# Assessment of Compliance with the Good Manufacturing Practice Criteria for Drinking Water in Sealed Containers among Manufacturers in Chachoengsao Province, Thailand

นิพนธ์ต้นฉบับ

Original Article

ผณินทร งามศิริ[1*] และ อัษฎางค์ พลนอก[2,3]

[1] สำนักงานสาธารณสุขจังหวัดฉะเชิงเทรา อ.เมือง จ.ฉะเชิงเทรา 24000
[2] ภาควิชาเทคโนโลยีเภสัชกรรม คณะเภสัชศาสตร์ มหาวิทยาลัยนเรศวร อ.เมือง จ.พิษณุโลก 65000
[3] อุทยานวิทยาศาสตร์ภาคเหนือตอนล่าง มหาวิทยาลัยนเรศวร อ.เมือง จ.พิษณุโลก 65000

* **ติดต่อผู้นิพนธ์:** panintorn.ngamsiri@gmail.com

*วารสารไทยเภสัชศาสตร์และวิทยาการสุขภาพ 2560;12(2):75-85.*

Paninitorn Ngamsiri[1*] and Assadang Polnok[2,3]

[1] Chachoengsao Provincial Health Office, Muang, Chachoengsao, 24000, Thaoland
[2] Department of Pharmaceutical Technology, Faculty of Pharmaceutical Sciences, Naresuan University, Muang, Phitsanulok, 65000, Thailand
[3] Science Park, the Lower North, Naresuan University, Muang, Phitsanulok, 65000, Thailand

* **Corresponding author:** panintorn.ngamsiri@gmail.com

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## บทคัดย่อ

**วัตถุประสงค์**: เพื่อประเมินการปฏิบัติตามหลักเกณฑ์วิธีการที่ดีในการผลิต (จีเอ็มพี) ของสถานที่ผลิตน้ำบริโภคในภาชนะบรรจุที่ปิดสนิททั้งโดยผู้ผลิตเองและผู้เชี่ยวชาญ **วิธีการศึกษา:** การศึกษาเชิงพรรณนาโดยผู้ผลิตและผู้เชี่ยวชาญประเมินสถานที่ผลิตน้ำบริโภคในภาชนะบรรจุที่ปิดสนิทในจังหวัดฉะเชิงเทราจำนวน 53 แห่ง โดยใช้แบบสอบถามที่สร้างมาจากแบบบันทึกการตรวจสถานที่ผลิตน้ำบริโภคในภาชนะบรรจุที่ปิดสนิท หรือแบบ ตส.3(50) ของสำนักงานคณะกรรมการอาหารและยา พร้อมทั้งเก็บตัวอย่างผลิตภัณฑ์ส่งตรวจวิเคราะห์คุณภาพทางเคมี กายภาพและจุลชีววิทยา ประเมินผลข้อมูลและนำเสนอในรูปแบบความถี่และร้อยละ **ผลการศึกษา**: การประเมินจีเอ็มพีด้วยตนเองของผู้ผลิตพบว่ามีสถานที่ผลิตไม่ผ่านเกณฑ์การประเมิน 12 แห่ง (ร้อยละ 22.64) โดยเฉพาะหมวดที่ 9 (การบันทึกและรายงาน) ประเมินตนเองไม่ผ่านมากที่สุด ส่วนผลการประเมินของผู้เชี่ยวชาญพบว่าไม่ผ่านเกณฑ์การประเมินจีเอ็มพี 20 แห่ง (ร้อยละ 37.74) โดยหมวดที่ 9 ไม่ผ่านมากที่สุดเหมือนการประเมินตนเอง รองลงมาคือ หมวดที่ 6 (การบรรจุ) เนื่องจากพบข้อบกพร่องรุนแรงคือ การบรรจุนอกห้องบรรจุ และพบว่าหมวดที่ 6 (การบรรจุ) มีผลประเมินตนเองว่าผ่านแต่ไม่ผ่านโดยผู้เชี่ยวชาญมากที่สุด คือพบใน 11 แห่ง (ร้อยละ 20.75) ผลวิเคราะห์ผลิตภัณฑ์พบปัญหาทางจุลชีววิทยามากถึงร้อยละ 28.30 เนื่องจากปนเปื้อน Coliform bacteria เกินมาตรฐาน พบว่าผลิตภัณฑ์ชื่อการค้าที่ประเมินผ่านจีเอ็มพีหมวดที่ 6 มีสัดส่วนที่ผ่านการตรวจทางจุลชีววิทยามากกว่า **สรุป:** หมวดที่ 6 (การบรรจุ) เป็นหมวดที่มีข้อบกพร่องรุนแรง และมีผลการประเมินแตกต่างกันมากที่สุดระหว่างการประเมินตนเองและโดยผู้เชี่ยวชาญ ดังนั้นผู้ผลิตและพนักงานเจ้าหน้าที่ควรให้ความสำคัญและสร้างความตระหนัก พร้อมทั้งควรกำหนดมาตรการในการป้องกัน เพื่อให้กระบวนการผลิตเป็นไปตามหลักเกณฑ์มาตรฐานจีเอ็มพี

