การพัฒนาระบบการพิจารณารับรองมาตรฐานสถานที่ผลิตยาในต่างประเทศ
Thai FDA Development of GMP Accreditation Approval System for Oversea Manufacturers

นิพนธ์ต้นฉบับ

Original Article

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บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาสถานการณ์และพัฒนาระบบการพิจารณารับรองมาตรฐานสถานที่ผลิตยาในต่างประเทศที่เหมาะสมกับประเทศไทย **วิธีการศึกษา:** แบ่งเป็น 2 ระยะ ระยะที่ 1 การวิเคราะห์สถานการณ์ระบบการพิจารณารับรองฯ โดยเก็บข้อมูลจากเอกสาร การสัมภาษณ์เจ้าหน้าที่รับผิดชอบการรับรองมาตรฐานฯ สำนักงานคณะกรมการอาหารและยา (อย.) และการสัมภาษณ์กลุ่มผู้รับอนุญาตนำเข้า ส่วนระยะที่ 2 เป็นการพัฒนาระบบการพิจารณารับรองฯ ให้เหมาะสมกับประเทศไทย เก็บข้อมูลจากการสัมภาษณ์ผู้บริหารของ อย. ที่มีประสบการณ์ด้านระบบการพิจารณารับรองฯ วิเคราะห์ข้อมูลโดยใช้ ความถี่ ร้อยละ และการวิเคราะห์เนื้อหา **ผลการศึกษา:** พบว่าการพิจารณารับรองฯ ดำเนินงานล่าช้าเนื่องจากพบข้อบกพร่องของเอกสารประกอบการพิจารณารับรองฯ โดยเอกสารที่พบข้อบกพร่องมากที่สุด คือ Plant Master File โดย อย. ได้แก้ไขโดยจัดทำคู่มือประชาชน แต่ยังพบว่ามีผู้รับอนุญาตฯ รอคิวนัดหมายตรวจสอบเอกสารเบื้องต้นเป็นจำนวนมาก ต่อมา อย.ได้ปรับปรุงกระบวนการทำงานและเพิ่มเจ้าหน้าที่ตรวจสอบเอกสารเบื้องต้น แต่ยังพบว่าผู้รับอนุญาตฯ ที่จองคิวส่วนใหญ่จัดเตรียมเอกสารไม่พร้อมจึงต้องยื่นขอคิวใหม่ ส่วนผู้รับอนุญาตฯ ที่มีเอกสารพร้อมก็ยังไม่ถึงคิวประเมิน ส่งผลให้ปริมาณงานของเจ้าหน้าที่ผู้ตรวจสอบไม่ลดลง ระบบการพิจารณารับรองฯ ที่ได้นี้จำเป็นต้องพัฒนาเป็น 2 ระยะ โดยระยะสั้น คือ การจัดการเบื้องต้นภายใน อย. ส่วนระยะยาว คือ การวางแผนพัฒนาระบบและแผนงบประมาณเพื่อคุ้มครองผู้บริโภคในอนาคต **สรุป:** ระบบการพิจารณารับรองฯ ที่เหมาะสมกับประเทศไทยที่ได้ ยังต้องพัฒนาอย่างต่อเนื่อง อย.ควรพัฒนาทั้งในส่วนการสนับสนุนการทำงานของเจ้าหน้าที่ และผู้รับอนุญาตฯ

คำสำคัญ: ระบบการพิจารณารับรองมาตรฐาน, สถานที่ผลิตยาในต่างประเทศ, การรับรอง, มาตรฐานการผลิตที่ดี

Editorial note

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Abstract

Objective: To explore and develop the GMP accreditation of oversea manufacturers suitable for Thailand. **Methods:** This study used an integrated research method. In phase 1, we performed document research on application and interviews on officers and group interviews on licensees. In phase 2, we performed interviews on executive officers of Thai Food and Drug Administration (FDA) who had experiences about GMP accreditation by purposive sampling. The data were analyzed using frequency, percentage and content analysis. **Results:** GMP accreditation approval process was delayed mainly because of application defects especially Plant Master File and a large number of applications were submitted. Public manual for GMP accreditation was made by Thai FDA. Even though the process was improved but the application process was still delayed because of limited workforce to inspect the documents. Defective documents and subsequent re-submission still slowed the whole process down. Informants reported that GMP accreditation process should be improved in 2 phases. In short-term phase, organization management of the FDA should be improved. In long-term phase, and plan for consumer protection should be developed. **Conclusion:** GMP accreditation approval process of oversea manufacturers suitable for Thailand should be improved to support the work of officers and the import licensees.

