1. **Title**: Requirements for Conducting Multi-Country Safety Surveillance of Vaccines in the Asia-Pacific region

2. **Background**:

Databases derived from electronic medical records (EMR) are increasingly used to conduct post-licensure vaccine safety studies. Within the United States (US), the Vaccine Safety Datalink (VSD) established by the Centers for Disease Control and Prevention, and the Food and Drug Administration's (FDA) Post-licensure Rapid Immunization Safety Monitoring (PRISM) are well-established systems that have been used to evaluate multiple products and safety events (Baggs 2011, Fahey 2015). In the European Union (EU) country-specific databases such as the Clinical Practice Research Datalink (CPRD) and the Health Improvement Network (THIN) in the United Kingdom, and national registries/databases (e.g., Nordic countries, France Germany), have been used in a similar capacity (Dodd 2013, Pasternak 2012). The strengths of these databases lie in their ability to record vaccine data linked to important in-patient and/or outpatient safety outcomes.

As the knowledge base in the US and EU continues to expand, less information is known about capabilities in the Asia-Pacific region to coordinate vaccine safety surveillance. A recent paper characterized the databases of the Asia-Pacific region though the focus was on medicines, not vaccines which gives rise to a different set of challenges (Lai 2015) including the requirement for data linkage with immunization registries, payment, coding systems, and vaccine formulations.

In the 2014 ISPE "Call-for-manuscripts" a proposal was accepted and has since been published titled: Importance of Feasibility Assessments Before Implementing Non-Interventional Pharmacoepidemiologic Studies of Vaccines (Williame 2016). We propose a follow-up paper that explores the feasibility of conducting vaccine safety studies in the Asia-Pacific region and additionally we will evaluate the capability of countries in the region to collaborate on multi-country studies. Unlike in the US and to some extent in the EU, information on national data sources and specialized databases for each country of the Asia-Pacific region has not been cataloged in the public domain. Opportunities to conduct vaccine safety research on emergent issues of existing vaccines and for new vaccines in development are limited to country-specific researchers and those with direct access to the data. In-depth knowledge of vaccine exposure data and linkage, or potential for linkage to outcome data will provide an opportunity to use a distributed network approach to assist with the rapid identification and investigation of safety issues with vaccines. Developing this capacity also has value in providing evidence for risk communication and strengthening vaccination policy in resource-poor countries with limited or no ability to conduct routine safety assessment of vaccines.

3. **Objective**:

The purpose of this project is to provide guidance on best practice for capture of data to support vaccine safety surveillance including countries with limited data capture. The aims of this project are:

   1. Referencing the Feasibility Tool box by Williame et al., we aim to develop a reference guide of databases for supporting vaccine safety research specifically for the Asia-Pacific region
      a. Types of data sources: claims data, inpatient / outpatient data, EMR data, patient reported events immunization registry and national death registry

   b. Exposure identification including sources of vaccine information, types of vaccines available, dose/batch capture, populations covered, and vaccine schedule including listing of common vaccines/coding systems
   c. Outcome identification including priority outcomes for study
   d. Existing/new linkages between datasets
2. Evaluate capabilities for multi-database analyses across Asia-Pacific
   a. Establish best practices for capture of data and recommendations for assessing quality of data capture
   b. Delineate requirements for a minimum dataset
   c. Access issues (ethical boards, privacy, cost, governance)
   d. Platforms (data management systems)
   e. Potential to translate to common data model platform

4. Rationale/Priority:

The International Society of Pharmacoepidemiology's (ISPE) call for manuscript proposal seeks proposal for guideline development or reference documents related to **real world evidence** and **communicating risks**. As such, the proposed manuscript proposal developed jointly by the Vaccine and the Asian Pharmacoepidemiology Network (AsPEN) SIGs will harness their expertise and resources to:

- Advance pharmacoepidemiology research capabilities in support of vaccine safety by cataloging database resources
- Use knowledge gained to provide guidance document on best practices for countries with limited data capture capabilities for vaccines
- Advocate for improved access to and quality of existing databases for multi-country vaccine safety surveillance
- To translate experience from multi-country studies in medicines in pharmacoepidemiology global community to multi-country studies in vaccines

5. Issue to be addressed:

The proposed joint ISPE SIG Vaccine and AsPEN working group will address the need for a resource dedicated to detailing databases in Asia-Pacific that can support observational research for emerging and existing vaccine safety issues. In addition, the working group will use the output to address capabilities for multi-country database assessment and advocate for enhancements to existing data collection systems.