**คำสำคัญ:** น้ำบริโภคในภาชนะบรรจุที่ปิดสนิท, หลักเกณฑ์วิธีการที่ดีในการผลิต, จีเอ็มพี, การประเมินตนเอง

## Abstract

**Objectives:** To assess the manufacturers' compliance with the Good Manufacturing Practice (GMP) criteria for drinking water in sealed containers by the self-assessment and experts. **Methods:** In this descriptive study, manufacturers and experts assessed all 53 plants in Chachoengsao Province using a questionnaire adapted from GMP inspection form mandated by the Thai Food and Drug Administration. Many samples of the drinking water were collected for chemical, physical and microbiological tests. **Results**: The self-assessment reviewed that 22.64% of the manufacturers were non-compliant with the GMP criteria, especially for Domain 9 (documentation and report) being the most failed aspect. Based on the expert assessment, 37.74% of the manufacturers were non-compliant with the GMP criteria. Similar to the self-assessment, Domain 9 was the most failed item followed by Domain 6 (water filling) that was seriously violated because of performing outside the filling room. In addition, domain 6 was assessed as compliant by the self-assessment but was found non-compliant by the experts up to 11 places (20.75%). Laboratory tests showed that 28.30% of them did not meet the microbiological standard with the presence of coliform bacteria. Water products compliant with GMP's Domain 6 standards were more likely to pass the microbiological test. **Conclusion**: Domain 6 (water filling) was found to be a serious violation and had the highest discrepancy between the self-assessment and expert assessment. Thus, the manufacturers and regulators should be aware of its importance. A preventive measure should also be initiated to ensure the operational procedure is in accordance with the GMP.

**Keywords:** Drinking water in sealed containers, Good Manufacturing Practice, GMP, self-assessment

## Introduction

Drinking water products have been evolved in various aspects including manufacturing process. However, with its fast business growth, certain problems have been realized. For example, there were products not meeting the manufacturing standards and manufacturers unaware of the existing laws and regulations. With a concern about the quality issue of the drinking water, the Thai Food and Drug Administration (FDA), Ministry of Public Health, listed the drinking water in sealed container or bottled drinking water in the category of standardized foods.[1] According to the Thai FDA regulations, standard foods do not require registration but their quality and labeling have to meet the standard requirements as specified in the Notification of the Ministry of Public Health.[2]

The manufacturer of drinking water is required to acquire manufacturing permission and food serial number from the Thai Food and Drug Administration or the provincial public health office. In addition to the two previous requirements, continuous monitoring of the factory and the manufacturing process is also required. To get permission, criteria based on the Good Manufacturing Practices (GMP) for sealed container drinking water must be met. GMP criteria compose of basic requirements for drinking water production and quality control processes to ensure safety of the drinking water.[3,4] All processes are designed to minimize the risk of unsafe products including physical, chemical and microbiological contaminations or impurities.

In Chachoengsao province, there were 115 food production facilities of bottled drinking water in the fiscal year of 2015. Of these 64 places that were inspected, 13 of them (20.31%) failed to meet the GMP criteria and/or had severe shortcomings. It was also found that 34.38% of the products did not meet the GMP criteria especially microbiological standards.[5] These findings were consistent with previous reports[6-12] which suggested that the quality of manufacturing factories and their bottled drinking water products was problematic despite the food regulations enforced since July 24, 2001. At the moment, measures to handle quality problems of the bottled drinking water include notification to the manufacturers for improvement and legal action for unsettled problems.[13] Despite the established measures, problems of bottled drinking water have been persistent. Obviously there has been a gap of knowledge about the issue. Previous studies on the assessment of the manufacturers' performance were based mainly on the healthcare providers' perspective. However, studies of assessment based on the manufacturers' perspective or self-assessment have been lacking. This present study aimed to determine the compliance of the manufacturers of the bottled drinking water with the GMP criteria. The findings could help improve the procedure to alleviate the quality problems of bottled drinking water manufacturing. Specific objectives of this study were to determine 1) the manufacturers' compliance to the GMP criteria for bottled drinking water as self-assessed by the manufacturers, 2) manufacturers' compliance as assessed by the experts, and 3) discrepancies of the assessed compliance between the manufacturers and the experts, and 4) associations between the assessed compliance to the GMP and the actual quality of the bottled drinking water.

## Methods

In this cross-sectional study, we evaluated the compliance with the GMP criteria on bottled drinking water among the manufacturers under the provision of Chachoengsao Provincial Public Health Office. The study was carried out from January to October, 2019.

In this study, the population included all 115 manufacturers of the bottled drinking water permitted by Chachoengsao Provincial Public Health Office, and the study sample was manufacturers that were eligible for the study based on inclusion and exclusion criteria. To be eligible, the manufacturers had to be listed in the monitoring plan in the fiscal year of 2015 and their informants were willing to participate in the study. We excluded manufacturers that were listed less than one year, and those out of business during the study period. For each participating manufacturer, the informant was identified as the owner or the chief operator.

The size of the manufacturer sample was based on the following formula,

$$n = \frac{NZ^2\alpha/2P(1-P)}{e^2(N-1)+Z^2\alpha/2P(1-P)},$$

where n was the desired sample size and N was the total number of all manufacturers of bottled drinking water (115 manufacturers, as of September 30, 2015). Z was the standardized value of the normal distribution at the confidence level of 95% with a 2-sided test ($Z_{\alpha/2}$ = 1.96). P, the proportion of manufacturers under the provision of Chachoengsao Provincial Public Health Office not meeting the GMP standards, was found to be 0.21 in the fiscal year of 2015. The sampling error (e) was set at 0.1. As a result, a total of 42 manufacturers were needed. However, our screening based on the inclusion and exclusion criteria resulted in a total of 53 manufacturers. To avoid bias from selecting a relatively small number of participants, all 53 manufacturers were recruited for participation.

