Research article

Perspectives on antimicrobial use in pig and layer farms in Thailand: legislation, policy, regulations and potential

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Abstract

Irrational use of antimicrobials is a major problem worldwide. The comprehensiveness of the existing legislation and veterinary pharmaceutical regulatory system has been critically evaluated and its practical implementation was assessed in this study. An archival review, a cross-sectional survey study, and an in-depth interview of key informants involving the layer and pig farm owners/managers of farms located in Chiang Mai, Lamphun and Chonburi Provinces were conducted. The Thai FDA is responsible for pre-marketing and authorizes relevant officials of DLD to enforce drug acts related to the post-marketing of veterinary drugs/biologics. These existing legislations and regulations were comprehensive enough to cover all areas of pharmaceutical activities developed to protect the health of the public and animals in the country; however, the enforcement of these rules may not be properly enforced or may be ineffectively executed. Additionally, the important regulatory tools such as the standards and guidelines have not been completely put into action. Regulations overseeing the veterinary pharmaceuticals at the farm level is not clearly stated and procedures are not systematically recorded in all farms. Some farmers can easily access veterinary pharmaceuticals, and veterinarian prescriptions were not needed. Additionally, the relevant benefits were among the most important reasons for choosing to use antimicrobials on farms, along with a lack of availability of better alternative products for the treatment of infections. Therefore, intensive and regulation enforcement, important regulatory standards and guidelines, financial issues and alternative products were considered to be the most effective means of reducing antimicrobial usage and abuse in Thailand.

Keywords: regulation, veterinary pharmaceutical, usage, farm, Thailand

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INTRODUCTION

Antimicrobial resistance has been recognized as being associated with enormous health and economic impacts on both animals and humans (World Health Organization, 2001; Gandra et al., 2014). Irrational use of medicines such as overuse, underuse or misuse is a major problem worldwide, as well as in Thailand and can promote the dynamic growth of antimicrobial resistance on farms (Padungtod et al., 2006; World Health Organization, 2010; Nuangmek et al., 2018a). Even though antimicrobial use is most likely posing a serious risk to human health, the practice of antibiotic treatment is still continued in livestock due to the lack of access to better alternatives for the treatment of infections in farm animals (Archawakulathep et al., 2014). Most drugs are used as both treatments and as feed additives for sub-therapeutic prophylaxis and as growth promoters. Veterinary drug formulas often contain a combination of different antibiotics; although their therapeutic effects are not always clearly stated (Office International des Epizooties, 2003; 2007).

Additionally, the KAP of pig and layer’ farmers in Thailand regarding antimicrobial usage revealed that the majority of the farmers surveyed had low levels of knowledge, neutral attitudes and employed poor antimicrobial practices. Such misconceptions, wrong beliefs and inappropriate practices can be a significant contributing factor in the cyclical increase in antibiotic resistance (Nuangmek et al., 2018b). Although the existing legislation and regulation are comprehensive enough to cover all areas of pharmaceutical activities to protect public and animal health in Thailand, the evidence of misuse or irrational use of antimicrobials on farms remains a significant concern (Archawakulathep et al., 2014). These problems can be found in almost all farming systems, but particularly in poultry and pig farms where antimicrobials are used extensively (Metlay et al., 2006). In Thailand, the pig and poultry industries have become the largest food-producing animal sectors. Pig production has the highest total consumption of antimicrobials (66.96%), followed by layer production (3.47%) (Animal Health Products Association, 2013). Chiang Mai–Lamphun (northern Thailand) and Chon Buri Provinces (eastern Thailand) were chosen as the focus of this study because they are associated with a high degree of density of animal raising, involving 46.57% of the layers and 26.57% of the pigs in the country (Department of Livestock Development, 2013).

To serve database as a baseline of regulatory systems for the policy makers in designing or updating policies and strategies for protecting the public from harmful and dubious drugs and practices, the comprehensiveness of the existing legislation and the veterinary pharmaceutical regulatory system were critically evaluated, and the relevant practical implementation measures were assessed in this study.

MATERIALS and METHODS

Study design and data collection

This study was conducted to critically assess the legal basis of the existing veterinary pharmaceutical regulatory system in Thailand, in order to evaluate antimicrobial usage on pig and layer farms. An archival review, in-depth interviews (with key informants selected from relevant stakeholders
involved in the pharmaceutical and veterinary sectors) and a cross-sectional survey of layer and pig farm owners/managers in Chiang Mai–Lamphun and Chon Buri Provinces using a validated self-administered questionnaire were used to gather data.

For the review process, an archival review guide was used as a data collection tool that was developed based on WHO guidelines (World Health Organization, 2008). It contained detailed descriptions on the general content of the legislation surrounding veterinary medicine and assesses the availability of the basic resources that are needed to implement the legislation on veterinary medicine in relation to the distribution and marketing authorization and regulatory the approvals that are associated with farm inspections and the enforcement of relevant laws in Thailand. The basic purpose for the archival review was to assess the comprehensiveness of the existing veterinary pharmaceutical regulatory system in controlling antimicrobial usage on layer and pig farms.

In-depth interviews were conducted with individuals selected based on their involvement in the regulatory system, and/or their roles as representatives of the pharmaceutical sector or other relevant stakeholder groups. A total of 18 key informants were selected from different relevant stakeholders (veterinary and medicine regulatory authorities working in the country, officials at the regional and provincial level, the president of the veterinary council of Thailand, the cooperative chairman, drug company managers, contract farming managers and pharmacists of drugstores) who were considered expert participants if they had work experience of more than 15 years. The purpose of the in-depth interviews was to obtain details and gain relevant insights involving: 1) the adequacy and comprehensiveness of the current legal provision in addressing all the veterinary pharmaceutical regulatory activities; 2) the access to and distribution of veterinary pharmaceuticals; 3) veterinary pharmaceutical usage on farms and the enforcement of the existing rules and regulations.

