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Malaysian generic pharmaceutical industries: perspective from healthcare stakeholders

Zhi Yen Wong^a, Mohamed Azmi Hassali^b, Alian A. Alrasheedy^b,
Fahad Saleem^b, Abdul Haniff Mohamad Yahaya^a and
Hisham Aljadhey^c

^aPharmacy Department, Hospital Teluk Intan, Teluk Intan, Perak, ^bDiscipline of Social and Administrative Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia and ^cCollege of Pharmacy, King Saud University, Riyadh, Saudi Arabia

Abstract

Objective The objectives were to document the published literature related to healthcare stakeholders' knowledge, attitudes, views and perceptions towards generic medicines or generic substitution in Malaysia and to suggest recommendations to improve generic medicines utilization in Malaysia according to different healthcare stakeholders' need.

Methods A systematic search of articles published in peer-reviewed journals from January 2001 to November 2013 was performed. The search used 11 electronic databases. The search strategy involved using Boolean operators for combinations of the following keywords: generic AND Malaysia, Malaysia AND pharmaceutical, Malaysia AND Medicine Policy, Malaysia AND Economic Transformation.

Key findings Twelve articles were included in this review. Two studies were conducted with generic manufacturers, one study with medical practitioners, six studies with community pharmacists and three studies with medicine consumers. Generic manufacturers expressed concerns about the generic medicines policy and drug approval system in Malaysia. In addition, medical practitioners, pharmacists and medicine consumers still have misconceptions about safety, quality, efficacy and bioequivalence of generic medicines. Furthermore, despite the availability of some pro-generic policies, there is a lack of implementation of these policies in the country.

Conclusion Different healthcare stakeholders have different concerns and views towards generic medicines as well as different levels of knowledge about them. The existing generic medicines policy and Economic Transformation Program should be implemented as planned. Educational and promotional campaigns should be carried out to improve utilization of generic medicines among all healthcare stakeholders in Malaysia.

Keywords generic medicines; generic pharmaceutical industry; healthcare stakeholders; Malaysia; perspective

Introduction

Globally, healthcare expenditures have increased significantly in the last two decades.^[1,2] Within this context, pharmaceutical costs have been reported as the second main driver for health care cost escalation, after healthcare professionals' wages.^[3] Similar trends have been noticed in the current Malaysian healthcare system. For example, the pharmaceutical expenditure increased from US\$ 1.55 billion in 2010 to reach US\$ 2.11 billion in 2013, representing 36% increase in only a span of 4 years.^[4] Greater use of generic medicines is one of the mechanisms suggested to contain the escalating cost of medicine.^[5–8] and the cost-saving benefit of generic medicine has been confirmed in previous studies.^[8,9]

Despite the Malaysian government's continuous effort to increase the generic utilization rate in Malaysia, the Malaysian prescription market is still dominated by patented drugs, which have a market share of about 60% of prescription sales by value.^[10] Malaysian pharmaceutical stakeholders consist of policymakers, pharmaceutical manufacturers, doctors, pharmacists and consumers. Different stakeholders might have different concerns and views towards generic medicines as well as different levels of knowledge about them. The presence of a strong, local, generic pharmaceutical industry, together with the support from the different healthcare stakeholders, can help to reduce pharmaceutical

Correspondence: Mohamed Azmi Hassali, Discipline of Social and Administrative Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Minden, Penang 11800, Malaysia.
E-mail: azmihassali@usm.my

expenditures. However, no study has yet been conducted to evaluate these different stakeholders' perspectives together. Therefore, the objectives were to document the published literature related to healthcare stakeholders' knowledge, attitudes, views and perceptions towards generic medicines or generic substitution in Malaysia and to suggest recommendations to improve generic medicines utilization in Malaysia according to different healthcare stakeholders' need.

Methods

An extensive literature search was carried out using many electronic databases available at the library of the authors' institution. A systematic search of articles published in peer-reviewed journals between January 2001 and November 2013 was performed. The search used 11 electronic databases and search engines including Google Scholar, ISI Web of Knowledge, Science Direct, SpringerLink, JSTOR, Wiley Online Library, Sage eReference, ProQuest, PubMed, Scopus and EBSCOHost (which includes CINAHL Plus with Full Text, Dentistry & Oral Sciences Source, Health Business Elite, Medline with full text, Psychology, and Behavioral Sciences Collection). The search strategy involved using Boolean operators for combinations of several keywords to identify the relevant articles. To make the search broad and comprehensive and to include as many relevant articles as possible, the stem word 'generic' was used to represent the keywords, i.e. generic medicine(s), generic drug(s), generic medication(s) and generics. For all the 11 electronic databases, the search was conducted using the keywords as follows: generic AND Malaysia, Malaysia AND pharmaceutical, Malaysia AND Medicine Policy, Malaysia AND Economic Transformation. The search was restricted to article titles. Equivalent terms in the thesauri or Medical Subject Heading (MeSH) browsers were used whenever possible. These searches were sup-

plemented by a hand search of the reference lists in the articles identified. In order to determine whether or not the articles met the required criteria, the lists of titles and abstracts from the searches were examined and where doubts remained, the whole paper was examined. Identified articles were arranged according to types of healthcare stakeholders.