Two experts in this study were recruited based on the following three criteria. To be eligible, they had to be a competent consumer protection officer appointed by the provisions of the Food Act B.E. 2522 (1979). They had to have a formal training from the FDA for the GMP inspector.

Last, they had to have a direct experience in inspecting the production facilities of the bottled drinking water for at least three years.

**Instruments**

In this study, three checklists were used. The first checklist was for the manufacturer's self-assessment on the GMP standards of bottled drinking water. This self-assessment checklist was modified from the inspection form for the manufacturer of drinking water in sealed container, Form 3(50) of the Thai FDA, which consisted of questions asking general information of the manufacturer, demographic information of the informant, and the GMP self-assessment. Questions for self-assessment were categorized into nine domains including 1) plant and location (23 questions), 2) equipment, machine and device (19 questions), 3) water source, water quality improvement and quality control (7 questions), 4) container (7 questions), 5) cleaning agent and disinfectant (3 questions), 6) water filling (11 questions), 7) hygiene (10 questions), 8) personnel and their hygiene (10 questions), and 9) documentation and report (4 questions). Response format for each question was a 3-point rating scale of 0-poor, 1-fair, and 2-good. With various weights for each of the questions, subtotal total scores for domain 1 to 9 were 20, 20, 14, 10, 3, 11, 10, 8, and 4, respectively with the grand total score of 100.

The second instrument was also adapted from the Form 3(50) of the Thai FDA but was intended to be filled out by the experts. The content, response scale and scoring method were similar to the one for self-assessment. Each of the two experts was responsible for different parts of the assessment. The third instrument was the interview form used by the experts in case of any discrepancies in the assessment results between the manufacturer and the expert. For example, the manufacturer could have rated a section as meeting the GMP criteria while the expert did not. The interview results obtained from the manufacturer were additionally analyzed for emerging issues relevant to the GMP standards.

**Data collection procedure**

To assess the production facility quality, the checklist was mailed to the manufacturer for self-assessment. Manufacturers willing to participate self-assessed and returned the checklist by mailing. The manufacturers were also instructed about the experts' assessment which would take place later. With no notice in advance, the experts approached and assessed the manufacturer at their site using the same kind of checklist. The researchers later compared the findings from self-assessment and those by the experts.

To assess the product quality, drinking water in sealed container was sampled at the manufacturing plant using the sampling method mandated by the Department of Health Sciences, Ministry of Public Health. For each drinking water product, a sample was drawn from the same production batch as guided by the consumer protection plan of the Thai FDA in the fiscal year of 2016.[14] For example, for drinking water products in the 500 – 900 mL containers, 12 units were sampled. For those in 1,000 - 1,500 mL and 5 – 20 liter containers, 6 units and 1 unit were sampled, respectively. All samples were tested for quality by the Regional Medical Sciences Center 6 Chonburi. Seven indicators of the drinking water quality were three physical properties including acid-base, nitrate content, and fluoride content, and four microbiological properties including the contaminations of *Coliform bacteria*, *Escherichia coli*, *Staphylococcus aureus*, and *Salmonella spp*.[14]

For manufacturers with more than one brand of drinking water, the product of the brand that was being produced while being inspected was selected as a sample. If no production at the time of inspection, the brand firstly registered as the standardized foods was selected.

This study was approved by the Ethics Committee for Human Research in Health Science of Naresuan University on November 7, 2015 (Issue no. 575/58).

**Data analysis**

To pass each of the nine domains of the self-assessment of the drinking water in sealed container, at least 60% of the possible total score had to be achieved and no severe defects were found. The severe defects were defined as those which could lead to contaminations that could potentially cause the unsafe consumption. These severe defects were as follows. Having no properly designed water filling room could lead to the poor contamination prevention. For manufacturers with a well-designed filling room, poor operation in the room or proper operation outside the room could lead to contamination. The severe defects also included any other incidents which were considered as a risk

for unsafe consumption by the experts. For the products of drinking water in sealed container to meet the standards, they needed to pass the criteria previously described as seven indicators mandated by the Thai FDA.

Data of demographic characteristics of the informants, general information of the manufacturers, and the GMP assessment results were summarized by descriptive statistics including frequency with percentage, arithmetic mean and range. Scores of GMP assessment by the informant and the experts were compared using the independent t-test. The associations between the assessment results and the actual water quality tests were determined using chi-square test or Fisher's exact test, as appropriate. Statistical significance for all statistical tests was set at a *P*-value of less than 0.05.

## Results

Of the 53 manufacturers of drinking water in sealed container in Chachoengsao province, the majority had less than 10 years of manufacturing operation (64.15%) (Table 1). More than half of these manufacturers were classified as "food production premise not recognized as factory" (54.72%) which means a place with a use of machine with the manufacturing capacity of less than five horse powers.[15] The majority had 3 – 4 workers (39.62%) and operated 6 days per week (60.38%). The majority manufactured one brand of drinking water product (81.13%). The most frequently found containers of the drinking water were 20-liter plastic cans (88.68%), followed by clear plastic bottles (66.04%), opaque plastic bottles (60.38%), and clear plastic cups (18.87%). No glass bottles were used.

Among 53 informants, the owners and chief managers were roughly equal in number (49.06% and 50.94%, respectively). About two-thirds were male (66.04%). The majority were in their 41 – 50 years of age (39.62%), followed by 31 – 40 years (26.42%). In addition, the majority had a bachelor's degree (30.19%), followed by high school degree (or equivalent vocational school degree) (26.42%).