A cross-sectional survey of layer and pig farm owners/managers in Chiang Mai, Lamphun and Chonburi Provinces was conducted using a validated self-administered questionnaire during the period of May 2015 through February 2017. The questionnaire containing personal information, general information on the regulation of veterinary medicines, and the knowledge, attitudes and practices of the owners/managers toward antimicrobial usage on farms. The sample size for the study was calculated using Epi Info™ 7 software (Centers for Disease Control and Prevention, 2014). A response distribution of 80% was assumed, with a confidence interval of 95% and a margin of error of 5%. The estimated minimum effective sample sizes for the layer and pig farm owners/managers were calculated to be 126 and 125, respectively. Eighty-five of the layer farms and 75 of the pig farms were located in the adjoining provinces of Chiang Mai and Lamphun Provinces in the northern region of Thailand, with 50 pig farms and 41 layer farms being situated in Chonburi Province, which is located in the central region of the country. Layer and pig farms in this study were classified as small, medium or large in size. The size of each stratum was determined by a proportionate allocation of the total number of layer and pig farms. Layer farms with 1,000 to 10,000 birds were categorized as small-scale; those with 10,001 to 50,000 birds were medium-scale; and those with more than 50,000 birds were classified as large-scale farms (Food and Agriculture Organization of the United Nations, 2014). Due
to variations in the size of individual pigs, livestock units rather than total numbers of animals were used to categorize the scale of the pig farms. Farms with 6 to 59 livestock units were categorized as small-scale; those with 60 to 600 livestock units were classified as medium-scale; and those with more than 600 livestock units were classified as large-scale farms (National Bureau of Agricultural Commodity and Food Standards, 2009). Farms included in the study were selected using a convenience sampling method.

Data analysis

The data obtained from the interviews with key informants were summarized, analyzed and presented in a descriptive way. Similarly, summaries were made from the archival review findings on the critical features of the existing legislation and veterinary medicine regulations. Quantitative data (close-ended questions) were edited, coded, and analyzed using SPSS Statistics version 16.0 software (Agresti, 1992). The relationship of the scale of the farms (small-, medium- and large-scale), farm registration (registered and non-registered farms), the study site (Chiang Mai-Lamphun and Chon Buri Provinces) and the current practices of antimicrobial usage on both layer and pig farms were analyzed using Chi-square statistics. P-values of <0.05 were considered statistically significant. Descriptive analyses were conducted and outputs were presented using frequency tables.

Responses to qualitative data obtained from open-ended questions were analyzed using summative content analysis (Hsieh and Shannon, 2005) as well as manifest and latent content analysis (Graneheim and Lundman, 2004). The text was read several times to attain a sense of the entire transcript and was then translated into English. For summative content analysis, the collected material was sorted into groups according to generated keywords that were repeated by different respondents. The frequency of the respondents using different keywords was calculated to explore the risk factors for rational antimicrobial usage on farms. Manifest and latent content analysis is a subjective interpretation of the content of textual data that is done by utilizing a process of systematic classification and abstraction of the relevant codes and themes. During the analysis, each statement that related to the same central meaning was coded. Similar codes were grouped together and then clustered into sub-categories and categories. Similar categories were assigned and then associated according to central themes (Eltayb et al., 2012). The analysis followed the structure described by Dahlberg et al.(2001).

RESULTS

In our review, we found that the existing legislation, policy and regulations related to the control of veterinary drugs in livestock and livestock products in Thailand can be summarized as follows.

Legislation, policy and regulations for antimicrobial use in livestock and livestock production in Thailand: Archival Review

The legislation of human being and veterinary medicines of Thailand is based on the Drug Act B.E. 2510 (1967) and its five amendments (Drug
The Thai Food and Drug Administration (FDA) under the Ministry of Public Health is responsible for licensing, registration, manufacturing and (re)packaging, export and import, distribution and storage, supply and sale, and the overseeing of information and the pharmacovigilance of veterinary medicinal products (including vaccines) within the country. It also authorizes relevant officials from the Department of Livestock Development (DLD), Ministry of Agriculture and Cooperatives and the Department of Fisheries (DOF) to enforce the drug acts related to the post-marketing procedures of veterinary drugs/biologics (Food and Agriculture Organization of the United Nations, 2012; Archawakulathep et al., 2014). The post-marketing procedure of veterinary drugs/biologics is under the responsibility of the FDA. The DLD activities also cover, check and monitor whether the approved products in the market conform to the proclaimed quality and safety standards of the surveillance programs developed for identifying unforeseen hazards, abuse, or any unsafe use of veterinary medicinal products (Food and Agriculture Organization of the United Nations, 2012).