6. Content:

The primary output of this project will be a manuscript that will identify existing databases in the Asia-Pacific region that can support observational research to inform vaccine safety, provide best practices for capture of data to support vaccine safety surveillance, and advocate for improved access to and quality of existing resources. The series of tables supporting the manuscript will serve as a reference guide for all vaccine researchers both internal to ISPE and globally. The best practices recommendations will apply to the global community.

SUPPLEMENTAL MATERIAL

7. Composition of Working Group:

Members from the joint AsPEN and Vaccines SIGs are uniquely qualified to develop these recommendations. First, the working group consists of pharmacoepidemiologists across government, industry and academia. Each of these colleagues has engaged in a diverse array of vaccine safety studies throughout the world. These collective experiences will ensure a well-defined assessment tool will be developed to assess existing data resources and understand the requirements for best practices. Second, the working group includes members affiliated with the ADVANCE consortium who can advise and support synergies with ADVANCE. Finally, this working group has conducted vaccine safety research across the world and inclusion of many colleagues from the Asia Pacific region through AsPEN will ensure a comprehensive evaluation of the region occurs. The co-chairs of the working-group have identified a potential PhD student who will work closely with the co-chairs to develop the survey, collate responses and draft the results section of the manuscript.

Nicole Pratt of the AsPEN SIG and James Stark of the Vaccines SIG will co-chair the working group.

Interested members from the following SIGs will participate in survey development, data collection, analysis, guidance development and manuscript preparation:

AsPEN SIG (7)

- **Tomomi Kimura, MD, PhD**

  Title: Director, Epidemiology, Medical Affairs
  Affiliation: Astellas Pharma Inc.
  Expertise: Tomomi is a physician-epidemiologist at Astellas Pharmaceuticals. Before joining Astellas, she was working for MSD (a subsidiary of Merck in Japan) and Janssen. She has been a member of ISPE and leads various industry taskforces for the Japan Pharmaceutical Manufacturers Association (JPMA) since 2006.
  Country: Japan

- **Kiyoshi Kubota, MD, PhD, FISPE**

  Title: President
  Affiliation: NPO Drug Safety Research Unit Japan and ISPE
  Expertise: Prior to serving as President of the NPO Drug Safety Research Unit, he was a Professor in the Department of Pharmacoepidemiology at the University of Tokyo. He has been a member of ISPE since 1995 and has led several groups including AsPEN and the Global Development Council. He has been an associate editor of Pharmacoepidemiology and Drug Safety since 2010.
  Country: Japan

- **Edward Chia Cheng Lai, PhD**

  Title: Assistant Professor

Affiliation: School of Pharmacy and Institute of Clinical Pharmacy and Pharmaceutical Sciences, College of Medicine, National Cheng Kung University, Taiwan.
Expertise: His expertise includes clinical pharmacy and pharmacoepidemiology with special interests of psychiatry, neurology and international multi-database pharmacoepidemiologic study. He is the current co-Chair of the AsPEN SIG.
Country: Taiwan

- **Yanfang Liu, MD, MPH**

  Title: Director, Epidemiology Asia Pacific
  Affiliation: Janssen, a division of Johnson and Johnson
  Expertise: Yanfang has greater than 10 years of experience in pharmacoepidemiology and epidemiology of vaccines for the Asia Pacific region and has authored several observational vaccine safety studies using electronic healthcare databases.
  Country: Singapore

- **Kenneth Man, PhD, MPH**

  Title: Senior Research Assistant
  Affiliation: Centre for Safe Medication Practice and Research, the University of Hong Kong; Research Department of Practice and Policy, UCL School of Pharmacy.
  Expertise: Kenneth is a Senior Research Assistant at Centre for Safe Medication Practice and Research, the University of Hong Kong. Kenneth is a medical statistician with expertise in the analysis of linked health-care data. He is the current co-chair of the Asian Pharmacoepidemiology Network (AsPEN) SIG. Kenneth is also a Visiting Scientist at the Research Department of Practice and Policy, UCL School of Pharmacy, London carrying out pharmacoepidemiology studies utilising multi-country datasets.
  Country: Hong Kong

