Introduction

This position paper is a collaborative effort of members of Philippine Clinical Research Professionals Inc. (PCRP) in the pursuit of PCRP's commitment to partner with key players in the field of clinical research.

PCRP is an association of clinical research professionals from the academe, pharmaceutical industry, contract research organizations (CROs), and other groups involved in clinical research. To date, PCRP has a membership of over 200 clinical research professionals. The vision of PCRP is for its members to be highly competent clinical research professionals committed to partner with key players in the field in raising the standards of clinical research practice in the country, so as to safeguard the rights and well-being of clinical trial subjects. More info about PCRP can be found at www.pcrp.org.ph

The Bureau of Quarantine (BOQ) of the Department of Health exercises the regulatory functions as the health authority in seaports and airports and with specific strategy to conduct surveillance and institute infection control measures to prevent the entry and spread of infectious diseases through effective entry-exit management at seaports and airports of entry.

Background

Clinical trials have long been conducted in the Philippines, especially local studies as these were part and parcel of how medical students and scientists need to advance science in the country. In the early 90's, the Bureau of Food and Drugs required new registered drugs to be monitored in the local market for three (3) years. This requirement spurned the rise of local post-marketing surveillance studies that are still being conducted up to this time.

The influx of randomized controlled clinical trials (RCTs) came in the late 90's with large pharmaceutical countries recognizing the opportunity that Philippines have over other Southeast Asian countries in terms of language facility, huge talent of doctors and nurses and the pool of patients that we could contribute. This influx resulted in the rise of contract research organizations (CROs) and more investments in clinical research in the country.

For the past 10 years, the growth of international, global clinical trials have been steadily rising. The impact of harmonization of how clinical trials are conducted, through ICH-GCP (International Conference on Harmonization- Good Clinical Practice) became the basis for the globalization of clinical trials. Philippines has become an emerging market for international trials. In 2009, *clintrials.gov* which is a global registry of clinical trials conducted all around the world lists Philippines as having close to 400 clinical studies (both completed and ongoing since Philippines was included in this global registry).

Global Clinical Trials and Why biological samples need to be shipped out of the country?

The Philippines is now becoming a major participant in global trials. The bulk of clinical trials being conducted in the country now has focused on international, multi-centre trials. A trial is thus being participated in by as much as 50 to 60 countries. One country may be participated by as as much as 10 to 20 hospitals.

Clinical trials involve the analysis of different variables and parameters in order to assess the efficacy and safety of the investigational product. One way to measure efficacy and/or safety is to perform various, protocol-specific analyses on human biological samples such as blood and tissue samples. Since trials are conducted globally and samples are collected from different hospitals/institutions, the need to control a potential source of variability in the measurement of the efficacy and/or safety endpoints is of absolute importance. Global trials, thus, commonly employ/contract only one laboratory to perform analyses of all samples collected globally. The laboratory contracted to do these are often located outside the Philippines, thus the samples need to be shipped out for analyses.

A sample flowchart of a clinical study can be found in Appendix 1 to demonstrate the different steps that a clinical trial patient will undergo – from screening to study end, to better understand the various processes involved in the conduct of a clinical trial.

BOQ Practice on outbound shipment of biological samples used in medical/clinical research

The BOQ is currently requiring an export license to be obtained for a single outbound shipment of a biological sample to be shipped to a central laboratory.

Historically, the BOQ based on the Quarantine Act of 2004, granted Export Permits for the entire duration of a clinical trial after the approval from the Food and Drug Administration (FDA) (previously Bureau of Food and Drugs, BFAD) has been obtained.

This was changed sometime in 2006-2007 where export licenses were granted on a one license per clinical study per year basis.

The requirements for both processes were the following:

- FDA (BFAD) approval
- description of the shipment
- duration of the study
- estimated amount of biologicals to be shipped out
- List of the participating sites with the corresponding names of the Principal Investigators

In 2009, BOQ came up with a new process that requires applicants to obtain a new export license for every shipment of biological samples. So a shipment date has to be stated in the application letter. The Export License/BOQ permit obtained will carry this date and is valid only on the indicated shipment date/s.

The new process has caused severe impact on the clinical research industry and it has affected us in a number of ways.

The Realities of the Current Licensing Process that Impact the Clinical Research Industry

1. There is huge variability in the nature of how clinical trials are conducted.

   Obtaining Export License that is good only for one shipment date may be equivalent to one defined visit of one clinical trial patient.

   With multiple sites, multiple clinical trial patients, multiple visits, and multiple blood draws, this process becomes almost impossible to comply with.

   The structure of clinical trials involves taking serial samples of these specimens from any one patient. The amount and frequency of blood draws would therefore depend on the clinical protocol and its objectives. This does not mean, however, that the exact dates of these specimen draws are predictable, as these depend on when a subject enters a study. Not only that as clinical trial patients come from multiple sites.

2. Timely reporting of laboratory results is an integral factor in the management of clinical trials.

   Results of laboratory data may impact on how the investigators/doctors will manage the care and well-being of their clinical trial patients. From pick-up at hospitals to delivery of shipment to Central Laboratories (most often located in Singapore) – this chain requires a very smooth flow otherwise, the samples are rendered useless.

3. A clear, concise, and written guideline on the process and its requirements (and rationale for such requirements) for shipment of biological samples collected from clinical trials could not be found.