DLD is an organization that plays a very important role in the regulation and control of all matters regarding livestock and livestock products. DLD also issues importation standards of livestock and livestock products with regard to environmental and animal welfare concerns that are addressed in the standards (Archawakulathep et al., 2014). To control the use of veterinary medicines in farm animals, the prescriptions from farm veterinarians who look after animal health and oversee farm management are required following the Ministerial Notifications of Ministry of Agriculture and Cooperatives on Livestock Farm Standard of Thailand on 3 November B.E. 2542 (1999), 15 May B.E. 2545 (2002), 21 May B.E. 2546 (2003) and 28 December B.E. 2551 (2008) (Notification of the Ministry of Agriculture and Cooperatives, 1999; National Bureau of Agricultural Commodity and Food Standards, 2002, 2003a, 2003b, 2003c, 2003d; Metlay et al., 2006). The notification is voluntary but compulsory for those who want to send their birds to slaughterhouses that have been approved for export. These ministerial notifications stipulated that the livestock standard farms (the farms certified for GAP by the DLD) must have certified farm veterinarians to look after the health of the animals. He/she must be qualified in accordance with the Veterinary Practitioner Act B.E. 2545 (2002) (Veterinary Profession Act B.E. 2545, 2002) and must have passed the farm veterinarian training course of the DLD and be licensed by the DLD. The treatment of animals by the farm veterinarians must comply with the Code of Practice for Control of the Use of Veterinary Drugs (THAI AGRICULTURAL STANDARD, TAS 9032-2009) issued by the National Bureau of Agricultural Commodity and Food Standards (ACFS), Ministry of Agriculture and Cooperatives that oversees the standards and policies of the country. The TAS 9032-2009, which is in compliance with the Code of Practice for Control of the Use of Veterinary Drugs (CAC/REP 38–1993) of Codex, describes the best practices for the use of veterinary drugs that are fed to food-producing animals in order to avoid any excesses of the maximum residue limits of veterinary drugs in animals, animal products and the animal products that are sold for human consumption. The farm veterinarian must have his/her prescription records kept for a period of at least two years, and present them when requested by the DLD (National Bureau of Agricultural Commodity and Food Standards, 2009).
With regard to animal feed control, animal feed must be safe for human consumption, and therefore, the registration, inspection, and control of animal feed are vigorously regulated by DLD, which is the main authority responsible for putting in place a system for the management and control of animal feed. The laws controlling animal feed in Thailand have evolved over time. Animal feed was previously regulated under the Animal Feed Quality Control Act B.E. 2506 (1963 Act) (Atthachai, 2017). The 1963 Act was replaced with the Animal Feed Quality Control Act B.E. 2525 (1983 Act). Then, in 1999, there was an amendment of the act. And very recently, the Animal Feed Quality Control Act B.E. 2558 (2015 Act) was announced in the Royal Gazette, which came into force on March 5, 2015. Under the 2015 Act, “Animal feed” including drinking water, and “especially controlled animal feed” must be registered prior to domestically manufacturing or importing animal feed into the Kingdom of Thailand. This term was not defined under the previous Animal Feed Quality Control Act (Animal Feed Quality Control Act B.E. 2558, 2015). However, the important regulatory tools such as standards and guidelines that equip drug regulatory authorities with the practical means of implementing those laws have to be put into place, since the sole existence of the law does not ensure its implementation. For the benefit of animal feed quality control, the Ministry of Agriculture and Cooperatives shall, with the advice of the Committee, have power to issue notifications on the name, category, type, characteristics or attributes of prohibited materials in animal feed mixtures including veterinary drugs (Animal Feed Quality Control Act B.E. 2558, 2015). The notifications of the Ministry of Agriculture and Cooperatives that were issued included prohibited drugs, active pharmaceutical ingredients and semi-finished products such as nitrofurans, nitroimidazoles, chloramphenicol, etc., that are often supplemented in animal feed mixtures (Notification of the Ministry of Agriculture and Cooperatives, 2016a). This government agency has banned all antimicrobial drugs used as growth promoters in food animals (Notification of the Ministry of Agriculture and Cooperatives, 2015). It is also required that legitimate cooperatives or farmers’ groups who produce especially controlled animal feed for their members or for farmers in their groups do not mix prohibited materials in animal feed mixtures (Notification of the Ministry of Agriculture and Cooperatives, 2016c). The notifications also control farmers producing controlled animal feed that is used to raise farm animals (Notification of the Ministry of Agriculture and Cooperatives, 2016b).

Regarding the distribution and marketing of drugs, before distributing modern and traditional drugs including veterinary medicinal products into Thailand, a pharmaceutical company or its distributor wishing to place a drug on the market must obtain a licence from the Thai FDA to manufacture, sell or import drugs into Thailand. An import licence must be renewed every year and is valid from 1 January to 31 December. After obtaining the import licence, the company must obtain the authorization to manufacture or import drug samples. Registration requirements differ for general drugs (which include generics, new medicines, and new generics) and traditional drugs. A drug product licence does need to be renewed annually. If a company has applied for an import licence and a drug product licence, but does not actually import that product within two consecutive years, the company would have its product licence
for that product withdrawn. After the manufacturing licence or import licence is obtained, modern and traditional drugs must be registered with the Thai FDA prior to being distributed in Thailand. As an exception, a drug imported for research, analysis, exhibition or charitable purposes does not require registration. Additionally, active pharmaceutical ingredients, semi-finished products, and sample drugs for registration purposes do not require product registration. With regard to the sale of drugs, the drug store requires a licence to sell, yet the hospitals or clinics can sell drugs directly to his or her patients without having applied for a licence to sell medicine. With regard to distribution to consumers, the marketing authorisation holder or distributor that holds the drug import licence and product registration licences, that have been approved by the Thai FDA, is responsible for the distribution of prescription drugs and over-the-counter drug products to hospitals, clinical institutes or pharmacies. However, the marketing authorization holder or distributor must register its company in order to get the drug import licence. It must also register a drug product with the FDA before distributing the drug product to consumers in Thailand. The marketing authorization holder or the legal distributor who have been approved by the FDA are responsible for the wholesale distribution of drug products to only hospitals, clinical institutes or pharmacies. Nevertheless, direct mailing or the remote selling of drugs is not allowed under the Drug Act B.E. 2510 (AD 1967) (Drug Act B.E. 2510, 1967; Alan et al., 2015). The surveillance data on the amount of antimicrobial importations and use are limited and not systematically recorded. In Thailand, types and amounts of veterinary drugs used vary widely depending upon the level and type of the farm involved. A variety of antimicrobials have been produced in or imported into this country. Reports on antimicrobial use are occasionally observed but not systematically recorded. The annual report concerning the production or the importation of drugs with regard to the formulation has been registered with the Thai FDA. The Thai FDA could then estimate the quantities of antimicrobials manufactured and imported into Thailand (Food and Agriculture Organization of the United Nations, 2012). However, antimicrobials used at the farm level have not been clearly listed and are not systematically recorded in all farms.