**The manufacturers' compliance to the GMP criteria for drinking water in sealed container by self-assessment**

Overall self-assessment revealed that 41 of 53 manufacturers (77.36%) were compliant with the GMP criteria (Table 2). For each of the nine domains, domain 9 (documentation and report) was the most frequently found to be the cause (22.64%) based on the 60% cut-off value of the individual domain total score. This was because most manufacturers were more likely to neglect the process of documentation and reporting, especially the processes of quality control of the raw water and finished product, and the maintenance of the equipment, machine and device. The manufacturers documented and reported mainly type and quantity of the finished products.

**Table 1** Demographic characteristics of the manufacturers of drinking water in sealed container (N = 53).

| | Number | % |
|---|---|---|
| Type of manufacturer | | |
| - food production premise not recognized as factory | 29 | 54.72 |
| - food production premise recognized as factory | 24 | 45.28 |
| Power of the production machine (horse power) | | |
| - less than 5 | 29 | 54.72 |
| - 5 or greater | 24 | 45.28 |
| Number of workers | | |
| - 1 - 2 | 12 | 22.64 |
| - 3 – 4 | 21 | 39.62 |
| - 5 – 6 | 13 | 24.53 |
| - 7 – 8 | 5 | 9.43 |
| - 9 or greater | 2 | 3.77 |
| Number of years of manufacturing operation | | |
| - 1 – 10 | 34 | 64.15 |
| - 10 or greater | 19 | 35.85 |
| Number of operation days per week | | |
| - 4 | 3 | 5.66 |
| - 5 | 8 | 15.09 |
| - 6 | 32 | 60.38 |
| - 7 | 10 | 18.87 |
| Number of brands of drinking water | | |
| - 1 | 43 | 81.13 |
| - 2 or greater | 10 | 18.87 |
| Type of containers | | |
| - 20-liter plastic cans | 47 | 88.68 |
| - clear plastic bottles | 35 | 66.04 |
| - opaque plastic bottles | 32 | 60.38 |
| - clear plastic cups | 10 | 18.87 |

The second cause of non-compliance was domain 5 (cleaning agent and disinfectant) which was reported by 3 of 53 manufacturers (5.66%). Being dependent on the machine installers, most manufacturers did not know how to clean or disinfect these machines, and how to keep the cleaning agent and disinfectant properly. The third cause was domain 3 (water source, water quality improvement and quality control) which was found in 3.77% of the manufacturers. This was mostly because the raw water and finished products were not

sampled for quality control tests. Another reason was the unavailability of complete test kits at the plant, or the disrupted use of the tests despite their availability. The fourth cause of the non-compliance was domain 6 (water filling) which was found in one manufacturer (1.89%). This was because the manufacturer reported a severe defect of which the filling process was done outside the water filling room, and the use of a disapproved extended plastic pipe to fill the water outside the filling room especially for the 20-liter plastic can. The other domains including domain 1 (plant and location), domain 2 (equipment, machine and device), domain 4 (container), domain 7 (hygiene), and domain 8 (personnel and their hygiene) were compliant with the GMP criteria as self-assessed by the manufacturers (Table 2).

**Table 2** The manufacturers' compliance to the GMP criteria for bottled drinking water by self-assessment (N = 53).

| Criteria domain | | Average score* [min – max] | Assessment result, N (%) | |
|---|---|---|---|---|
| | | | Compliant | Non-compliant |
| Domain 1 | Plant and location | 93.37 [62.50 - 100] | 53 (100) | 0 (0.00) |
| Domain 2 | Equipment, machine and device | 92.22 [62.50 - 100] | 53 (100) | 0 (0.00) |
| Domain 3 | Water source, water quality improvement and quality control | 84.16 [39.29 - 100] | 51 (96.23) | 2 (3.77) |
| Domain 4 | Container | 92.74 [65.00 - 100] | 53 (100) | 0 (0.00) |
| Domain 5 | Cleaning agent and disinfectant | 88.05 [50.00 - 100] | 50 (94.34) | 3 (5.66) |
| Domain 6 | Water filling | 93.40 [31.82 - 100] | 52 (98.11) | 1 (1.89) |
| Domain 7 | Hygiene | 94.20 [62.50 - 100] | 53 (100) | 0 (0.00) |
| Domain 8 | Personnel and their hygiene | 94.16 [62.50 - 100] | 53 (100) | 0 (0.00) |
| Domain 9 | Documentation and report | 76.65 [0 - 100] | 41 (77.36) | 12 (22.64) |
| Overall assessment | | 91.11 [70.75 - 100] | 41 (77.36) | 12 (22.64) |

* A total score of 100%.

**The manufacturers' compliance as assessed by the experts**

After the manufacturer's self-assessment, the experts' assessment was conducted. While 77.36% of the manufacturers were compliant with the GMP criteria by self-assessment, only 33 of 53 (62.26%) meet such criteria as assessed by the experts (Table 3). Similar to that by self-assessment, the most frequently cause of non-compliance as assessed by the experts was domain 9 (documentation and report) which was found in 15 of 53 manufacturers (28.30%). In accordance with self-assessment, most manufacturers were more likely to neglect the process of documentation and reporting especially the processes of quality control of the raw water and finished product, and the maintenance of the equipment, machine and device. In addition to self-assessment, the manufacturers perceived documentation and report as unimportant and irrelevant to business gain or benefit.