- **Nicole Pratt, PhD**

  Title: Associate Professor and Chief Investigator
  Affiliation: Centre of Research Excellence in Postmarket Surveillance of Medicines and Devices, University of South Australia
  Expertise: Nicole is an Associate Professor at the Quality Use of Medicines and Pharmacy Research Centre, Sansom Institute, University of South Australia. Nicole is a biostatistician with expertise in the analysis of linked health-care data. She is the past co-chair of the Asian Pharmacoepidemiology Network (AsPEN) SIG. Nicole has experience linking the Australian Childhood Immunisation Registry with the National Death Registry for vaccine safety surveillance and was an expert member of the Australian Therapeutic Goods Administration (TGA) Advisory Committee on the Safety of Vaccines (ACSOV).
  Country: Australia

- **Sawaeng Watcharathanakij, R.Ph., PhD**

Title: Assistant Professor
Affiliation: Faculty of Pharmaceutical Sciences, Ubon Ratchathani University, Thailand
Expertise: His research interest includes identifying optimal measurement model for temporal relationship between causes and outcomes in pharmacoepidemiology, drug utilization study and drug use evaluation from database.
Country: Thailand

Vaccines SIG (7)

- **Bob Chen, MD, MA, FISPE**

  Title: Medical Officer
  Affiliation: Clinical Trials Team, Centers for Disease Control and Prevention
  Expertise: Conducted research on the epidemiology and pharmacoepidemiology of vaccines and vaccine-preventable diseases (VPD) for ~30 years at CDC. Played leading role in modernizing the vaccine safety infrastructure in the U.S. and elsewhere, including the Vaccine Adverse Event Reporting System (VAERS), Vaccine Safety Datalink (VSD), Clinical Immunization Safety Assessment (CISA) Network, the Brighton Collaboration, and the Safety Injection Global Network (SIGN). He has coauthored ~250 scientific publications, many of which were the results of multi-national, multi-site studies. He is an Associate Editor of Vaccine and founding Chair of ISPE VAXSIG.
  Country: United States

- **Catherine Cohet, PhD**

  Title: Senior Epidemiology Expert
  Affiliation: Glaxo Smith Kline Division of Vaccines
  Expertise: Catherine had greater than 10 years of experience in epidemiology and pharmacoepidemiology of vaccines. She has participated on several multi-national consortiums including the ADVANCE project.
  Country: Belgium

- **Katherine Duszynski, BSc GDPH**

  Title: Coordinator/PhD Candidate
  Affiliation: Vaccine Assessment Using Linked Data Safety Study, University of Adelaide, University of South Australia
  Expertise: Katherine has some 15 years of experience undertaking pharmacoepidemiological investigations in the primary care and pediatric settings. Her doctoral work examines the application of Australian health administrative data for vaccine safety assessment in young children including, evaluation of data quality and statistical methodologies.
  Country: Australia

- **Wan-Ting Huang, MD**

  Title: Chief Medical Officer

Affiliation: Office of Preventive Medicine, Taiwan Centers for Disease Control
Expertise: Wan-Ting's work and research area include public health surveillance, vaccine epidemiology, and training/supervision of Field Epidemiology Training Program (FETP) fellows. She is a board member of ISPE and involved in several international collaborative vaccine safety projects.
Country: Taiwan

- **Alena Khromava, MD, MPH**

  Title: Senior Director, Pasteur Pharmacoepidemiology Lead
  Affiliation: Sanofi Pasteur
  Expertise: Her current area of interest is in epidemiologic methods used in vaccine safety and benefit-risk assessment of vaccines. Prior to joining Sanofi Pasteur, she completed Epidemic Intelligence Service at the US Centers for Disease Control and Prevention in Immunization Safety Branch. She is currently leading work package 3 of the ADVANCE consortium.
  Country: Canada