   This lack of documentation presents a major problem when we are preparing clinical trial budgets because of the need to justify the shipment costs.

   Clinical research has always been guided by a sound, justified need – the safety and well-being of clinical trial patients and the integrity of its data. It also goes hand-in-hand with the need for a sound, justified financial program. The impact of obtaining hundreds and hundreds of Export Licenses will translate to a huge expense if we compare Philippines to other Southeast Asian countries in terms of how much is being paid for Export License as the other SEA countries have no such thing. This puts a question on the viability of including Philippines as a participating country in clinical trials.

4. The new process has a huge impact on clinical operations

   The logistical challenges are extremely cumbersome and are hindering with the planned smooth flow of operations that clinical trials need to have in order to succeed. And with the rise in the number and magnitude of clinical trials being done in the Philippines, this stunts the potential growth of the industry and impacts our competitiveness as a major player in the region.

   Severe adverse increase in operational costs – CRA hours have to be increased to accommodate the numerous applications, licensing costs of the Export Permits, messengerial, courier, freight and telecommunication charges have drastically increased. Man-hours of even the site staff have to be factored-in because they too have been affected by this process.

We feel that on the Bureau's side, the workload of having to change dates of import licenses and granting new ones are becoming taxing and cumbersome, with the frequency of having to do these tasks and having to accommodate all these requests.

To reiterate the impact of the huge increase in operation - on the business side of things, increased cost in doing clinical trials diminishes the country's viability as a major player in the clinical research industry.

The country's unique attributes that put us ahead of other nations in the region, like having a population that can speak and understand English, for example, can be set aside when a Sponsoring company considers the cost of doing clinical trials. Other countries whose requirements are not as stringent and costly might be considered over the Philippines, even if we have the more capable doctors and study sites and the desired patient population.

Export License Requirements from other countries in the Region

Country	Export License Requirement for Biological Samples
Hongkong	No requirement
Malaysia	No requirement
Singapore	No requirement
Tawan	Yes, export license for the study after regulatory approval. Requirements to obtain export license : Regulatory approval, name and address of Central Laboratory; at least 1 approval from Ethics of participating hospital. Export license is valid for up to 3 years.
Thailand	Yes. Requirement for regulatory approval is needed.
South Korea	No requirement
Vietnam	Yes, export license for the study after regulatory approval. Requirements needed : Regulatory approval, name & address of Central Laboratory; Export License valid for 1 year

With reference to tabulation, 4 of the 7 countries do not require export licenses for biologicals. Of the 3 countries that do require it, 2 have validities for a year or more. None of these countries require one export license per shipment.

Our country is not at par with our neighbors in the region, in terms of exporting biological samples used in clinical research and in other regulatory processes in the conduct of clinical research.

PCRP's Recommendations

PCRP is working hard to partner with key players in the clinical research industry so that sound, logical, practical guidelines and processes are put in place to level up Philippines to the rest of the countries that are active in the conduct of clinical research.

PCRP's Recommendations in obtaining Export Permit for Outbound Shipment of Biological Samples for Use in Clinical/Medical Research

1) The Bureau of Quarantine has to develop a written guideline/memo/communication on the export licensing process and its requirements. This would help prevent confusion within the industry and will facilitate the understanding of one of our country's regulatory processes. This would also put the Philippines at par with our neighboring countries in SEA with sound and firm guidelines on exportation.

2) PCRP recommends for an annual Export License for every clinical trial. This Export License will cover all participating sites/investigators of the clinical trial.

3) PCRP recommends that an annual listing of outbound shipments be provided by the courier companies, regardless of the shipper and consignee. Courier companies are the last person that handles the outbound shipments. But we recommend also that to make this work, consultation with the courier companies must be ensued to check the viability of this idea. After all, guidelines and processes must be practical, workable and sustainable.

Conclusion

The use of human biological specimens is critical for clinical/medical research. In reality, patient specimens that have a minimal likelihood of containing pathogens are exempt from many shipping requirements. The public and more so, the clinical study participant, must have confidence that researchers will handle and use such materials sensitively and responsibly.

PCRP acknowledges the role of BOQ to safeguard and protect the public from entry and spread of infectious diseases and other biological hazards. This same principle is also an important concern for PCRP.

We are all involved in the health industry, we are all guardians of our society's health and well-being. It is therefore our duty to ensure that quality health care is accessible, obtainable and would be available at fair cost to all people. A streamlined regulatory process, including the BOQ, is thus urgently needed.

The clinical supply chain (from importation and exportation) must then be clear-cut, well-thought-of, well-designed with no blockage from all parties concerned in the conduct of clinical trials – FDA, hospitals, Bureau of Customs, BOQ, courier companies, and the other industries that are linked in the whole operation on clinical/medical research.

Communication of the new guidelines will pave the way for less work for all concerned (less labor, less expense) which will translate with more ease (without sacrificing the evaluation and review of outbound shipments by concerned agencies of the government) and will ensure that new investigational products and drugs will get into the market sooner, for the benefit of patients afflicted with different diseases.

With streamlined processes and with written guidelines for the country, PCRP believes that Philippines as a country will become more competitive and will provide for more capability in conducting global clinical trials. The country has to get up to the speed of globalization. Alignment of regulatory policies and processes with the rest of the world will make us a stronger participant in global clinical trials.

Thank you very much.

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