**Implementation status of veterinary medicine regulatory system**

The results of the in-depth interviews of the key informants were used to evaluate the implementation status of the regulatory system pertaining to veterinary medicines. Regarding the adequacy and comprehensiveness of the current legal provisions that have been employed to address all the veterinary pharmaceutical regulatory activities, all the key informants agreed that the Drug Act B.E. 2510 (1967) and its five amendments are comprehensive enough to cover all areas of pharmaceutical activities to protect the health of the public and animals in Thailand. However, they stressed that the important regulatory tools such as the standards and guidelines that have been enacted to equip drug regulatory authorities with the practical means of implementing those laws have to be put into action, since the sole existence of the law does not ensure its implementation. Therefore, the medicine regulatory authority who has the power to issue notifications must also be empowered to put into action the proper guardrails.
The majority of the key informants believe that veterinary pharmaceuticals used on farms, especially independent farms can be easily accessed and obtained over the counter, and acknowledge the fact that veterinarian prescriptions are not needed when antimicrobials are purchased. These factors could support overuse or irrational use of antimicrobial on farms. Regulation regarding the distribution of veterinary pharmaceuticals at the farm level is not clearly stated and procedures are not systematically recorded in all farms. In Thailand, the types and amounts of veterinary drugs that are used vary widely depending upon the level and type of the farm involved. Reports on antimicrobial use are occasionally observed but not systematically recorded in all type of farms. The Thai FDA could estimate the antimicrobial use in Thailand from the quantities of antimicrobials manufactured and imported. Pharmaceutical companies and/or their distributors wishing to place a drug on the market must obtain a licence from Thai FDA to manufacture, sell or import drugs. The rules governing the data on the veterinary medicine distributed to drug stores, clinician or farmers in the country are occasionally observed. If tighter control of the distribution channels and stricter law and regulation enforcement are achieved, these could restrict the distribution of veterinary drugs to the farms.

All the key informants agreed that there is weak enforcement of legislation and regulation on farms in Thailand. For control of the usage of veterinary drugs on farms, livestock farms must have farm veterinarians onsite to look after the health of the animals. The treatment of the animals by the farm veterinarians must comply with the TAS 9032-2009. However, veterinarian prescriptions are not needed when antimicrobials are purchased. Insufficient and poor veterinary services are common, especially in farms that have not been registered by the DLD or on independent farms. The Ministry of Agriculture and Cooperatives stipulated that the livestock standard farms (farms certified for GAP by the DLD) must have onsite farm veterinarians to look after the health of the animals. The notification of livestock farm standard is voluntary but compulsory for those who want to send their birds to slaughterhouses that are approved for export. Even with the appropriate regulations for the control of veterinary drug use on farms, those regulations cannot be enforced on all farms. The situation is exacerbated where there is weak law and regulation enforcement on farms. With regard to contract farming, farmers are managed with an integrated system by relevant companies. The contract farmers are not allowed to use feeds and pharmaceutical products obtained from other sources. Treatment and prevention of diseases are also under the supervision of the DLD-registration farm veterinarians that have been provided by the contract companies. Additionally, the contract farmer must comply strictly with the company rules.

Cross-sectional survey

A cross-sectional survey of layer and pig farm owners/managers in Chiang Mai, Lamphun and Chon Buri Provinces was conducted using a validated self-administered questionnaire. Of a total of 126 respondents of the layer farms, almost half (48.4%) were contract farmers, while 37.3% were independent farmers. Additionally, 50.8% of respondents were small-scale farms, followed by medium to large-scale farms (49.2%). The majority of the
respondents (90.5%) had registered with the appropriate government agency. Distribution of the respondents were located throughout Chiang Mai-Lamphun Provinces (67.5%) and Chon Buri Province (32.5%). Out of a total of 125 respondents of pig farms, 53.6% were contract farmers, while 24.0% were independent farmers. Additionally, 55.2% were small-scale farms and medium to large-scale farms (44.8%). The majority of the respondents (96.0%) had registered with the DLD. Sixty percent and 40% of the respondents were located in Chiang Mai-Lamphun and Chon Buri Provinces, respectively (Table 1).

Table 1 General characteristics of layer and pig farmers located in Chiang Mai, Lamphun and Chon Buri Provinces participating in this study

| Characteristics                  | Layer farm (n = 126) No (%) | Pig farm (n = 125) No (%) |
|----------------------------------|-----------------------------|---------------------------|
| Pattern of farm                  |                             |                           |
| Independent farm                 | 47 (37.3)                   | 30 (24.0)                 |
| Cooperative member               | 18 (14.3)                   | 28 (22.4)                 |
| Contract farming                 | 61 (48.4)                   | 67 (53.6)                 |
| Farm size                        |                             |                           |
| Small scale                      | 64 (50.8)                   | 56 (44.8)                 |
| Medium to large scale            | 62 (49.2)                   | 69 (55.2)                 |
| Farm registration status         |                             |                           |
| Registration                     | 114 (90.5)                  | 120 (96.0)                |
| Non-registration                 | 12 (9.5)                    | 5 (4.0)                   |
| Study site                       |                             |                           |
| Chiang Mai, Lamphun Province     | 85 (67.5)                   | 75 (60.0)                 |
| Chon Buri Province               | 41 (32.5)                   | 50 (40.0)                 |