Keywords: GMP accreditation, oversea manufacturer, approval, good manufacturing practice

Journal website: http://ejournals.swu.ac.th/index.php/pharm/index

Introduction

The Food and Drug Administration (FDA) of Thailand had developed and launched the first Good Manufacturing Practice (GMP) of Medicinal Products in 1978 as guided by the World Health Organization (WHO). In 1984, Thai FDA had promoted industrial sectors to develop the standards of drug manufacturing, and GMP certificated firms that passed GMP inspections. This policy had been continued until June 5, 2003, the Ministry of Public Health (MOP) mandated all local pharmaceutical firms producing modern medicinal products to comply with the GMP. [1] With the effort to join the pharmaceutical inspection cooperation scheme (PICS) which is an international co-operative committee for developing GMP inspection standards toward the international one, the MOP revised the GMP and mandated the compliance into effect since October 5, 2012. Since there was a change in manufacturing control such as legal enforcement and GMP

details, local pharmaceutical firms have been forced to improve pharmaceutical quality accreditation which could result in international quality of pharmaceutical products.

In Thailand, pharmaceutical product market is highly competitive. Low-cost finished pharmaceutical products have been imported from various countries such as the People's Republic of China, India, and South Korea, with suspected quality.[2] Vigilance on finished product quality on domestic manufacturers is therefore insufficient to assure the quality of the products available in the country. With such premise, nondomestic pharmaceutical manufacturers of the products imported to Thailand are also subject to quality accreditation to hold GMP standards at least equal to those mandatory to local manufacturers. The Thai FDA thus issued the GMP Accreditation of an Oversea or Non-Domestic Manufacturer which was enforced since October 1, 2012. As a result, registration process of imported products from oversea manufacturers has been changed. Specifically, nondomestic manufacturers whose finished products have not been registered with the Thai FDA must be accepted by the agent before applying for the import of the finished products to the country.

With such legal requirement, import licensees are required to file quality accreditation documents mandatory by GMP standards for nondomestic manufacturers to the FDA for accreditation before the registration of the imported products.[3] The process is depicted in Figure 1.

To get accreditation for oversea manufacturers, the import licensee usually submitted relatively similar documents to two units separately, but almost simultaneously, namely the Pre-marketing Control Unit and the Post-marketing Control Unit of the Thai FDA (Figure 1). Specifically, the Post-marketing Control Unit examined the manufacturer plant information based on GMP standards. Once the plant quality was approved, the licensee was given the manufacturer approval letter. This letter was an additional piece of document referred to as the "plan information" that the licensee needed to submit to the Pre-marketing Control Unit in addition to the first set of submitted documents. The Pre-marketing Control Unit usually reviewed product information especially quality, safety and efficacy of the finished products, in addition to the "plant information" additionally submitted later. The final stage was the registration number of the imported finished product granted by the Pre-marketing Control Unit.

Based on the process mentioned above, with no collaborated document sharing between the Pre-marketing Control Unit and the Post-marketing Control Unit, the licensee unfortunately had to submit two relatively similar documents almost simultaneously to the two units. The duration until getting approval from the Post-marketing Control Unit was usually shorter than the one from the Pre-marketing Control Unit. In addition, the licensee needed to submit the approval letter from the Post-marketing Control Unit to the Pre-marketing Control Unit by themselves because of no sharing or transferring of documents between the two units (Figure 1).

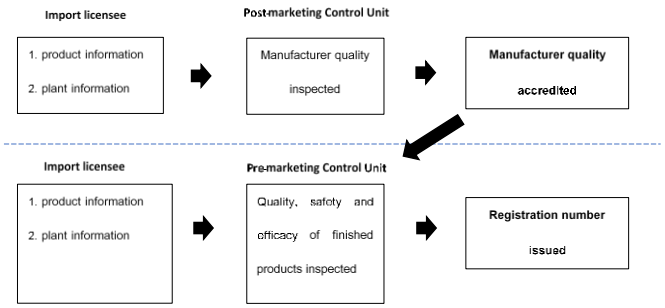

Figure 1 The registration process for importation of pharmaceutical finished products to Thailand.

Based on the execution from October 1, 2012 to March 31, 2016 enforced by the new regulations for accreditation on oversea manufacturers, several issues had been found.[4] For example, many filed submissions for accreditation on oversea manufacturers had been rejected. In addition, there had been a lack of officers to sufficiently handle submission filing, and to provide information, answer, and advice for the import licensees. In the past, the approval was done based only on evaluation of filed documents; no on-site inspection on oversea manufacturers was done even with a suspect on the manufacturer's quality. This is because there has been no rules allowing collecting on-site inspection fees from the oversea manufacturers. Furthermore, there has been no rules for import licensees to follow once the accreditation of their oversea manufacturers is approaching expiration within 3 years.