- **Sonali Kochhar, M.D**

  Title: Medical Director
  Affiliation: Global Healthcare Consulting
  Expertise: Sonali has over 15 years of leadership experience for Global Phase I-IV Clinical Research, Epidemiology and Safety Studies for Vaccines conducted in the USA, Europe, Asia, Africa and India in adult and pediatric populations.
  Country: India

- **James Stark, PhD**

  Title: Director, Epidemiology
  Affiliation: Worldwide Safety and Regulatory, Pfizer Inc.
  Expertise: James is an infectious disease epidemiologist with multiple years of experience studying vaccine safety and vaccine preventable diseases at both Pfizer and the New York City Department of Health and Mental Hygiene. At Pfizer, he conducts safety studies from data sources around the world. He is Adjunct Faculty at the College of Global Public Health at New York University and the Vice-Chair of the Vaccine SIG.
  Country: United States

8. Conflict of Interest:

Bob Chen: No relationships to disclose

Catherine Cohet: Employed by GSK, pharmaceutical company (commercial entity), holds GSK stock

Katherine Duszynski: No relationships to disclose

Edward Lai: No relationships to disclose

Yanfang Liu: Employed by Janssen R&D, pharmaceutical company (commercial entity), holds GSK and Johnson and Johnson stock

Wan-Ting Huang: No relationships to disclose

Alena Khromava: Employed by Sanofi Pasteur, pharmaceutical company (commercial entity), holds Sanofi Pasteur stock

Tomomi Kimura: Employed by Astellas Pharma Inc., pharmaceutical company (commercial entity), holds Astellas stock

Sonali Kochhar: No relationships to disclose

Kiyoshi Kubota: No relationships to disclose

Kenneth Man: No relationship to disclose

Nicole Pratt: No relationships to disclose

James Stark: Employed by Pfizer Inc., pharmaceutical company (commercial entity), holds Pfizer stock

Sawaeng Watcharathanakij: No relationships to disclose

9. **Budget**:

A budget of $11,800 will be used to support this research project.

Task	Estimated Cost
Survey monkey subscription (subscription with unlimited questions)	$300
PhD student assistance (create survey monkey tool, collate responses, draft results section of manuscript, travel to mid-year ISPE meeting, student abstract submission)	$8,000
ISPE Toronto mid-year meeting (room hire and catering)	$1,000
ISPE Prague meeting (room hire and catering)	$1,000
Manuscript submission fee	$1,500
Total	**$11,800**

10. **Target Journal**:

Pharmacoepidemiology and Drug Safety published by John Wiley and Sons. This journal has a diverse global audience including epidemiologists, statisticians, vaccinologists, public health practitioners and physicians.

11. Bibliography:

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Dodd CN, Romio SA, Black S, et al. International collaboration to assess the risk of Guillain Barre Syndrome following influenza A (H1N1) 2009 monovalent vaccines. Vaccine 2013;31:4448-58.

Fahey KR. The Pioneering Role of the Vaccine Safety Datalink Project (VSD) to Advance Collaborative Research and Distributed Data Networks. EGEMS (Wash DC). 2015 Dec 29;3(1):1195

Lai ECC, Man KKC, Chaiyakunapruk N, et al. Databases in the Asia-Pacific region: the potential for a distributed network approach. Epidemiology 2015;26:815-820.

Pasternak B, Svanstrom H, Molgaard-Nielsen D, et al. Risk of adverse fetal outcomes following administration of a pandemic influenza A(H1N1) vaccine during pregnancy. JAMA 2012;308:165-74.

Williame C, Baril L, van den Bosch J, et al. Importance of feasibility assessments before implementing non-interventional pharmacoepidemiologic studies of vaccines: lessons learned and recommendations for future studies. Pharmacoepidemiology and drug safety 2016;25:1397-1406.

12. Timeline:

Event	**2017**			**2018**								
	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep
Formation of joint working group												
Kickoff meeting												
Monthly conference calls												
Data collection tool development												
Data resource assessment development												
Survey data resources												
1st face to face meeting – Toronto												
Analyze data and produce tables												
Gap analysis of data source capability												
Develop draft guidance												
Draft manuscript												
Review of manuscript												
2nd face to face meeting – Prague												
Finalize manuscript and submission												