In this review, both qualitative and quantitative studies that reported healthcare stakeholders' knowledge, attitudes, views and perceptions towards generic medicines or generic substitution were included. Healthcare stakeholders in this case were government or institution policymakers, doctors, pharmacists, and consumers or patients. Systematic reviews, case studies, commentaries, essays, legal analyses, consensus statements and letters to editors were excluded from the review. Articles reporting clinical trial results for evaluating the efficacy of generics versus branded originator medicines were also excluded from this review. Similarly, articles mentioning bio-similar products were also excluded. Each study was reviewed by the researchers, and disagreement was resolved by consensus.

A total of 455 titles and abstracts were identified by three authors from electronic searches of the 11 databases and search engines, and wherever possible, a review of the reference lists. Of these, 436 titles and abstracts not related to healthcare stakeholders' knowledge, attitudes, views and perceptions towards generic medicines or generic substitution and duplicated citations were examined and excluded. The full text of 19 articles was retrieved and distributed among the authors for further assessment. All authors agreed that 7 of the 19 manuscripts did not assess healthcare stakeholders' perspectives towards generic medicines, but rather looking broadly at pricing and cost issues, general intellectual rights laws, regulatory guidelines and trade agreements were excluded. The QUORUM flow chart for selection in this review is shown in Figure 1.

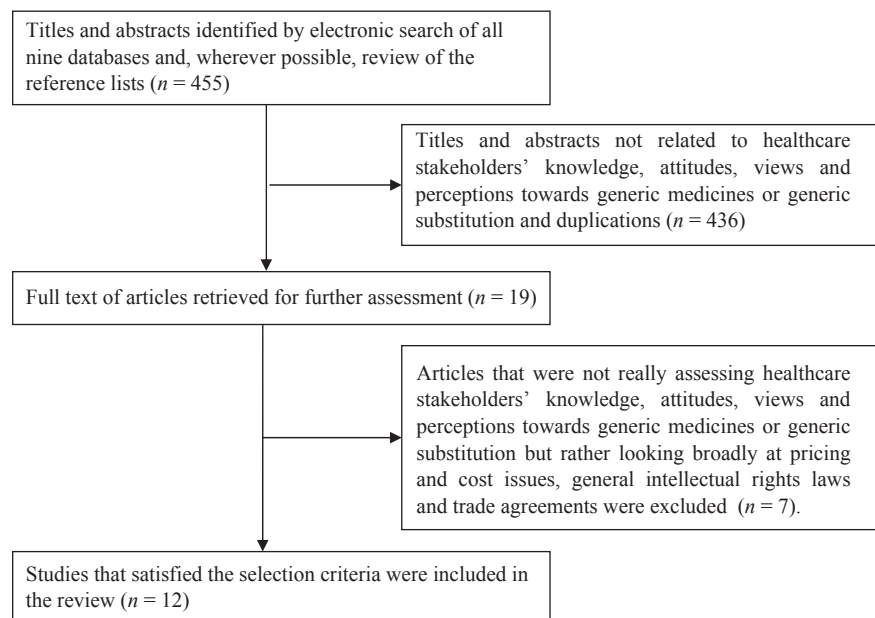


Figure 1 QUORUM flow chart of the review process.

Results

Description of included studies

A summary of studies included in the review investigating healthcare stakeholders' knowledge, attitudes, views and perceptions towards generic medicines or generic substitution is shown in detail in Table 1. The studies discussed in this review article are arranged according to target groups: generic manufacturers, medical practitioners, pharmacists and medicine consumers.

Methodological quality

Each article was reviewed by all the authors and a consensus meeting was convened to ensure quality assurance. The most prominent limitation identified was a lack of generalization of study results, as the studies were restricted to certain geographical areas, governorates or provinces.^[13,16,19,21,22] Five studies suffered from low response rates.^[11–13,15,17–19] Four studies used convenience sampling,^[16,20,22] and two studies were of a small sample size,^[14,16] which might have had an impact on generalization.

Issues or perspective from different healthcare stakeholders

An overview of the issues from different healthcare stakeholders, comments and future recommendation are shown in detail in Table 2.

Discussion

Government/policymakers

Few policies were formulated by the Malaysian government to improve the usage of generic medicines, including the Malaysian generic medicines policy, the Economic Transformation Program (ETP), and their reluctance to agree with the Trans-Pacific Partnership Agreement (TPPA). In 2006, Malaysia adopted a national medicines policy (NMP), which encourages generic manufacturing, generic prescribing, generic dispensing, generic substitution and generic medicine use in Malaysia.^[23] Moreover, one new strategy was introduced in 2012 to give priority to locally manufactured medicines in terms of pharmaceutical procurement.^[24] In the current generic medicines policy, which is part of the NMP 2012, healthy price competition in medicines are encouraged via the following strategies:^[24]

- i. Prescribing by using generic name or International Nonproprietary Name (INN) shall be practiced at all levels
- ii. Promoting the use of generic names or INN in procurement of medicines
- iii. Priority shall be given to locally manufactured medicines in terms of pharmaceutical procurement
- iv. Using the generic names or INN with or without the trade names in labelling for dispensed medicines should be encouraged
- v. Establishment or formation of formulary of interchangeable medicines

- vi. For all interchangeable medicines, generic substitution shall be allowed and encouraged
- vii. Appropriate incentives or allowances should be introduced to encourage the use and manufacturing of generic medicines in Malaysia.