Other studies have shown the process of accreditation for oversea manufacturers in certain countries which are different from that of Thai FDA. In Australia, the Therapeutic Goods Administration has Regulatory Guidelines Good Manufacturing Practice (GMP) Clearance for Overseas Manufacturers demand different documents necessary for

accreditation of oversea manufacturers according to countries. The discrepancy of the required documents among various countries depends on their trade agreement with Australia, activities in the oversea manufacturers, the finished products produced, and the GMP regulatory agents in the oversea countries. [5] The maintenance of accreditation is clearly specified by Australia's Therapeutic Goods Administration.[5] In Singapore, fees for on-site inspection has been mandated with fee amounts according to the locations of the oversea manufacturers. [6] In Thailand, the accreditation for oversea manufacturers has been in a relatively early stage. The have been a large number of problems such as personnel, rules and regulations, standard procedure, and operational outcomes. With the concern and need to improve the accreditation process, the researchers aimed to understand the process and problems of accreditation for oversea manufacturers of the imported pharmaceutical products. Understanding on the issue could be useful for improving the accreditation process suitable for Thailand which was defined as the one that is faster, more efficient, and more compliant to the GMP of individual countries of the oversea manufacturers.

Methods

This study was a cross-sectional analysis and was divided into two phases, specifically 1) situational analysis on the Thai FDA' s existing accreditation process for the oversea manufacturers, and 2) the analysis on the proposed accreditation process suitable for Thailand.

In **phase one or situational analysis**, accreditation on oversea manufacturers of various countries was examined qualitatively and quantitatively. First, by means of documentary research, issues and/or problems were extracted from accreditation application documents submitted for inspection, results of document inspection, reports of accreditation process. From the issues and/or problems found, the questions regarding problems, issues and possible solutions for interviews were formed. The semi-structured or guided interviews were performed on two groups of informants, specifically (1) individual interviews on 5 FDA officers in the accreditation process and 3 external experts in the accreditation (a total of 8 informants), and (2) group interview on 9 import licensees (or delegates) consisting of 3 accredited and the other 6 not accredited.

The data obtained in the first phase were detailed situations and related problems, and possible solutions. Data were analyzed using descriptive statistics including frequency and percentage. Qualitatively, content analysis was performed to explore themes emerging from the interview content of accreditation process for oversea manufacturers suitable for Thailand. Based on the findings, the proposed accreditation process and possible solutions were drafted for the second phase of the study.

In **the second phase**, the proposed accreditation process and possible solutions were further tested for possibility or appropriateness by opinions from 3 experts which were Thai FDA executives with knowledge, understanding and experience in accreditation process. These expert informants were selected by purposive sampling. Data collection was done by means of a semi-structured or guided interview. Their opinions and recommendations were analyzed by ways of content analysis and summarized.

This study was approved by the Ethics Committee for Human Study, Faculty of Pharmacy, Silpakorn University (approval date: May 27, 2016).

Results

Phase 1: Situation of the existing accreditation process

Accreditation process for oversea manufacturers was based on the data from October 2015. The process could be divided into 4 steps specifically document preparation as shown in Table 1, appointment with the officer for accreditation application document inspection, and decision making by the committee for accreditation with or without the need for on-site inspection (Figure 2).

In this situational analysis, **problems and proposed solutions in the process of accreditation** were identified as follows. First, there was a lack of FDA workforce especially those to preliminarily inspect the filed documents. It was found that from August 1, 2015 to September 30, 2016, despite two more teams added to the existing five teams of officers (two or more persons for each team) for preliminary inspection of documents, there was a delayed inspection among 155 of 260 submissions (59.61%). All relevant FDA officers interviewed agreed that more personnel should be added to sufficiently handle the workload. However, only one of the three FDA executive experts agreed with such solution. To improve the accreditation process with no additional

workforce, the three experts also proposed risk management, systematic thinking process, and information technology.

Table 1 **List of documents for GMP accreditation request for oversea manufacturers for the imported finished pharmaceutical products.**

Oversea manufacturers approved by PICS Member	Oversea manufacturers NEVER approved by PICS Member
1. A request letter for accreditation approval	1. A request letter for accreditation approval
2. A list of finished pharmaceutical products manufactured for GMP accreditation request of oversea manufacturer	2. A list of finished pharmaceutical products manufactured for GMP accreditation request of oversea manufacturer
3. Plant Master File for PICS member or Certified/Audited by PICS	3. Plant Master File for non-PICS member
4. Report on the latest GMP inspection results by country-specific regulatory agency or other acceptable international regulatory agency (if any)	4. Report on the latest GMP inspection results by country-specific regulatory agency or other acceptable international regulatory agency (if any)
5. A photocopy of the latest Certificate of GMP issued by government agency, private agency, or other acceptable international regulatory agency, or other comparable certificates issued by acceptable government or private agencies.	5. A photocopy of the latest Certificate of GMP issued by government agency, private agency, or other acceptable international regulatory agency, or other comparable certificates issued by acceptable government or private agencies.
6. A form to check for document completion or the Plant Master File for **PICS member** or Certified/Audited by PICS	6. A form to check for document completion or the Plant Master File for **Non PICS member** or Certified/Audited by PICS, and manufacturing details of the imported pharmaceutical products especially plant, machines, devices, and plant layout
	7. Details of the imported pharmaceutical products especially plant, machines, devices, and plant layout (for oversea manufacturers inspected by the agency that was **Non PICS member**)