**Table 3** The manufacturers' compliance to the GMP criteria for bottled drinking water as assessed by the experts (N = 53).

| Criteria domain | | Average score* [min – max] | Assessment result, N (%) | |
|---|---|---|---|---|
| | | | Compliant | Non-compliant |
| Domain 1 | Plant and location | 77.97 [52.50 - 100] | 51 (96.23) | 2 (3.77) |
| Domain 2 | Equipment, machine and device | 79.13 [60.00 - 100] | 53 (100) | 0 (0.00) |
| Domain 3 | Water source, water quality improvement and quality control | 82.85 [55.36 - 100] | 50 (94.34) | 3 (5.66) |
| Domain 4 | Container | 80.38 [60.00 – 100] | 53 (100) | 0 (0.00) |
| Domain 5 | Cleaning agent and disinfectant | 83.96 [50.00 – 100] | 50 (94.34) | 3 (5.66) |
| Domain 6 | Water filling | 72.04 [22.73 – 100] | 41 (77.36) | 12 (22.64) |
| Domain 7 | Hygiene | 77.64 [60.00 – 100] | 53 (100) | 0 (0.00) |
| Domain 8 | Personnel and their hygiene | 77.62 [50.00 – 100] | 49 (92.45) | 4 (7.55) |
| Domain 9 | Documentation and report | 68.40 [0.00 - 100] | 38 (71.70) | 15 (28.30) |
| Overall assessment | | 78.21 [57.00 - 99.5] | 33 (62.26) | 20 (37.74) |

* A total score of 100%.

The second cause of non-compliance based on the expert assessment was domain 6 (water filling) which was found in 12 of 53 manufacturers (22.64%). This was worrisome since self-assessment revealed only 1.89% of the manufacturers with this problem. The experts also found a severe defect which was filling outside the filling room and using disapproved extended plastic pipes to fill the water outside the filling room especially for the 20-liter plastic can. The malpractice of filling 20-liter cans outside the filling room was because the cans were heavy and difficult to move. Such malpractice was more prone to a higher risk of contamination. This malpractice was more prevalent among manufacturers whose manufacturing permission was granted before the GMP criteria were enforced. Therefore, at present, their plants' layout was non-compliant to the GMP criteria.

The third cause was domain 8 (personnel and their hygiene) which was found in 4 manufacturers (7.55%). It was found that in spite of the availability of the worker's clothes,

the worker's negligence led to clothing non-compliance especially mask and hair cap. Such non-compliance occurred because workers perceived clothing as a hindrance to their task. In addition, the workers were also non-compliant with hand washing before the filling task. In addition, some sinks were not suitable for use or even not usable. In terms of hygiene training, most manufacturers did not have training program in place. Most production plants were small so the on-site training for all workers could be disruptive to the daily production process. Therefore they were informally allowed to place signs showing hygienic instructions in front of the filling room. However, most workers did not pay adequate attention to follow the instruction.

The fourth cause was domain 3 (water source, water quality improvement and quality control) which was found in 5.66% of the manufacturers. Most manufacturers did not sample the raw water and finished products for quality test submission. Based on GMP criteria, the manufacturers were required to submit the samples for quality test at least once a year. Since the cost of quality test was relatively high (5,900 Baht per sample), such mandate was not strictly followed. In addition, basic test kits, for example, tests for water hardness, chlorine, and microbes, were not readily available on-site, or were not used despite their availability. This malpractice was evident as documentation of the tests was not completed. As a result, this shortcoming also impaired domain 9 (documentation and report) of the manufacturer's performance.

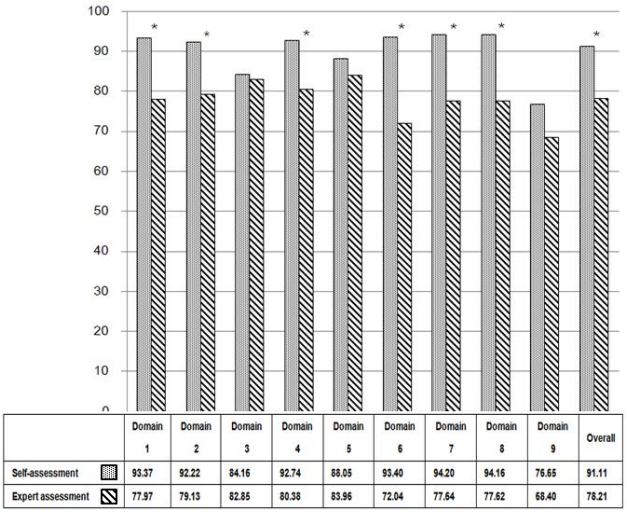
The fifth cause of the non-compliance was domain 5 (cleaning agent and disinfectant) which was found in 5.66% of the manufacturers. Some manufacturers did not know about the procedure for cleaning and disinfecting the water filter and filler. Cleaning agents and disinfectants were not kept in a well-compartmented room. This was because most manufacturers relied almost solely on the maintenance service provided by the device installers.

Another cause of non-compliance was domain 1 (plant and location) which was found in 3.77% of the manufacturers. Severe defects were revealed. Specifically the water filling room area was not adequately compartmented which could possibly lead to contamination. This incident was found in the manufacturer that had been more than 15 years of operation. Since its operation started long before the GMP criteria for drinking water in sealed container were enforced, the plant layout did not comply with the criteria. The experts reported that domain 2 (equipment, machine and device), domain 4 (container), and domain 7 (hygiene) complied with the GMP criteria (Table 3).

**Discrepancies of the assessed compliance between the manufacturers and the experts**

Self-assessment by the manufacturers resulted in a mean overall score of 91.11% which was higher than that by the experts (78.21%) with a statistical significance (*P*-value < 0.05). Once individual domains were considered, self-assessed mean total scores of domain 1 (plant and location), domain 2 (equipment, machine and device), domain 4 (container), domain 6 (water filling), domain 7 (hygiene), and domain 8 (personnel and their hygiene) were higher than those assessed by the experts with statistical significances (*P*-value < 0.05, for all) (Figure 1).