The quantitative data obtained from close-end questions, as shown in Table 2, reveal the highest rate of response for positive practice items included layer farmers who did not mix prohibited antimicrobial drugs into the feed of food-producing animals (97.6%). There was a lower rate of response for positive practice items among farmers who tested for sensitivity before choosing antimicrobial drugs for use on layer farms (3.2%). Fewer respondents were located in Chon Buri Province (58.5% vs. other locations 24.7%, $P = 0.003$), with regard to farm registration (33.3% vs. other 0%, $P = 0.0001$). Of pig farmers concerned with test sensitivity, only 17.6% responded accordingly, in contrast to the majority of respondents in the medium and large-scale farms (87.2% vs. other 12.8%, $P <0.0001$). This survey found that 32.5% and 59.2% of the respondents of the layer and pig farmers employed veterinarians who were responsible for drugs prescriptions. With regard to farm registration of layer farms, there was a higher level of response (66.7% vs. other 33.3%, $P =$
0.011), while in the medium and large-scale farms of pig farmers, responses were greater (80.8% vs. other 19.2%, $P = 0.001$). Regarding the authorized personnel that kept records of the veterinary drugs used on farms, they were found at layer and pig farmers by 67.5% and 46.4%, respectively. We found that medium to large scale-farms of layers responded accordingly (77.6% vs. other 22.4%, $P = 0.0001$). Farmers in layer and pig farm responded that drug withdrawal periods should be adhered to in order to avoid very high rates of drug residues (about 92%). Additionally, 53.6-73.8% of the respondents incorrectly believed that the primary reason for using antimicrobials on farms were associated with the economic costs and benefits, whereby the medium to large-scale layer farms wrongly believed this statement (57.1% vs. other 42.9%, $P = 0.03$).
Table 2 Association of demographic characteristics with practice statements regarding the usage of antimicrobials and antimicrobial resistance of layer and pig farm owners/managers in Chiang Mai, Lamphun and Chon Buri Provinces

| Statement                                                                 | Layer farm (n = 126) | Pig farm (n = 125) |
|--------------------------------------------------------------------------|----------------------|--------------------|
|                                                                          | Usually response No (%) | P value (X2 test) | Usually response No (%) | P value (X2 test) |
|                                                                          | Farm size | Farm registration | Study site | Farm size | Farm registration | Study site |
| 1. Antimicrobial use on farms by veterinarian prescriptions.              | 41 (32.5) | 0.866 | 0.011* | 0.586 | 74 (59.2) | 0.001** | 0.383 | <0.0001** |
| 2. The farm owner/manager is the top authority for drug purchases.      | 49 (38.9) | 0.261 | 0.135 | 0.020* | 52 (41.6) | 0.001** | 0.910 | 0.023* |
| 3. Prevention is the main purpose of antimicrobial use on farms.         | 24 (19.1) | 0.033* | 0.382 | 0.0001** | 50 (40.0) | 0.001** | 0.749 | <0.0001** |
| 4. Farmers consult a veterinarian regarding the decision to use antimicrobials drugs on the farm. | 54 (42.9) | 0.478 | 0.314 | 0.0001** | 70 (56.0) | 0.036* | 0.001** | 0.292 |
| 5. Use antimicrobial drugs in the absence of a disease outbreak.         | 31 (24.6) | 0.254 | 0.36 | 0.0001** | 30 (24.0) | 0.002** | 0.774 | <0.0001** |
| 6. Antimicrobials administration follows the drug recommendations and the advice of the consulting veterinarian. | 93 (73.8) | 0.48 | 0.055 | 0.004** | 79 (63.2) | 0.002** | 0.543 | <0.0001** |
| 7. Use multiple antimicrobial drugs at the same time.                    | 64 (50.8) | 0.105 | 0.048* | 0.0001** | 55 (44.0) | <0.0001** | 0.380 | 0.247 |
| 8. Test sensitivity before choosing antimicrobials use on the farm.      | 4 (3.2) | 0.603 | 0.0001** | 0.003** | 22 (17.6) | <0.0001** | 0.122 | <0.0001** |
| 9. Farmers use the same antimicrobial drugs for long periods of time on the farm. | 54 (42.9) | 0.278 | 0.782 | 0.0001** | 61 (88.8) | <0.0001** | 0.257 | 0.189 |
| 10. Farmers don’t mix prohibited antimicrobial drugs into the feed of food producing animals. | 123 (97.6) | 0.811 | 0.851 | 0.223 | 0 (0.0) | 0.062 | 0.062 | 0.232 |
| 11. Drug withdrawal periods shall be adhered to avoid drug residues.     | 116 (92.1) | 0.387 | 0.565 | 0.378 | 115 (92.0) | 0.591 | 0.078 | 0.178 |
| 12. The economic costs and benefits of farm are the most important reason for choosing to use antimicrobial drugs on farm. | 93 (73.8) | 0.030* | 0.839 | 0.585 | 67 (53.6) | 0.178 | 0.826 | 0.074 |
| 13. Antimicrobial usage for protection against diseases on farms          | 99 (78.6) | 0.505 | 0.837 | 0.163 | 86 (68.8) | 0.739 | 0.167 | 0.293 |
| 14. Authorized person keep record their use of veterinary drugs and maintain it for further inspection. | 85 (67.5) | 0.073 | 0.0001** | 0.89 | 58 (46.4) | <0.0001** | 0.505 | <0.0001** |

Notes: * was significant at the 0.05 level, ** was significant at the 0.01 level. Study site: Chiang Mai-Lamphun vs. Chon Buri Province, Farm size: small-scale farm vs. medium and large-scale farm, Farm registration: non-registered and registered.
Issues related to rational antimicrobial use on farms

Responses to open-ended questions were analyzed using summative content analysis. In the analysis of the data when farm owners tried to clarify what rational antimicrobial use on farms should be, three categories and four sub-categories emerged which ended in one theme, namely ‘Rational antimicrobial use on farms relies on financial status’. In Table 3, the analysis followed the structure that had been described by Dahlberg et al. (2001). This theme evolved from the comments of layer and pig farmers that mainly dealt with their daily life practices. Farmer’s clarifications lacked scientific facts and biological or theoretical explanations of antibiotic resistance. Instead, farmers discussed issues in relation to rational antimicrobial use on farms depending on the benefits to the farm as the most important reason for choosing to use antimicrobial drugs on farms.