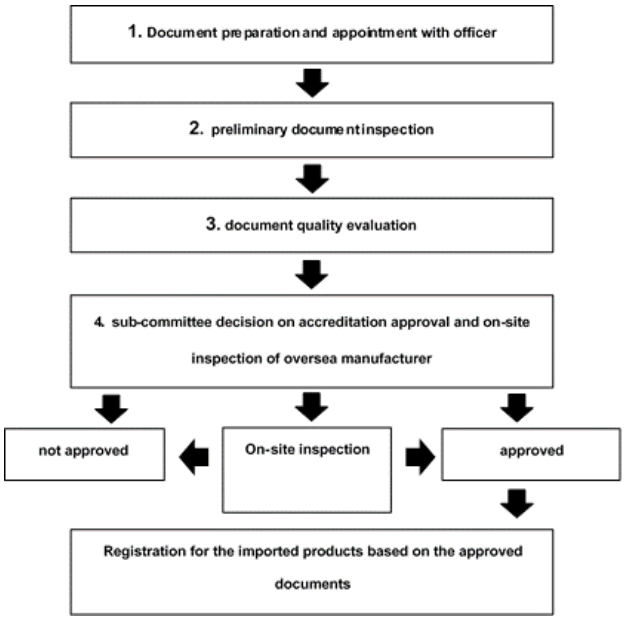

Figure 2 **The GMP accreditation process for oversea manufacturers of Thailand FDA.**

Second, it was found that accreditation process for oversea manufacturers was unclear. Once approved, the oversea manufacturer GMP accreditation lasted only 3 years, while the registration number of the imported products was life-long, i.e., no expiration. It was found that the process was divided into three steps (1) the initiative of the process (October 1, 2012 to July 31, 2015), (2) the modification of the process according to the public manual on accreditation (August 1, 2015 to September 30, 2016), and (3) the addition of the workforce and the modification of appointment for the preliminary document inspection. In addition, there had been unclear rules on accreditation extension, accreditation amendment, temporary accreditation suspense, accreditation discontinuation, and on- site inspection of the oversea manufacturers. These problems were agreed by all interviewees and experts. To alleviate these problems, it was recommended that more elaborate rules and regulations to handle all steps and personnel of the accreditation process be developed including preliminary document inspection, on- site oversea manufacturer inspection, accreditation status maintenance, accreditation extension, and accreditation discontinuation.

Regarding the performance of inspecting the document, 11.76% of the interviewees agreed that the problem existed (i.e., 2 external experts of 17 interviewees). Of the 17 interviewees, 52.94% of them which were all 9 import licensees reported that it was unforeseeable to know what kind of additional documents the officer would ask for. They recommended that clear and specific rules on document inspection be developed, and officers relevant to the process be trained before launching and periodically thereafter.

In terms of document inspection, 5 officers and 3 experts of the total of 17 interviewees (47.06%) reported that it was impossible to detect fraud or fabricated documents regarding oversea manufacturers. They proposed that these filed documents need approval from reputable international agencies. In addition, a database should be developed for vigilance in case of fraud documents.

It was found that there was an unfair control on the domestic manufacturers compared to their oversea counterparts. While domestic manufacturers had been on-site inspected periodically, those oversea ones had not been so by the government PICS agents. For oversea manufacturers, Thai FDA only inspected documents for GMP standards compliance. There was a recommendation that this problem

could be relieved by on- site inspection of oversea manufacturers for those never been inspected for GMP by PICS related regulatory agencies in their own countries. This recommendation was agreed by all 4 experts, 1 of 4 officers, and 5 of 9 import licensees resulting in 10 of 17 agreement rate, or 58.82%. Therefore, it was proposed that Thai FDA should establish an annual oversea inspection schedule in addition to the plan to enhance the performance and potential of the workforce, as well as the plan to outsource experts for oversea manufacturer on-site inspection.

The submission of accreditation request for oversea manufacturers was also an obvious, if not prevalent, problem. In duplicate addition to the submission to the Post-marketing Control Unit, once the oversea manufacturer was accredited, documents similar to the first submission was redundantly requested by the Pre-marketing Control Unit. The problem was agreed upon by 88.24% of the interviewees (3 of 4 experts, 3 of 4 officers, and all 9 import licensees). To relieve the problem, they proposed that a database of oversea manufacturers with their filed documents should be developed. This database should be easy for retrieval and update for all involving FDA personnel and units so that the re-submission of documents is unnecessary. This solution was agreed by 88.23% of the interviewees (all 4 experts, all 8 officers, and 7 of 9 import licensees).