In 2010, the ETP was formulated as part of Malaysia's National Transformation Program to elevate the country to developed-nation status by 2020, targeting a gross national income per capita of US\$ 15 000.^[25] The ETP's targets will be achieved through the implementation of 12 National Key Economic Areas (NKEA), which include the healthcare sector.^[25] The government aims to further grow this sector by increasing local generic manufacturing for exports under a listing of entry point projects (EPP).^[26] A few of the strategies under EPP were to:^[26,27]

- i. Promote Malaysia as a member in the Organisation of the Islamic Cooperation and the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Cooperation Scheme (PIC/S) to widen the export opportunities
- ii. Upgrade the domestic manufacturing plants
- iii. Have good relationships between multinational corporations and domestic manufacturers
- iv. Ministry of Health (MOH) off-take procurement agreement with new local manufactured pharmaceuticals. Under this scheme, the MOH will become the main buyer of the manufacturer's future production for 3 years with the condition that the product must be manufactured in Malaysia. The agreement could be extended for another 2 years if the manufacturer demonstrates that the product can be registered and marketed in other countries
- v. Develop comprehensive national pharmaceutical data

In addition, the Malaysia government's reluctance to agree with the TPPA (which would cause patent periods to be extended for foreign companies' drugs) could cause an increase of generic drug sales in the future. The Malaysian government is reluctant to agree with TPPA due to the strong voices of opposition from non-profit organizations and generic pharmaceutical associations (both local and foreign).^[28–30]

Despite the availability of some pro-generic policies, there is a lack of implementation and enforcement through legislations.^[12,17,21,31] In comparison with developed countries (e.g. USA, Australia) where pro-generic medicine policies and initiatives are in place including generic substitution policy, interchangeable medicines formulary, differential copayment system that encourage patients to accept generic medicines, incentives/profit margin to encourage pharmacists to recommend generic medicines, and extensive educational campaigns targeting both healthcare professionals and patients, the situation in Malaysia is still by far behind these countries.^[32] However, the situation in Malaysia is relatively comparable with south-east Asian countries such as Thailand. Moreover, the situation in Malaysia is relatively comparable with Japan in terms of the challenges related to negative perceptions and misconceptions about safety, quality and efficacy of generic medicines among healthcare professionals and medicine consumers.^[32] Therefore, the Malaysian government is urged to formulate strategies, indicators and

Table 1 A summary of studies included in the review investigating healthcare stakeholders' knowledge, attitudes, views and perceptions towards generic medicines or generic substitution

Author	Study location	Method	Number of participants	Target group	Findings	Limitation
Fatkun et al. (2013) ^[11]	National survey	Mail survey	14	Generic manufacturers	A small portion of the respondents indicated that the regulatory provision (i.e. Bolar provision) is either effective (21.4%) or highly effective (14.3%) in promoting early post-patent entry of generic medicines. Government policies and regulations were perceived to be fairly effective in promoting generic medicines in Malaysia by 42.9% and 35.7% of the respondents respectively. Majority of the respondents were dissatisfied with generic prescribing (64.3%), public awareness of generic medicines (50%), but satisfied with the generic medicine dispensing (57.1%). Uses of the patent clustering by branded innovator companies and market competition from imported generic medicines were two main barriers to post-patent entry of generic medicines in Malaysia. 85.1% of the respondents claimed that they actively prescribed generic medicines.	Inability to obtain response from all potential respondents. Therefore, non-response bias cannot be ruled out with certainty.
Fatkun et al. (2013) ^[12]	National survey	Mail survey	14	Generic manufacturers		Inability to obtain response from all potential respondents. Therefore, non-response bias cannot be ruled out with certainty.
Chua et al. (2010) ^[13]	Penang state	Mail survey	87	General practitioners	Only 4.6% of the respondents correctly identified the regulatory bioequivalence standards for generic products. 33% of the respondents had doubts about the efficacy of generic medicines while only 10.3% thought that generic medicines produced more side effects than their counterpart branded originator medicines. Majority of the physicians (84.4%) and patients (88%) accepted the recommendations made by pharmacists regarding generic substitution.	The low response rate is one of the limitations of the study. Moreover, the study was conducted in one state (State of Penang). Hence, the generalization of the findings to all GPs in Malaysia is not possible.
Ping et al. (2008) ^[14]	Penang state	Questionnaire based study	34	Community pharmacists, physicians and patients		Lack of generalizability of results because of the small sample size and the short study period.
Chong et al. (2011) ^[15]	National survey	Mail survey	157	Community pharmacists, physicians and patients	The pharmacists recommended generic substitution for 84.7% of the branded originator medicines requests. Majority of the physicians (87.9%) and patients (88.9%) accepted the recommendations made by pharmacists regarding generic substitution.	The reasons for pharmacists, physicians and patients to support or oppose generic substitution were not directly assessed. Furthermore, a major limitation of this study is the low response rate as only 157 pharmacists responded and participated in the study, giving a response rate of 11.1%.
Babar and Awaisu (2008) ^[16]	Four states in Malaysia (Penang, Selangor, Negeri Sembilan and Johor)	Interviewer-administered survey	40	Community pharmacists	Approximately 47% of the pharmacists preferred to recommend branded originator medicines over generic medicines and 62% of them did not favour the compulsory generic substitution concept. 85% of the customers accepted pharmacists' recommendations for generic substitutions.	The sample size was low (i.e. pilot study). It was conducted only in four states using a convenience sampling method and involved only 10 community pharmacies in each state. Hence, generalization of results to the entire country is not possible.
Chong et al. (2010) ^[17]	National survey	Mail survey	219	Community pharmacists	Majority of the pharmacists (87.2%) were on favour to generic substitution for most cases and 93.6% of them agreed that pharmacists should be given the generic substitution rights.	Different contribution rate from different regions might lead to over-representation or under-representation of community pharmacists in some areas. Due to lack of national data on demographic and characteristics of community pharmacies, it is not possible to determine whether the sample was representative of Malaysian community pharmacists. Moreover, low response rate is a major limitation of this study. Therefore, generalization of results is limited. However, the study could provide valuable baseline data.