The discrepancies in assessment results could be viewed in terms of proportions. The majority of manufacturers were compliant with the GMP criteria as assessed by themselves and the experts (33 manufacturers or 62.26%). Twelve manufacturers (22.64%) were not approved by either self-assessment or the experts; while 8 (15.09%) were approved by self-assessment but not the experts. Approval by the experts but not the manufacturer themselves was not found in any manufacturers (Table 4).




| | Domain 1 | Domain 2 | Domain 3 | Domain 4 | Domain 5 | Domain 6 | Domain 7 | Domain 8 | Domain 9 | Overall |
|---|---|---|---|---|---|---|---|---|---|---|
| Self-assessment | 93.37 | 92.22 | 84.16 | 92.74 | 88.05 | 93.40 | 94.20 | 94.16 | 76.65 | 91.11 |
| Expert assessment | 77.97 | 79.13 | 82.85 | 80.38 | 83.96 | 72.04 | 77.64 | 77.62 | 68.40 | 78.21 |

**Figure 1** Comparisons of scores of compliance to GMP criteria (as percentage) between self-assessment and expert assessment (N = 53). * Statistical significant at *P*-value < 0.05.

**Table 4** Frequency and percentage of the GMP compliance results by the manufacturers' self-assessment and the expert assessment (N = 53).

| | | Expert assessment | |
|---|---|---|---|
| | | Compliant with GMP | Non-compliant with GMP |
| Self-assessment | - Compliant with GMP | 33 (62.26%) | 8 (15.09%) |
| | - Non-compliant with GMP | 0 (0.00%) | 12 (22.64%) |

Regarding individual domains, the highest discrepancy of being approved by self- but not expert-based assessment was found in domain 6 (water filling) (11 manufacturers or 20.75%), especially on the issue of the filling process and filling room (Figure 2). Despite the availability of information and knowledge, ignorance was a major cause of this poor practice. The problem was found mostly in the filling into 20-liter containers which was relatively heavy to move. As a result, they used the extended plastic pipe to fill the containers outside the filling room. This risk of contamination thus was more likely.


**Figure 2** Frequency and percentage of the GMP compliance results by the manufacturers' self-assessment and the expert assessment on domain 6 (water filling) (N = 53).

In addition, the assessment discrepancy on domain 1 (plant and location) was found in two manufacturers (3.77%). We found a serious defect which was an unavailability of the well-compartmented filling room. This problem could lead to contamination while filling. Assessment discrepancies regarding domain 3 (water source, water quality improvement and quality control), domain 8 (personnel and their hygiene), and domain 9 (documentation and report) were found in one (1.89%), 4 (7.55%), and 3 (5.66%) manufacturers, respectively; while none were found in domain 2 (equipment, machine and device), domain 4 (container), domain 5 (cleaning agent and disinfectant), and domain 7 (hygiene).

**Associations between the assessed compliance with the GMP and the actual quality tests of the bottled drinking water**

Based on quality control results, 18 samples of the water product passed all criteria (33.96%) while 35 samples (66.04%) failed physicochemical and/or microbiological criteria. Specifically, 26 samples (49.06%) failed physicochemical criteria of which acid-base criteria were not met and 15 samples (28.30%) failed microbiological standards because the contamination of *Coliform bacteria* was higher than standard criteria (Table 5).

**Table 5** Results of quality control tests of the drinking water in sealed container (N = 53).

| Tests and criteria | Test results | | | |
|---|---|---|---|---|
| | Passed | | Failed | |
| | N | % | N | % |
| **Physicochemical properties** | | | | |
| - acid-base (pH 6.5 - 8.5) | 27 | (50.94) | 26 | (49.06) |
| - fluoride (not more than 0.7 mg/L) | 51 | (96.23) | 2 | (3.77) |
| - nitrate (not more than 4 mg/L) | 53 | (100.00) | 0 | (0.00) |
| *Conclusion* | *27* | *(50.94)* | *26* | *(49.06)* |
| **Microbiological properties** | | | | |
| - Coliform bacteria (less than 2.2/100 mL by MPN method) | 38 | (71.70) | 15 | (28.30) |
| - *Escherichia coli* (absent) | 51 | (96.23) | 2 | (3.77) |
| - *Staphylococcus aureus* (absent) | 52 | (98.11) | 1 | (1.89) |
| - *Salmonella spp.* (absent) | 53 | (100.00) | 0 | (0.00) |
| *Conclusion* | *38* | *(71.70)* | *15* | *(28.30)* |
| **Overall conclusion** | **18** | **(33.96)** | **35** | **(66.04)** |

* MPN = Most Probable Number for the quantitative analysis of Coliform bacteria

It was found that manufacturers that passed the physicochemical tests were more likely to be compliant with the GMP criteria as assessed by the experts (Table 6). Even among those that failed the physicochemical tests, there were more manufacturers that were compliant than those non-compliant with the criteria. Similar patterns were also found in microbiological tests and overall results. These associations were not statistically significant.