Table 3 Exploring rational antimicrobial use on farms: an example of data analytical steps by content analysis

| Text | Codes | Subcategories | Category | Theme |
|------|-------|---------------|----------|-------|
| ‘Rational antimicrobial use on farms happens when reducing or restricting amount of antimicrobials, however high production on farm is sustainable’, ‘Intensive law and regulation enforcement can lead to reducing antimicrobials use on farms’, ‘Financial compensation, bonuses and punishments were considered to be the most effective means of reducing antimicrobial usage on farms’, ‘Alternative products substitute usage of antimicrobial and growth promoters on farms can cause rational antimicrobial use on farms’; … etc | Reducing antimicrobials use on farms occurred due to stricter law and regulation enforcement, considered financial compensation, bonuses and punishments, and usage alternative products substitute of antimicrobial and growth promoters on farms can cause rational antimicrobial use on farms | Rational antimicrobial use on farms relation to intensive law and regulation enforcement, the economic costs and benefits, financial status of farms and alternative products substitute. | Intensive legislation and regulation enforcement, benefits of farms and alternative products substituted in relation to rational antimicrobial use on farms | Rational antimicrobial use on farms relies on benefits of farm. |

The analysis followed the structure described by Dahlberg et al. (2001).

Category 1: Intensive legislation and regulation enforcement in relation to rational antimicrobial use on farms

The majority of farm owners indicated the need for intensive legislation and regulation enforcement in relation to rational antimicrobial use on farm. The respondents had high levels of overall knowledge regarding the legislation and regulation for controlling antimicrobial usage and antimicrobial affects; however, they admitted that some of the antimicrobial usage taking place on farms is improper. Even with appropriate legislation and regulations for the control of antimicrobial usage on farms, the legislation and regulations cannot be enforced on all farms. This study indicates that some improper antimicrobial usage that occurs on farms would require strong enforcement of laws and regulations by the relevant agencies.
Category 2: Benefits to farms in relation to rational antimicrobial use

The majority of farm owners identified the perceived benefits in relation to rational antimicrobial use. Some of them referred to the rational antimicrobial use on farms as indicated in the following sub-categories.

‘The economic costs and benefits of farms are the most important reason for choosing to use antimicrobial drugs on farms.’

‘Financial compensation, bonuses and punishment were considered to be the most effective means of reducing antimicrobial usage.’

The farm owners, especially those on small-scale farms, had wrongly believed that the antimicrobials were most important for protection against diseases on farms and that farmers made decisions of antimicrobial drug use based on the relevant economic costs and benefits. Generally, respondents worried less about their animals' health and antimicrobial resistance than they did about financial issues. However, antimicrobial usage on contract farms was found to be more proper than on the other types of farms, such as with regard to the antimicrobial administration on farms that are pre-scripted by veterinarians. This was also the case with regard to farmers choosing the antimicrobial drugs that are used on farms by sensitivity tests and the use of antimicrobials on farms when there is a disease outbreak. This likely occurred because antimicrobial usage on contract farms involved decisions being made by the veterinarians and according to the relevant company policy. Additionally, the financial policy of the company, such as financial compensation, bonuses and punishments, were considered to be the most effective means of reducing antimicrobial usage on farms. This study indicated that layer and pig farm owners/managers, especially on small-scale farms and not contract farms, should be given more awareness of antimicrobial resistance, with regard to its consequences and its causes, in order to support rational antimicrobial use on farms.

Category 3: Alternative products used to substitute antimicrobial and growth promoters in relation to rational antimicrobial use

The majority of the farm owners indicated that alternative products could be used to substitute the usage of antimicrobial and growth promoters, which could reduce antimicrobial use on farms. Even with appropriate legislation and regulations for the control of antimicrobial usage on farms, the legislation and regulations cannot be enforced in all farms. Some farm owners still employ improper practices of antimicrobial usage on farms. Some farm owners avoid using irrational antimicrobial usage, while they seem to be concerned about the health of their animals and the financial issues that are associated with the farms. Even though antimicrobial use is most likely posing a serious risk to human health, antimicrobial treatments continue to be used on livestock due to the lack of better alternatives for the treatment of infections. In order to maintain rational antimicrobial use on farms, alternative products that can be used to substitute for antimicrobial and growth promoters are necessary. Additionally, other scientific approaches which play a role in treatment and control are needed, as well as the use of natural substances or autogenous vaccinations.
DISCUSSION