Chong et al. (2011) ^[18]	National survey	Mail survey	219	Community pharmacists	<p>21.4% of respondents perceived generic medicines as inferior in quality compared to branded originator medicines and approximately 56% of them agreed that therapeutic failure is a serious problem with some generic medicines.</p> <p>75.8% of the pharmacists considered generic substitution of narrow therapeutic index drugs inappropriate.</p> <p>5.5% of the respondents agreed that generic medicines produce more side effects than brand original products whereas 30.6% of them hold neutral view.</p> <p>Pharmacists surveyed had difficulty in ascertaining bioequivalent status of generic products in Malaysia.</p> <p>37.5% and 58.4% of the respondents agreed that locally manufactured generic medicines were equal to imported generic products in terms of quality and safety and efficacy respectively.</p>	<p>The low response rate may cause non-response bias as non-respondents might be different, particularly as those who responded might have a more positive attitude.</p> <p>The data was not normally distributed and hence the use of more powerful statistical techniques to detect the differences between pharmacist groups was not possible.</p>
Hassali et al. (2012) ^[19]	Penang state	Mail survey	48	Community pharmacists	<p>Only 28.3% of the respondents were familiar with the term 'generic medicines'.</p> <p>Only 43.9% of the respondents claimed that they purchased generic medicines in the past.</p> <p>Some of the respondents perceived generic medicines as inferior to branded originator medicines in terms of quality (38.9%) and effectiveness (34.8%)</p>	<p>Low response rate and hence the risk of non-response bias, as those who responded might have a more positive attitude.</p> <p>The survey was conducted in only one state (i.e. Penang state). Thus, the results cannot be generalized to the whole country.</p> <p>The convenience sampling technique influence generalization of results.</p> <p>The study was conducted in one state. Hence, results cannot be generalized to the whole country.</p>
Al-Gedadi et al. (2008) ^[20]	Penang state	Questionnaire based study	400	Consumers	<p>67.5% of the respondents did not know what generic medicines were.</p> <p>42% of them claimed that they had used generic medicines in the past.</p> <p>Lack of efficacy (27%), safety (27%) and quality (25%) were the main reasons for not using generic medicines.</p>	<p>The study was conducted only in two states in Malaysia. Therefore, it is not possible to generalize the results to other parts of the country.</p> <p>In addition, the study was conducted in urban areas, rural communities were not represented.</p> <p>The participation rate was not calculated and those who refused to take part might have different views.</p> <p>Many participants did not obtain prescription medicines from the pharmacy, hence they might have less experience with generic medicines.</p> <p>The study used a convenience sampling technique that limits the generalization of the results. Also, the study was conducted in one region.</p> <p>The study design was cross-sectional. Hence, the changeover time in the behaviour towards generic medicines cannot be assessed.</p>
Thomas and Vitry (2009) ^[21]	Kuala Lumpur and Selangor state	Interviewer- administered- survey	203	Consumers		
Abzakh et al. (2013) ^[22]	Klang Valley	Questionnaire based survey	456	Consumers	<p>Only two out of six variables (i.e. performance risk-technology and physical risk) were in positive relationship with consumer resistance towards generic medicines.</p>	

Table 2 Overview of issues from different healthcare stakeholders, comments and future recommendations