It was a long waiting list for appointment with the officers during August 1, 2015 to September 30, 2016. Based on the public manual on accreditation process available during that period of time, import licensees were guided to contact the officer at the Post-marketing Control Unit for the further in-person appointment. The date and time for the in-person appointment for preliminary document inspection was supposed to be e-mailed to the licensee within 7 days. Unfortunately, it was found there had been as high as 155 of a total 260 accreditation requests in the waiting list for preliminary document inspection (59.61%). The waiting time till the in-person preliminary document inspection was usually 2 to 4 months. This problem was agreed upon by 82.35% of the interviewees (1 of 4 experts, all 4 officers, and all 9 licensees). They suggested internet-based e-submission for preliminary document inspection instead of in- person appointment, so that the burden on a limited number of officers could be lessened and the waiting list could be shortened.

The next problem was incomplete documents. The most incomplete document was found in Plant Master File part (73 of 80 accreditation request submissions, or 91.25%), followed by Certificate of GMP (46 of 80 accreditation request submissions, or 57.50%), pharmaceutical items for approval under the accreditation of oversea manufacturers (40 of 80 accreditation request submissions, or 50.00%), and the latest report on GMP inspection results (40 of 80 accreditation request submissions, or 50.00%). Since as high as 91.25% of the submitted documents were found with at least one defect, further burden could be expected. This was because the import licensees needed to re- submit the documents to replace the defective ones and the officers needed to inspect them unnecessarily.

In addition, for import licensees who could not re-submit the documents before the deadline after the notification of incomplete documents, their accreditation request could unfortunately be rejected. This could be even more problematic for documents that needed to obtain from the oversea manufacturers since the manufacturer could have no such documents or the documents were considered a private intellectual property not supposed to share. This problem was agreed upon by 70.59% of the interviewees (all 4 experts, all 4 officers, and 4 of 9 licensees). The majority of interviewees (88.23%) agreed that fewer documents necessary for evaluation should be required (3 of 4 experts, 3 of 4 officers, and 2 of 9 import licensees). In addition, all 3 FDA executive experts agreed that the list of documents did not adequately reflect the performance of GMP inspection on oversea manufacturers. They also suggested that risk management should be used to improve the accreditation process and the relevant list of required documents. However, they insisted that the requests with no crucial documents should be rejected.

The last problem was that there was a large proportion of submitted accreditation requests that were ignored by the import licensees. From October 1, 2012 to July 31, 2015, 108 of 256 submissions (42.19%) were ignored by the licensees. A lack of understanding in the accreditation process and the required documents was mostly the reason of such discontinuation or withdrawal. The problem of a lack of knowledge and understanding was agreed upon by 70.59% of the interviewees (all 4 experts, all 4 officers, and 4 of 9 import licensees). In addition, all 3 FDA executive experts agreed with the solutions acquired from interviews, group interviews,

and document study. They also proposed the additional easy access to the database, advice, and forms with more accessible website, training, and media for E-learning. They though that such improvement could help submission discontinuation or withdrawal. The solutions to the problems emerging from document study, interviews with FDA officers and experts, group interviews with import licensees were used to propose the new accreditation process as shown Figure 3.