The Drug Act B.E. 2510 (1967) and its five amendments determine the legislation of oversight on human being and veterinary medicine in Thailand (Drug Act B.E. 2510, 1967; Archawakulathep et al., 2014). The Thai FDA is responsible for the pre-marketing of drugs/biologics including licensing, registration, manufacturing and (re)packaging, export and import, distribution and storage, supply and sale, information and the pharmaco-vigilance of veterinary medicinal products (including vaccines) in Thailand. The FDA also authorizes relevant officials of the DLD to enforce the appropriate drug act in relation to the post-marketing of veterinary drugs/biologics (Food and Agriculture Organization of the United Nations, 2012; Archawakulathep et al., 2014). The post-marketing process of veterinary drugs/biologics activities is also covered to check and monitor whether the approved products on the market conform to the proclaimed levels of quality and safety. This would also include the surveillance programs for the overseeing of unforeseen hazards, abuse, or any unsafe use of veterinary medicinal products in the country (Food and Agriculture Organization of the United Nations, 2012). To control the use of veterinary medicines in farm animals, veterinarian prescriptions are required according to the Ministerial Notifications of Ministry of Agriculture and Cooperatives on Livestock Farm Standards of Thailand (National Bureau of Agricultural Commodity and Food Standards, 2008). Veterinarians who look after the health of animals must be qualified in accordance with the Veterinary Practitioner Act B.E. 2545 (2002) (Veterinary Profession Act B.E. 2545, 2002) and pass the farm veterinarian training course of the DLD and be licensed by the DLD. The treatment of animals by farm veterinarians must comply with the Code of Practice for Control of the Use of Veterinary Drugs (TAS 9032-2009) (National Bureau of Agricultural Commodity and Food Standards, 2009). Additionally, medicated feed is regulated under the Animal Feed Quality Control Act (Animal Feed Quality Control Act B.E. 2558, 2015). This legislation and the relevant regulations are comprehensive enough to cover all areas of pharmaceutical activities to protect the health of the public and animals in Thailand. This is similar to the legislation and regulation of veterinary pharmaceuticals found in Indonesia, Laos, the Philippines and Malaysia (Stür et al., 2002; Food and Agriculture Organization of the United Nations/World Health Organization, 2004; Food and Agriculture Organization of the United Nations, 2009; Ministry of Health, 2009). However, it is different from the existing regulations in Myanmar where a national policy on the sale or use of antimicrobials in animals and animal feed does not exist (Archawakulathep et al., 2014). However, the important regulatory tools such as the standards and guidelines that equip drug regulatory authorities with the practical means of implementing those laws must be put into action. To improve the regulations to optimize rational use on farms, guidelines on responsible use of antimicrobial agents in livestock production are recommended and have been mostly developed by relevant authorities. Thailand has begun the development of the prudent use guidelines for antimicrobial use in food animals, in line with the Philippines (Food and Agriculture Organization of the United Nations, 2009; Archawakulathep et al., 2014). For example, the veterinary council developed prudent use guidelines on antimicrobial use on farms and the DLD will reserve four groups of critically important antimicrobials for treatment only (polymyx-
in, cephalosporins, fluoroquinolones and beta-lactams). This will be done to restrict the use of medicated feed on farms (Food and Agriculture Organization of the United Nations, 2012).

Regarding the distribution and access of medicines, veterinary pharmaceutical usage on farms can be easily accessed and obtained over the counter. Typically, veterinarian prescriptions are not needed when antimicrobials are purchased. Although, in Thailand notifications of Livestock Farm Standard of Thailand (National Bureau of Agricultural Commodity and Food Standards, 2008) are required. Veterinarians who look after the health of animals on registered farms must be qualified, trained and licensed by relevant authorities (Veterinary Profession Act B.E. 2545, 2002; National Bureau of Agricultural Commodity and Food Standards, 2009). Additionally, animal treatment must comply with the Code of Practice for Control of the Use of Veterinary Drugs (TAS 9032-2009) (National Bureau of Agricultural Commodity and Food Standards, 2009). However, the evidence of misuse or irrational use of antimicrobials on some farms still occurs. The notification of Livestock Farm Standards of Thailand is voluntary, but it is compulsory for those who want to send their birds to slaughterhouses that are approved for export. Insufficient and poor veterinary services are common, especially among farms that have not been registered by the DLD or on independent farms. Therefore, appropriate regulations for the control of veterinary drug use on farms cannot be enforced in all farms. These factors could support the misuse or irrational use of antimicrobial on farms. The situation is exacerbated when there are weak laws and non-regulated enforcement on these farms.

Thailand possesses sufficient legislation and regulation for controlling and monitoring the distribution of veterinary pharmaceuticals (Drug Act B.E. 2510, 1967; Alan et al., 2015). However, records of veterinary pharmaceutical distribution throughout the country is not clearly stated and not systematically enforced. The Thai FDA could estimate the quantities of antimicrobials used from the manufactured and imported quantities (Drug Act B.E. 2510, 1967). The distribution of veterinary pharmaceuticals at the farm level is not clearly stated and is not systematically recorded in all farms, while types and amounts of veterinary drugs used vary widely depending upon the level and type of farm involved. Rules on the data collected on the veterinary medicine distributed to drug stores, clinicians or farmers are occasionally observed. Tightening the control of the distribution channels and stricter law and regulation enforcement would help to restrict the distribution of veterinary drugs to the farms. The distribution of active pharmaceutical ingredients (APIs) for registration purposes do not require product registration. Not only are most of APIs to distribute to pharmaceutical production companies who have import licence and product registration licences, some of them illegal directly leakage to farms that are home to food-producing animals. It is the supply and demand of cheap drugs with APIs and the amount of drugs in the feed that are the persistent problems. In Thailand, ingredients like colistin or amoxicillin premixes are registered in higher concentrations than in Japan or the European Union (EU). Additionally, the farm mixers may not have the capability of mixing these substances well and may not have obtained proper licensing or meet proper monitoring standards set by the relevant authority, which is in contrast with the practices found in the EU (European Commission, 2014). The lack of restrictions on medicated feed
production, the high concentrations of medicated premixes, including the uncontrolled access to antimicrobials without veterinary oversight, all could drive antimicrobial resistance rates even higher in Asia, including in Thailand. These practices contribute to the irrational use of drugs in the feed of food-producing animals in Thailand (Vincent ter, 2017).