Stake holders	Issues	Comments	Recommendation
Government or Policy maker Generic Manufacturers	<ul style="list-style-type: none"> • Implementation and support of the use of generic medicines in the country • Expressed ambiguous perceptions about the effectiveness of Malaysian government policies and regulations in promoting generic medicine • Expressed an unclear view of regulatory exception provision (i.e. Bolar provision) in which development of generic medicines was allowed before the branded originator product's patent expired • Dissatisfied with level of generic medicine prescribing • Patent clustering by branded innovator companies • Earlier entry of imported generic medicines 	<ul style="list-style-type: none"> • Few strategies were formulated: <ol style="list-style-type: none"> a) Malaysian generic medicine policy b) Economic Transformation Program c) Reluctance of Malaysia government to agree with the Trans-Pacific Partnership Agreement (TPPA) • There is a lack of implementation and enforcement through legislations. • General practitioners claimed they actively prescribe generic medicines. However, the study was conducted in only one state (Penang state) and was based on practitioners' self reporting. • No existing data for generic medicines prescribing. • Reluctance of Malaysia government to agree with the TPPA • Due to trade policy initiatives and the difficulty of local generic medicine manufacturers in conducting bioequivalence (BE) studies. • Inadequate number local BE centres available in Malaysia. 	<ul style="list-style-type: none"> • Malaysia government is urged to formulate strategies, indicators and targets to monitor the stage of policy implementation. • Frequent review of these policies will be a good option so that the policies' weaknesses can be identified and be further improved. • Appropriate implementation of the formulated policies in national medicines policy and Economic Transformation Program • National data on generic medicine prescribing should be collected.
Medical practitioners	<ul style="list-style-type: none"> • Low level of knowledge of the basis of BE testing. • Misconceptions about safety, quality and efficacy of generic medicines 	<ul style="list-style-type: none"> • Resulted in misconceptions about generic medicines. • Lack of awareness regarding the BE standard set by Malaysia Drug Control Authority (MDCA). • Only one study was conducted in Malaysia assessing general practitioners' views on generic medicines. • Medical practitioners practiced in public hospitals and clinics might have different views on generic medicines 	<ul style="list-style-type: none"> • The number of local BE centres needs to be increased. • A discounted price to conduct BE studies should be given to local generic manufacturers • Tax exemption and various incentives should be given to local generic manufacturers. • The concept of BE, the basics in pharmacodynamic and pharmacokinetic principles and facts of generic medicines should be incorporated into current medical curricula. • Educational efforts to promote MDCA and National Pharmaceutical Control Bureau (NPCB) responsibilities and the approval system of medicines. • Use of emails, official newsletter, mass media and social website • Formation of discussion group involving different healthcare stakeholders • Need of nationwide study to assess perspectives of medical practitioners.
Pharmacists	<ul style="list-style-type: none"> • Expressed doubts about the quality, safety and efficacy of locally manufactured generic medicines. • Lack of confidence in Malaysia's generic approval system • Mixed results were obtained for generic substitution rate 	<ul style="list-style-type: none"> • Both imported and locally manufactured generic medicines have to comply with same quality control standards and requirements set by MDCA. • Possible difference in these findings might be due to nature of the studies. • Pharmacist working in rural and urban might have different views towards generic medicines • Consumers in urban area are more knowledgeable and can afford to buy brand original products • These studies were conducted in year 2007 and pharmacists' view might have changed. • Quality of pharmaceutical products manufactured in Malaysia was of high quality and internationally recognized • It is important to be implemented via a holistic approach that considers different aspects. 	<ul style="list-style-type: none"> • Education effort to increase pharmacists' awareness towards the generic approval system in Malaysia. • Views and perspectives from pharmacists working in public hospitals and in clinics are yet to be explored.
Consumers	<ul style="list-style-type: none"> • Misconceptions about safety, quality, efficacy and BE of generic medicines • Supporting implementation of generic substitution policy. • Lack of knowledge about generic medicine • Expressed concerns about safety, efficacy and quality of generic medicines 	<ul style="list-style-type: none"> • Education interventions are needed. • It is essential have a guide on therapeutically interchangeable drug products to help healthcare professionals to perform generic substitution appropriately • Need of nationwide study • Coverage of consumers in both public and private sectors, and rural and urban areas. • Continuous media campaigns on television, radio, use of social media and the internet should be used to educate patients or consumers about generic medicines. • Reassurance of quality, safety and efficacy of generics by healthcare professionals is needed 	

targets to monitor the stage of policy implementation. Frequent review of these policies will be a good option so that the policies' weaknesses can be identified and be further improved.

Generic manufacturers

The public will not enjoy the cost-saving benefit of generic medicines without the availability of generic medicines in the domestic market. In fact, low availability of generic medicines in the market will cause a direct economic implication to patients, as patients will have to dig deep into their pockets to pay for branded originator medicines.^[33] Therefore, the role of generic manufacturers is essential in this regard. However, in a recent study, Fatokun *et al.* reported that generic manufacturers expressed ambiguous perceptions about the effectiveness of the Malaysian government's policies and regulations in promoting generic medicine.^[12] In addition, they expressed an unclear view of the Malaysia regulatory exception provision (i.e. Bolar provision) in which development of generic medicines was allowed before the branded originator product's patent expired.^[12] Therefore, these concerns held by generic manufacturers need to be considered and addressed via appropriate implementation of the formulated policies in NMP and ETP.