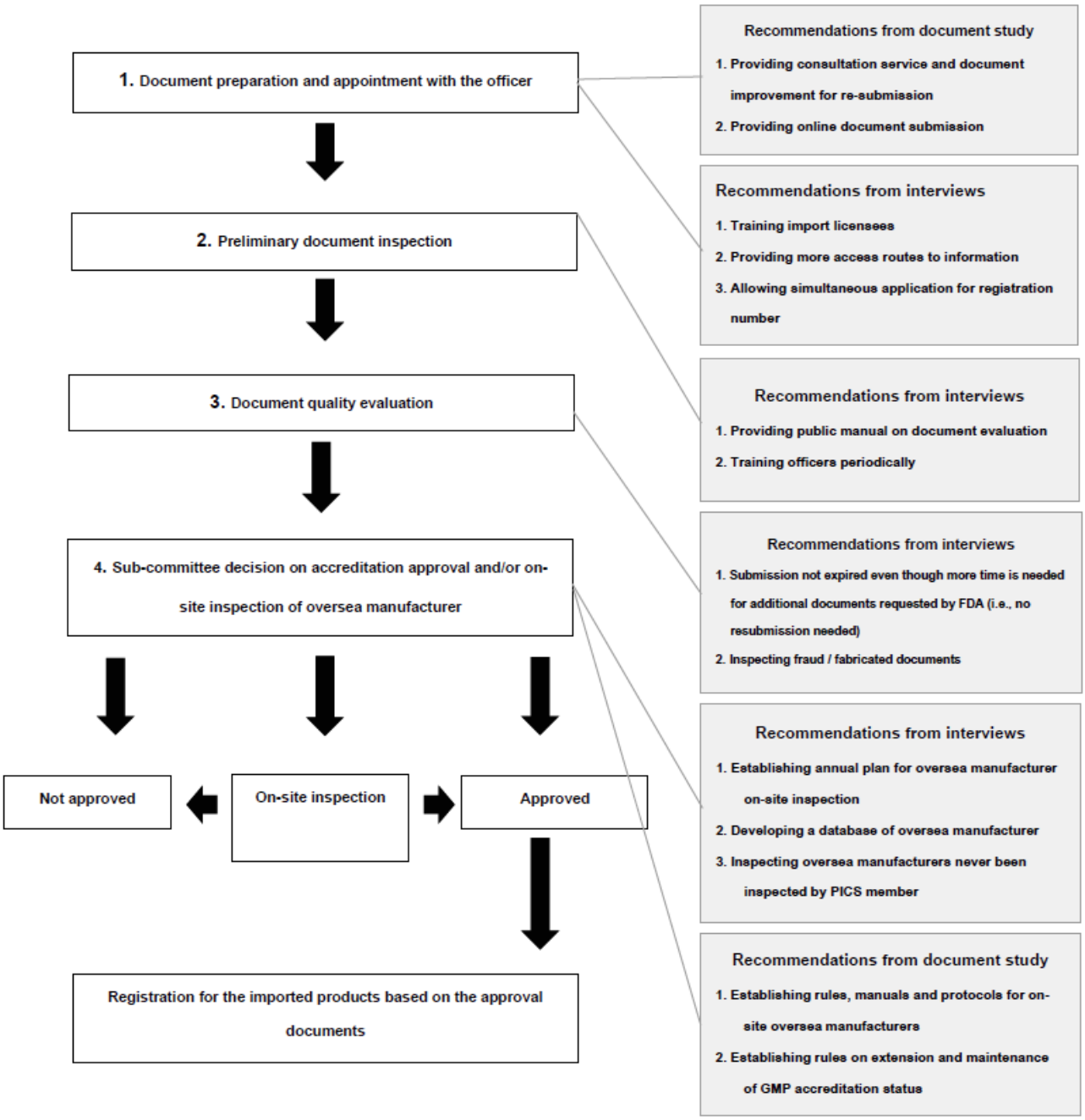

Figure 3 Draft of GMP accreditation process for oversea manufacturers suitable for Thailand (from study Phase 1).

Phase 2: Development of accreditation process for oversea manufacturers of Thai FDA

The proposed solutions from the first phase of the study, accompanied with results from further interview with FDA executive experts, could be used to form the new accreditation process for oversea manufacturers (first phase) as summarized in Figure 4. The details of the newly developed accreditation process are as follows.