There are a number of issues worth mentioning in relation to rational antimicrobial use on farms in Thailand. In general, the adequacy and comprehensiveness of the current legal provision in addressing all the veterinary pharmaceutical regulatory activities cannot be equally enforced in all farms. This survey (as shown in Table 2) found layer and pig farmers employed veterinarians who were responsible for drug prescriptions at only 32.5% and 59.2%, while farmers who tested for sensitivity before choosing antimicrobial drugs for use on layer farms was low (3.2%). Notably, pig farms did not usually employ authorized personnel in the farms and layer and pig farmers did not effectively keep records of their use of veterinary drugs on these farms at levels of 67.5% and 46.4%. This common practice was found on registered farms more than on other farms; however, practice was not often consistent. This study indicated that existing legislation and regulation for enforcing antimicrobial use on farms may not be presently ineffective. Some of the farm owners avoided using irrational antimicrobial usage on farms; however, they did tend to be concerned about the health of their animals and the financial concerns associated with their farms. Additionally, the majority (53.6-73.8%) of the respondents incorrectly believed that economic costs and benefits are the most important reasons for choosing to use antimicrobial drugs. This incorrect perception could be promoting irrational antimicrobial use on farms in Thailand. Even though antimicrobial use is most likely posing a serious risk to human health, antimicrobial treatments continue to be used on livestock due to a lack of better alternatives for the treatment of infections. In order to maintain rational antimicrobial use on farms, intensive legislation and regulation enforcement must be employed. Additionally, financial issues such as financial compensation, bonuses and punishments must be kept in perspective and alternative products that can be substituted for antimicrobial and growth promoters need to be considered as the most effective means of reducing antimicrobial usage in Thailand. This would be in line with the findings of research that has been conducted in Switzerland (Vivianne et al., 2014).

CONCLUSION

The legislation governing human being and veterinary medicine in Thailand is based on the Drug Act B.E. 2510 (1967) and its five amendments. The Thai FDA is responsible for pre-marketing and authorizes relevant officials of the DLD to enforce the relevant drug act related to the post-marketing practices of veterinary drugs/biologics. The existing legislation and regulation are comprehensive enough to cover all areas of pharmaceutical activities to protect the health of the general public and animals in Thailand; however, the enforcement of these rules and regulations is ineffective. Regulations overseeing the veterinary pharmaceuticals at the farm level is not clearly stated and procedures are not systematically recorded in all farms. Some farmers can too
easily access veterinary pharmaceuticals, and veterinarian prescriptions are not needed when antimicrobials are purchased. Additionally, the economic costs and benefits of the farms are considered the most important reason for choosing to use antimicrobial drugs among farmers. Additionally, there is a lack of better alternative products for the treatment of infections. These factors will continue to promote irrational antimicrobial use. This study have discovered issues that could assist policy makers in designing or updating policies and strategies for contributing to the sustainable mitigation of antimicrobial resistance and can help to conserve the therapeutic potential of antimicrobials for future generations of which the major strategic are as follows.

1. Provide clear guidelines and potential strategies. In order to curtail irrational antimicrobial usage, clear guidelines and potential strategies must be provided for antimicrobial use on farms which generated the strategies include
   a) Support development of guidelines and standards on rational use of veterinary drugs to ensure prudent and safe antimicrobial use in livestock.
   b) Support systematically recording of antimicrobials use in all farms.
   c) Advocate the requirement of prescription for veterinary pharmaceuticals, setting monitoring program and follow–up system to ensure the effectiveness and success of these issues.
   d) Raise awareness and educate of farm owners on AMR and its effect, especially on small–scale farms and independent farms.
   e) Raise number of veterinarians and veterinary services in remote areas.
   f) Support implement quality control measures for own medicated feed on farm by using a feed mixer.
   g) Advocate financial policy such as financial compensation, bonuses and punishments, which were considered to be the most effective means of reducing antimicrobial usage on farms.
   h) Foster relevant stakeholders must cooperate to achieve the goal of reducing antimicrobial consumption of Thailand of which follow the Global Action Plan on Antimicrobial Resistance.

2. Enforcement of laws and regulations. Strict enforcement of laws and regulations, effective monitoring, tracking and inspection of drugs along the supply chains must be considered. The strategies of this issue as follows.
   a) Restrict distribution wholesale of drug products directly to farmers or others who are not licensed retail outlets.
   b) Foster monitoring and tracking of APIs distribution in order to protect APIs illegal directly leakage to farms.
   c) Raise inspections and enforcement to control over–prescribed antimicrobials as a consequence of financial incentives that are offered by pharmaceutical companies.
   d) Raise intensive enforcement of legislations and regulations, effective monitoring, tracking and inspection of veterinary pharmaceutical medicines and pharma–vigilance have along the supply chains.
   e) Support promulgated the notification of livestock GAP farms will be compulsory standard, in order to strict enforcement legislation and regulation of antimicrobial use on farm.
3. Support alternative products and scientific approaches for treatment and control. Even though antimicrobial use is most likely posing a serious risk to human health, however antimicrobial treatments continue to be necessary used on livestock. In order to maintain rational antimicrobial use on farms, support of alternative products and scientific approaches for treatment and control such as autogenous vaccinations, natural substances, microbial-derived products; non-nutritive phytochemicals; immune-related products; chemicals, enzymes, and innovative drugs that can be used to substitute for antimicrobial and growth promoters are necessary.

CONFLICT of INTEREST

The authors report that no conflicts of interest exist. The authors alone are responsible for the content and writing of this paper.

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