Besides that, the members of the Malaysian generic industry who were surveyed were satisfied with the generic medicine dispensing rate. However, they were dissatisfied with the level of generic medicine prescribing, the generic education given to healthcare professionals, and public awareness of generic medicines.^[12] However, in a study conducted by Chua *et al.*, most of the surveyed medical practitioners (85.1%) claimed that they actively prescribed generic medicines in their practices.^[13] However, the study was conducted in only one state (Penang state) and was based on practitioners' self reporting.^[13] In fact, there were no existing data available for the national generic medicine prescribing rate in Malaysia. Therefore, official data on nationwide generic medicine prescribing, including both public and private sectors, should be collected. The data collected will serve as an indicator to monitor the impact of government's ongoing effort in promoting generic medicine prescribing.

According to the Malaysian Organization of Pharmaceutical Industries (MOPI), local manufacturers are capable of producing 80% of the medicines in the Malaysian National Essential Drugs List (NEDL).^[34] In fact, Malaysia's generic market share has continued to grow over the years. In 2011, generic drug sales consisted of 41.5% of total prescription sales by value, with an increment of 4.7% over a period of 2 years.^[10] Hence, the role of local generic manufacturers is increasingly important in maintaining the affordability and availability of prescription medicines in Malaysia.

A nationwide study conducted in 2010 reported that branded innovator companies' uses of patent clustering (i.e. acquisition of multiple patents surrounding the basic patents of the drug products) and market competition from imported generics were the two of the main barriers to local production of generic medicines in Malaysia.^[11] By identifying these barriers, the government can help to formulate strategies to facilitate the entry of generic medicines into Malaysia market. The Malaysia government's recent reluctance to agree with the

TPPA was a good move to combat the patent extension by branded originator companies.^[10] Earlier entry of imported generic medicines into the Malaysia drug market was due to trade policy initiatives and the difficulty of local generic drug manufacturers in conducting bioequivalence (BE) studies.^[11] Limited number of BE centres in Malaysia had cause difficulty for the local generic drug manufacturers to conduct BE studies, and the BE centres are mostly university based and non-profit orientated.^[31] In fact, as of 10 December 2013, there are only five local centres that are listed in the National Pharmaceutical Control Bureau (NPCB), in the Ministry of Health Malaysia Compliance Program for Bioequivalence Centre.^[35] Therefore, the number of local BE centres needs to be increased to cater the local generic drug manufacturers' demand as the current number of BE centres are inadequate.^[31] In addition, in order to boost the production of generic medicines by local manufacturers, a few further recommendations were made. First, a discounted price to conduct BE studies should be given to local generic manufacturers. Second, tax exemption and various incentives should be given to local generic manufacturers.

Medical practitioners

In Malaysia, dispensing of prescription medicines still follows a traditional 'dispensing doctors' system in which medical practitioners still dispense medicines as a part of their professional practice.^[36] This is because the 1952 Poison Act in Malaysia granted the right for registered medical practitioners to prescribe and dispense medicines in their clinics.^[37] Hence, the influence of medical practitioners on selecting either generic or branded originator medicines for patients cannot be ignored. In fact, medical practitioners' influence on consumers' acceptance of generics medicine has been confirmed by previous studies.^[38-41]

In a local study conducted by Chua *et al.*, most of the general practitioners (GPs) surveyed (85.1%) claimed that they actively prescribed generic medicines in their practices.^[13] However, the GPs surveyed had a low level of knowledge of the basis of BE testing. Moreover, they had misconceptions about safety, quality and efficacy of generic medicine among the GPs.^[13] Therefore, the concept of BE, the basics in pharmacodynamic and pharmacokinetic principles and facts of generic medicines should be incorporated into current medical curricula so that medical graduates will easily accept generic medicines. Additional efforts will be needed to change the prescribing habits of doctors from the older generation.^[42]

In fact, the Malaysia Drug Control Authority (MDCA) at its 92nd meeting in 1999 decided to include BE studies requirements for the registration of generic products of certain categories of oral, immediate-release products due to the increasing number of generic products in the market and the increasing complaints regarding the products' efficacy.^[43] BE is required if a product is intended to be substituted for an approved medicinal product, and only drugs that are intended for systemic use will require BE testing.^[44] The MDCA has adopted the basic principle outlined by the European Medicines Agency with some adaptations to suit local requirements including Biopharmaceutics Classification system (BCS) in which bioavailability and BE studies can be waived if the

