 Thai HIV-positive women on HAART and willing to use hormonal contraception provided as a standard low-dose COC pill for two months.

The study of ATV/r-based HAART in Thai HIV-infected children

This trial will study the pharmacokinetics of ATV/r in HIV-infected Thai children.
CURRICULUM VITAE
Suwapit Prasertthanawut

PERSONAL
Date of Birth: 7 April 1988
Address: HIV-NAT, The HIV Netherlands Australia Thailand Research Collaboration and Thai Red Cross AIDS Research Centre, 104 Ratchdamri Road, Pathumwan, Bangkok 10330, Thailand
Phone: 0-2652-3040-9 Ext.136 (Office), 086-388-0213 (Mobile)
Email: suwapit.p@hivnat.org

EDUCATION
Bachelor of Pharmacy, 2007-2011
Faculty of Pharmacy, Srinakharinwirot University

POSITION
Present: Clinical research associate
August 2012 – August 2013:
- Junior clinical research associate (Monitor) at The HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT)
April 2012 - August 2012:
- CRA Assistant at The HIV Netherlands Australia Thailand Research Collaboration (HIV-NAT)

TRAINING EXPERIENCE
August 2012 11th HIV/AIDS workshop 2012 by THAI AIDS SOCIETY
June 2012 International “Standard Course in Clinical Trials” by faculty of Medicine, Chulalongkorn University
May 2012 Good Clinical Practice & Human Subject Protection by HIV-NAT
October 2011 CRA Internship at Bayer company