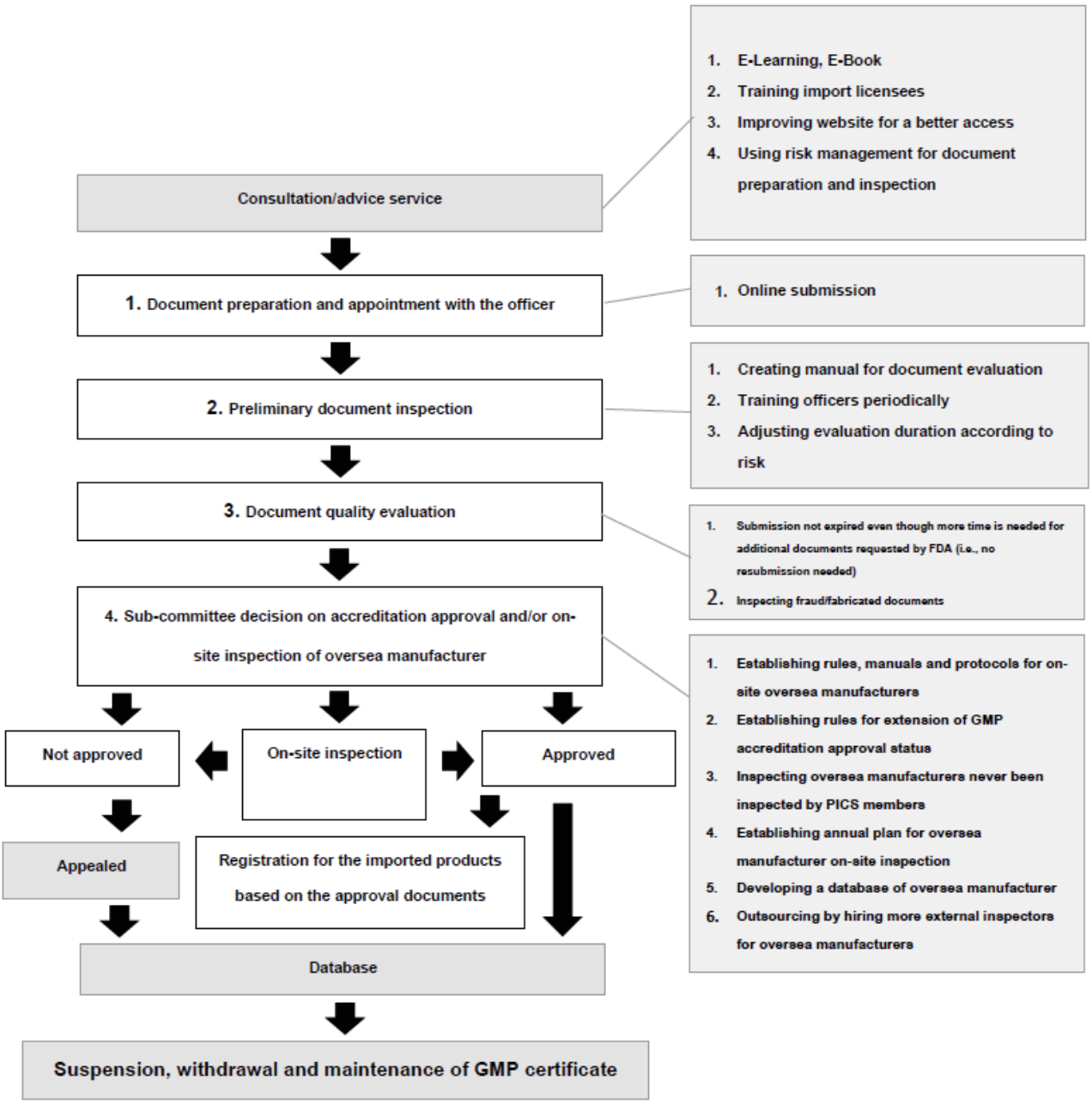

Figure 4 Draft of GMP accreditation process for oversea manufacturers suitable for Thailand (from study Phase 2).

First, the module of advice service to import licensees should be separated from the other regular service, i.e., document inspection. Second, internet-based technology such as E-book E-Learning could be in place to help the working process of the officers. Third, the oversea manufacturers should be approved for accreditation before the registration of imported finished products could be requested so that burden and expense in the registration process could be reduced. Fourth, risk management should be in place to select submitted documents suitable for the given duration of inspection to avoid submission discontinuation or withdrawal. Fifth, Thai FDA should consider outsourcing external experts on inspection on oversea manufacturers to alleviate the burden on and improve the potential of the existing workforce. Last, to be transparent and fair for the import licensees and the oversea manufacturers, appeal process should be in place.

Structure, process and outcomes of the accreditation process of oversea manufacturers

Based on the findings previously mentioned, the improvement of accreditation process for oversea manufacturers could be summarized based on the concept of structure, process and output in two phases namely short- and long-term phases as follows.

In the short-term phase, the managerial change within the relevant units of Thai FDA was proposed. In terms of structure, the training for systematic thinking for personnel should be implemented. This could help manage the workflow more efficiently, especially the on-site inspection on oversea manufacturers and the document inspections with comparable standards among various evaluators. On the other hand, import licensees should also be educated and trained more about the process of and documents necessary for accreditation request. For learning materials, manuals and training sessions should be created and more readily available especially online e-learning materials in Thai and English language. Finally, accreditation website should be improved for a better access.

For the process aspect of the structure-process-output framework, protocols should be more elaborate to cover all steps of accreditation request including document inspection, on-site inspection of oversea manufacturers, and maintenance, extension and withdrawal of accreditation status. Database of oversea manufacturers should be developed for a better access and retrieval not only for import licensees, but also for officers in Post- and Pre-market Control Units as well. This database could help duplicate submission of documents for those oversea manufacturers already accredited. The database could also be useful for officers to use for vigilance on fraud or fabricated documents. Regarding the working flow, risk management should be employed to prevent and minimize risks potentially found in the manufacturing as guided by the GMP standards. Risk management could help evaluate the tasks where various factors of all involving countries are taken into account such as the latest inspection results, regulatory agents of the countries, bilateral trade agreement with Thailand, location of the oversea manufacturers, the country's GMP standards, type of finished pharmaceutical products, and the time of inspection.

Lastly, for the output component of the structure-process-output framework, the number of accredited oversea manufacturers as well as the GMP inspection on the domestic manufacturer was the crucial output of the improvement.