product is categorized under BCS Class I (i.e. high solubility and high permeability).^[45] In Malaysia, as in most countries, the accepted criteria to demonstrate BE is when the 90% confidence intervals for the logarithmically transformed C_{max} ratio and AUC ratio (generic: branded innovator products) fall within the range of 80% to 125%.^[44,46] The C_{max} in this case refers to maximum plasma drug concentrations and AUC is the area under the plasma-drug concentration versus time curves. Despite this tight regulatory limit, the GPs surveyed still expressed reservations about generic medicines' safety and efficacy. This might be due to doctors' lack of awareness regarding the BE standard set by MDCA. This is confirmed by the studies that reported that only 4-6% of the respondents correctly identified the BE standard for generic products.^[13] This misconception, if not corrected, could have a negative impact on medical practitioners' confidence in generics and then subsequently affect the country's generic prescribing rate. First, more educational efforts should be carried out to promote MDCA and the National Pharmaceutical Control Bureau's (NPCB) responsibilities besides increasing prescribers' awareness towards the regulatory limit of generic medicines. Use of emails, official newsletters, mass media, and social media can ease the transfer of this information to medical practitioners. In addition, discussion groups involving doctors, pharmacists, policy makers, and manufacturers can be set up by the government in order to facilitate a mutual exchange of information between the different healthcare stakeholders.^[47] Insights and the perceptions of different healthcare stakeholders can be explored further, and strategies can be formulated to tackle the barriers identified. Additionally, only one study that was conducted in Malaysia assessed GPs' views on generic medicine. Medical practitioners who practice in public hospitals and clinics might have different views on generic medicines from those who practice in the private sector since most medications dispensed in the government sector are generic.^[21] Hence, a nationwide study covering doctors practicing in the private and in the public sector should be carried out in the future.

Pharmacists

Despite traditional dispensing roles, the pharmacist profession has transformed into a profession that involves in patients' medication reviews and health promotion campaigns and that provides drug information and pharmaceutical care to patients.^[48] In the context of generic medicines, pharmacists play an important role. The pharmacists are responsible for education given to healthcare professionals about generic medicines and for patient education to avoid potential brand confusion resulting from generic substitution, providing reassurance about the safety, quality, and efficacy of generics, and selecting bioequivalent generic medicines for substitution.^[49-51] Hence, pharmacists' opinions and knowledge about generic medicines are important in both medicine consumers' and medical practitioners' acceptance of generic medicines.

A local study conducted by Hassali *et al.* reported that some of the pharmacists expressed doubt about the quality, safety, and efficacy of locally manufactured generic medi-

cines compared to imported generic medicines manufactured by international companies.^[19] This implies a lack of confidence in Malaysia's generic approval system among the surveyed pharmacists. In fact, both imported and locally manufactured generic medicines have to comply with the same quality control standards and requirements set by MDCA. In terms of quality, both parties have to follow good manufacturing practice (GMP) requirements, guidelines for pharmaceutical development, product testing (i.e. both compendial and non-compendial testing), and the content of the common technical documents for regulatory submission has been adopted from competent, regulatory agencies in the European Union, the USA, and the International Conference on Harmonization (ICH).^[31,44] In terms of BE, both local and international generic manufacturers must provide evidence of BE.^[44] MDCA and NPCB are again urged to carry out more promotional campaigns to increase other healthcare stakeholders' awareness towards the generic approval system in Malaysia.

In terms of the generic substitution rate, mixed results were obtained. A study conducted by Babar *et al.* reported that 47% of community pharmacists prefer to recommend branded originator medicines over generic medicines.^[16] In contrast, a study by Chong *et al.* found that community pharmacists recommended generic substitution for 84.7% of the branded originator medicines requests.^[15] A possible reason for the difference in these findings might be the nature of the studies. The study by Babar *et al.*^[16] was conducted in only four states (i.e. Penang, Selangor, Negeri Sembilan, and Johor) whereas the study by Chong *et al.*^[15] was nationwide. Hence, the results from Babar *et al.* study might be limited. However, the Chong *et al.* study also suffered from a low response rate (11.1%) which can cause non-response bias as non-respondents might be different, particularly those who responded might have a more positive attitude and practiced proactive generic substitution.^[15] In addition, pharmacists in rural and urban areas might have different views towards generic medicines. Pharmacists in urban area might recommend generic substitution more frequently as patients or consumers in urban areas are usually more knowledgeable. Knowledge of generic medicine was found to be positively correlated with their acceptance of generic medicine.^[52] However, different trends may be seen for pharmacists in urban area as consumers in urban areas can better afford to buy branded originator medicines compared to those in rural areas. Hence, the generic substitution rate might be lower in urban areas. Hence, a nationwide study is recommended to explore pharmacists' view from both urban and rural area towards generic medicine. Also, these studies were conducted in 2007, and pharmacists' view might have changed after 6 years because the Malaysia National Medicine Policy was published in 2007,^[23] and various strategies were formulated in the policy to improve generic utilization in Malaysia. As Babar *et al.*'s and Chong *et al.*'s studies focused on community pharmacists,^[15,16] views and perspectives from pharmacists working in public hospitals and in clinics are yet to be explored. Their perceptions and knowledge might be different from community pharmacists because, as noted earlier, most medicines dispensed in the government sector are generic medicines.^[21]