**Table 6** Associations between quality control test results and expert-based GMP assessment (N = 53).

| Test results | Expert-based GMP assessment results, N (%) | | *P*-value* |
|---|---|---|---|
| | Compliant | Non-compliant | |
| Physicochemical properties | | | 0.50 |
| - Passed | 18 (33.96) | 9 (16.98) | |
| - Failed | 15 (28.30) | 11 (20.75) | |
| Microbiological properties | | | 0.40 |
| - Passed | 25 (47.17) | 13 (24.53) | |
| - Failed | 8 (15.09) | 7 (13.21) | |
| Overall results | | | 0.09 |
| - Passed | 14 (26.42) | 4 (7.55) | |
| - Failed | 19 (35.85) | 16 (30.19) | |

* Chi-square test or Fisher's exact test, as appropriate

**Table 7** Associations between microbiological test results and expert-based assessment by GMP criteria domains (N = 53).

| Expert assessment by GMP domains | Microbiological test results | | | | *P*-value* |
|---|---|---|---|---|---|
| | Passed | | Failed | | |
| | N | % | N | % | |
| Domain 1: Plant and location | | | | | |
| - Compliant | 37 | (69.81) | 14 | (26.42) | 0.49 |
| - Non-compliant | 1 | (1.89) | 1 | (1.89) | |
| Domain 2: Equipment, machine and device | | | | | |
| - Compliant | 38 | (71.70) | 15 | (28.30) | N/A |
| - Non-compliant | 0 | (0.00) | 0 | (0.00) | |
| Domain 3: Water source, water quality improvement and quality control | | | | | |
| - Compliant | 37 | (69.81) | 13 | (24.53) | 0.19 |
| - Non-compliant | 1 | (1.89) | 2 | (3.77) | |
| Domain 4: Container | | | | | |
| - Compliant | 38 | (71.70) | 15 | (28.30) | N/A# |
| - Non-compliant | 0 | (0.00) | 0 | (0.00) | |
| Domain 5: Cleaning agent and disinfectant | | | | | |
| - Compliant | 37 | (69.81) | 13 | (24.53) | 0.19 |
| - Non-compliant | 1 | (1.89) | 2 | (3.77) | |
| Domain 6: Water filling | | | | | |
| - Compliant | 33 | (62.26) | 8 | (15.09) | 0.02 |
| - Non-compliant | 5 | (9.43) | 7 | (13.21) | |
| Domain 7: Hygiene | | | | | |
| - Compliant | 38 | (71.70) | 15 | (28.30) | N/A |
| - Non-compliant | 0 | (0.00) | 0 | (0.00) | |
| Domain 8: Personnel and their hygiene | | | | | |
| - Compliant | 38 | (67.92) | 13 | (24.53) | 0.57 |
| - Non-compliant | 2 | (3.77) | 2 | (3.77) | |
| Domain 9: Documentation and report | | | | | |
| - Compliant | 27 | (50.94) | 11 | (20.75) | 1.00 |
| - Non-compliant | 11 | (20.75) | 4 | (7.55) | |

* Chi-square test or Fisher's exact test, as appropriate

# N/A = not applicable

With a great concern of microbiological safety of the drinking water, significant association between microbiological test result and GMP assessment was found in domain 6 (water filling) (*P*-value = 0.02) (Table 7) of which a serious defect was found. Those assessed as compliant with the GMP standard were more likely to pass the microbiological test (62.26%) while those non-compliant were less likely (9.43%).

## Discussions and Conclusion

The study on the compliance with GMP criteria of bottled drinking water products revealed that 22.64 % and 37.74% of the manufacturers did not meet the criteria as assessed by themselves and experts, respectively. This was because, once permitted, most manufacturers usually had not improved or controlled their manufacturing processes as guided by the GMP criteria. Our finding was consistent with previous studies of which such non-compliance with the GMP criteria was also found.[5,6,8,10,12]

The most troublesome aspect of quality was domain 9 (documentation and report) which did not meet the GMP criteria in 22.64% and 28.30% of the manufacturers as evaluated by the manufacturer themselves and experts, respectively. This was consistent with studies by Kongjing and Lerkiatbundit[5] and Polying and Sungsitthisawad[6] where they found that all manufacturers did not pass the criteria of this domain. They reported that the manufacturers did not complete documentation and report. Few manufacturers documented only their product sales. This ignorance on documentation and report was prominent in the process of quality control on raw water and finished product and the process of maintenance of equipment, machine and device. Manufacturers viewed documentation and report as uncritical and not benefit-driven.

We also found that a relatively high number of manufacturers (22.64%) did not meet the GMP criteria of domain 6 (water filling) as evaluated by experts. This poor performance was based on the finding that manufacturers filled the container with water outside the filling room with the extended plastic pipe. This practice was considered a severe defect or violation to the GMP criteria. The practice was prevalent among large containers, i.e., 20-liter cans, which were relatively too heavy to move. As a result, the risk of contamination was high. Manufacturers with at least 15 years of operation were more likely to face this problem since their plant layout was done and the operation was started long before the GMP criteria for drinking water in sealed container were enforced in 2001. The improper plant layout was difficult

to improve. The filling process was therefore unhygienic and prone to contamination. Since the filling pipe could not be thoroughly cleaned and disinfected, microbes could grow and contaminate the finished products. In addition, the reckless workers could also cause the water contaminated with microbes to splash from the floor and contaminate the container. Filling pipe lying down on the floor was used without cleaning and disinfecting. Furthermore, exposure of the water at the pipe outlet with the worker's hand could also cause contamination.[7] Our finding was also consistent with the study by Bootsingh[8] where 6.0% of manufacturers used the extended plastic filling pipe. It was also consistent with the study by Kongjing and Lerkiatbundit[4] which found that 85.70% of manufacturers did not fill the water in the filling room and were more likely to face contamination. Our result was also in line with the study by Polying and Sungsitthisawad[6] reporting that 11.11% of manufacturers had no filling room and did not use the designated filling nozzle.