For the long-term phase, development of system and budget for future consumer protection was planned. It was suggested that have a plan for on-site inspection on oversea manufacturers never been inspected by their own regulatory agents in countries of PICS members. It was also recommended that international agreement on mutual recognition on GMP evaluation results among PICS countries should be made. This could alleviate the burden of on-site inspection on oversea manufacturers. In addition, online e-submission for accreditation request should be developed. Finally, there should be persons specifically assigned for providing advice on the accreditation process. This could reduce burden on the whole workforce and provide more accurate information to the public.

Discussions and Conclusion

This study explored the problems and possible solutions in the development of accreditation process for oversea manufacturers of the finished pharmaceutical products. Further discussions are as follows. First, risk management was proposed to improve the accreditation process to for a more efficient and less time-consuming protocol for products with different risk profiles. This proposal could be supported by the studies on accreditation process of Australia[5],

Singapore[6], and Malaysia[7], where differences in protocols, required documents, and processing duration were found among the countries depending on the mutual recognition arrangement (MRA), GMP certification, GMP regulatory agencies, manufacturing process, and types of finished pharmaceutical products. These studies recommended risk management for the accreditation process which was consistent with the opinion from the three experts in our study where risk management should be implemented in the step of determining required documents to lessen the burden caused by requesting unnecessary documents.

Second, there was a need for the mutual recognition arrangement (MRA) among countries. Once the trust between regulatory agencies among these countries are made, the sharing of knowledge and data and the acceptance or transferal of accreditation from the FDA of the manufacturer's country could be possible. With the MRA, the burden for on-site inspection could be reduced which could further expedite the inspection process. At present, Thailand has joined the ASEAN Sectorial Mutual Recognition Arrangement (MRA) for Good Manufacturing Practice (GMP) Inspection of Manufacturers of Medicinal Products which requests that all ASEAN members accept GMP Certificates and/or GMP Inspection Reports according to PICS issued by the GMP inspectors in the ASEAN Listed Inspection Service.[8] Since Thailand has also joined PICS[9], one of the FDA executive export asserted that such MRA could alleviate the burden of accreditation process and the time and expense for on-site inspection on oversea manufacturers. The whole process of MRA is based on the trust in inspection standards shared by member countries.

Third, an up-to-date database was proven again a vital part of all agencies. FDA officers, import licensees, and an external expert all agreed that oversea manufacturers already accredited should be in the database. They also proposed the online E-submission system to reduce the burden of duplicate document submission and inspection especially those oversea manufacturers already accredited. This was also consistent with the study of Tonmaithong where online electronic accreditation system (E-Accredit) was found to offer a faster and more efficient accreditation of oversea manufacturers.[10]

Fourth, the pre-submission consultation or advice for document preparation should be provided. This service could help reduce the premature withdrawal or cancellation of submission because of incomplete or defective document which was found as high as 91.25%. This proposed service could help reduce the burden on licensees for filing additional documents and the officers for reviewing such additional filing. This service should be independent from the document inspection process. This proposal was sound since Australia has provided this kind of service for licensees. In phase 2 of our study, an expert also supported the idea of having a consultation service system to prevent incomplete/defective document submission. The expert also stated that the plans for taskforce, rules, organization structure, and budget needed to be urgently made.

Fifth, working efficiency among officers should be enhanced to overcome a lack of workforce and performance inconsistency among these officers. Regarding a limited number of officers, 3 FDA executive experts had some disagreement. One of the three stated that there was relatively an adequate number of officers but efficiency was insufficient. However, the second expert argued that more data were needed to justify an appropriate number of officers; while the third expert agreed about the lack of officers. However, all three FDA executive experts suggested that systematic thinking process should be introduced to the officers to enhance efficiency and information system fully implemented to reduce workload. They also recommended a consultation service, online electronic leaning system, and outsourced freelance inspectors for oversea manufacturers to alleviate the problem of limited workforce. Ultimately, they supported the idea of improving the officer's efficiency as the first priority.

In conclusion, results from our study could suggest certain practical points. To improve understanding among import licensees, and reduce the cancellation on document submission, Thai FDA should develop more accessible routes for information, workflow, and document preparation which include public manuals/leaflets, websites, and online E-learning materials. To enhance efficiency of the FDA officers, database of oversea manufacturers should be developed for the use of the Pre- and Post-marketing Control Units. Last, to improve quality of other imported health-related products, FDA could also implement the proposed system found in our study.

For future research, prospective studies should be done to prove efficiency of the new system for accreditation of oversea manufacturers. Risks in the process of document preparation and submission for manufacturer's GMP should be studied. Vigilance on quality of imported finished

pharmaceutical products from the accredited oversea manufacturers should be studied.

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