Acceptance of pharmacists' recommendation of generic substitution by patients and medical practitioners^[14–16] is an important facilitator to the successful implementation of the generic medicines policy in Malaysia.^[32] However, misconceptions held by pharmacists about safety, quality, efficacy and BE of generic medicines can be a barrier to wide use of generic medicines.^[18] Therefore, educational interventions are needed to correct the misconceptions among pharmacists. In fact, Malaysian-manufactured pharmaceutical products are of a high quality and internationally recognized. This can be seen through Malaysia's participation as a member of the Pharmaceutical Inspection Cooperation Scheme (PIC/S) since 2002.^[53] PIC/S is an international instrument between countries and pharmaceutical inspection authorities, which together provide an active and constructive cooperation in the field of GMP.^[54] Pharmaceutical products from members of PIC/S are of high quality because PIC/S ensures that all members comply with PIC/S standards at all times (i.e. assessment of new applicants and reassessment of existing member inspectorates).^[55]

Regarding pharmacists' view on a future generic substitution policy, the majority of the surveyed pharmacists were in favor of generic substitution,^[17] but they mentioned that in certain cases, generic substitutions were inappropriate, such as, for narrow therapeutic index (NTI) drugs.^[18] However, they did not favor the compulsory generic substitution concept.^[16] In fact, to implement generic substitution and generic prescribing successfully, it is important to be implemented via a holistic approach that considers different aspects. For example, agreement, cooperation and communication between pharmacists and medical practitioners are important for the successful substitution. Moreover, physicians should be able to disallow generic substitution for the cases in which generic substitution is not appropriate. Moreover, patients should be given the opportunity to make an informed choice to consume either branded original medicines or generic medicines. Moreover, it is essential to have a guide on therapeutically interchangeable drug products to help healthcare professionals to perform generic substitution appropriately and to avoid any pitfalls or errors that may arise from inappropriate generic substitution.^[32] The British National Formulary (BNF) in the United Kingdom (UK), the Schedule of Pharmaceutical Benefit Scheme (PBS) in Australia and the lists of interchangeable products in Finland and Sweden are examples of such references.^[56]

Patients/consumers

Consumers are the end users of the medicines and have the ultimate choice to decide to consume either branded originators or generic medicines. Hence, their perceptions and knowledge about generic medicine will have a great influence on their acceptance of generic medicines.^[57] Most of the consumers in Malaysia did not know what generic medicines were.^[20,21] Many of the consumers expressed concern about the safety, efficacy, and quality of generic medicines.^[20,21] In addition, only approximately 40% of the consumers surveyed had used generic medicines in the past.^[20,21] However, these studies were conducted in 2007 and people's views and knowledge might have changed especially in the recent few years because of the various strategies that were formulated in

the generic medicines policy in 2007 to improve acceptance of generics among consumers in Malaysia. Moreover, rural consumers' knowledge was neglected in both of these studies.^[20,21] A recent publication by Abzakh *et al.* was conducted to investigate the dimension of perceived risk and consumer resistance towards generic medicine in Malaysia.^[22] Two main barriers were identified. The first one was worry about the efficacy of generic medicines (Performance risk-technology). The second barrier was time risk because consumers expressed concern that they were wasting time by searching and buying to discover a safe and correct way to consume the product, and to possibly change the product in case of poor performance or the product's inability to perform as expected.^[22,58] The time factor is an interesting barrier that needs to be further explored. Thus, based on the analysis of the current literature, a nationwide study covering consumers in both public and private sectors, and rural and urban areas needs to be conducted to reassess and evaluate the current level of knowledge and awareness of medicine consumers about generic medicines. In addition, media campaigns on television, radio, through social media, and through the Internet should be used to educate consumers about generic medicines. However, the educational effects last for only a short period of time,^[59] so continuous effort should be carried out in a systematic manner to ensure that patients are well educated about generic medicines.^[60] More importantly, patients' reassurance of quality, safety, and efficacy of generic medicines by healthcare professionals is needed. In fact, medical practitioners and pharmacists are in the best position to educate patients as most patients and consumers in Malaysia have a high trust in recommendations by their pharmacists and medical practitioners.^[14–16,20]

Limitations

The review has a number of limitations. Although the literature search was comprehensive and carried out using several electronic databases and search engines, all studies relevant to the topic might not have been retrieved. Moreover, the review focused on the recent literature, i.e. from 2001 and onwards. However, this is justified because older studies might not be relevant to current practices. Perceptions and views do change over time, and a large number of generic medicines have been marketed in the last two decades.^[57] Moreover, the policies and promotion programmes have been introduced recently, which might have an effect on healthcare stakeholders' perceptions and views. Also, information technology and easy access to information about generic medicines (e.g. via the Internet) has become more common in recent years. Thus, including the recent literature makes this review more contemporary and more relevant to today's practice.^[57]

Conclusion

The present literature review revealed that lack of awareness about the regulatory approval system of generic medicines. Moreover, negative perceptions about safety, quality, and efficacy of generic medicines still persist among different healthcare stakeholders in Malaysia. Furthermore, there was a gap between policy formulation and its implementation in Malaysia. Hence, the existing generic medicines policy and

ETP should be implemented as planned. Educational and promotional campaigns more should be carried out to promote utilization of generic medicines among all healthcare stakeholders in Malaysia.

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