Contrary to the self-assessment which indicated that all but one manufacturer were compliant with the GMP criteria on domain 6 (water filling), discrepancy between such self-assessment and the expert assessment was found in 11 manufacturers (20.75%). This seriously poor practice involved mainly the filling process and filling room. The manufacturers reported that they understood the GMP criteria. Unfortunately, with some limitations previously described, they could not fully comply with them. We recommended that the manufacturers acquire machines and devices, such as filling machine and nozzle with adequate capacity to prevent contamination. We also recommended a rail system to move large and heavy containers such as 20-liter cans of finished products to the storage room.[7]

In terms of product quality, 49.06% of the finished products did not meet the GMP criteria for physicochemical properties. The most prominent problem was that the pH was not within an acceptable range, mostly lower than the normal limit. Most manufacturers with this problem were those using reverse osmosis which could remove impurities such as copper, fluorite, nitrate, and colloids. Such process made the water softer or more purified. As a result, carbon dioxide dissolved more in the water and hence a lower pH. Chongworagun[9] compared acid-base status between manufacturing processes using and not using a reverse osmosis system. It was found that reverse osmosis was significantly associated with a lower pH ($P$-value < 0.05). This was also consistent with the study of Polying and Sungsitthisawad[6] which found that 24.07% of bottled drinking water products did not meet the pH criteria mostly with a lower than normal limit and the study of Kongjing and Lerkiatbundit[5] which revealed that 14.70% of the products did not meet the acid-base criteria.

Regarding microbiological standards, the most crucial indicator of drinking water safety, our study found that as high as 28.30% of the products did not meet the GMP standards since the contamination of *Coliform bacteria* was higher than the standard criteria. This bothersome finding was consistent with other previous studies. In studies of Polying and Sungsitthisawad[6], Kongjing and Lerkiatbundit[5] and Meksawasdichai and Ruengorn[10], contamination with *Coliform bacteria* was found in 31.48%, 35.29% and 22.00% of finished products of drinking water, respectively. In addition, in the study of Setthetham and Jiaramae[11] investigating the drinking water available at sub-district health promoting hospitals, contamination of *Coliform bacteria* was found in 98.2% of the samples. The contamination of microbes in drinking water has been considerably prevalent and of great concern.

In an attempt to alleviate the microbial contamination problem in drinking water, Thai FDA in cooperation with the Nutrition Research Institute of Mahidol University studied the causes of *Coliform bacteria* contamination.[7] The study found seven major causes including poor quality control of the raw water, microbial accumulation in the filters and filter materials, defect in the disinfection process, microbial colonization in the water reservoir especially of non-circulating or standing water, contamination due to no cleaning or disinfection of the filters after a long pause of production, inappropriate filling process and finished products management post-filling, and poor cleaning process and storage of the containers.

Our study also found a relationship between microbiological results and domain 6 (water filling) of the GMP criteria. Domain 6 was found to have the most serious defect and the highest discrepancy between self-assessment and the expert-based assessment. On the other hand, other domains were not associated with the overall assessment result. The relationship found in our investigation was consistent with other previous studies. Kongjing and Lerkiatbundit found that manufacturers that met microbiological standards had a significantly higher GMP domain 6 score than those that did not ($P$-value < 0.05).[5] The

study of Wongpattanawut[11] revealed that scores of GMP criteria were significantly associated with the passing results of physical, chemical and microbiological analyses (*P*-value < 0.05). The study of Meksawasdichai and Ruengorn also reported that manufacturers that met the GMP criteria had a significant relationship with better microbiological quality.[10] However, the study of Polying and Sungsitthisawad[6] found no relationships between *Coliform bacteria* contamination and the GMP quality, both on overall assessment and nine individual domains.

Based on findings from our study and the previous others, defect in domain 6 (water filling) was the most troublesome problem with the lowest proportion of manufacturers meeting the GMP criteria, the highest discrepancy between results from self-assessment and expert-based assessment, and the relationship between results of water quality test and the domain assessment. We recommend that the GMP inspector pay more attention in close monitoring on the domain assessment while manufacturers strictly follow the GMP standards. We realized that not only the domain of water filling but also all others need a close attention. Since all manufacturing processes affect each other in a consequential fashion, a defect in any particular step or process could potentially lead to contamination in the finished products. Following every single GMP standard strictly is highly crucial.

In terms of mode of assessment, even though self-assessment by the manufacturers was a valuable mode to help the manufacturers realize the importance of compliance with the GMP standards, expert- or inspector-based assessment should be mandated for a close monitoring on domains with serious defects or problems. Since the usefulness of self-assessment is evident, we recommended ways to improve the assessment process for the routine practice. To make the self-assessment judging and scoring easier and less biased, we recommended that the description of good, fair and poor levels for each item should be detailed. Scoring system with additional pictorial explanation could also help the judging process. To be more concise and less time-consuming, number of items could be reduced. The provincial health offices should use the results of the GMP compliance assessment and the product quality tests to categorize the risk of poor manufacturers. Those with the highest risk should be urgently and closely monitored. In addition to monitoring, the provincial health offices and other related agencies should also provide GMP compliance trainings regularly for the manufacturers and their workers to maintain a robust attention on quality assurance. Last, competency of the consumer protection officers or inspectors should be strengthened. These workers are valuable resource since they are geographically close to the manufacturers. They are prompt for an urgent monitoring and help for the manufacturers when needed.

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Editorial note
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