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Advancing pharmaceuticals and patient safety in Saudi Arabia: A 2030 vision initiative

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ABSTRACT

Low-quality medicines deliver sub-optimal clinical outcomes and waste precious health resources. It is important to ensure that public funds are spent on healthcare technologies that meet national regulatory bodies such as the Saudi Food and Drug Authority (SFDA), quality standards for safety, efficacy, and quality. Medicines quality is a complicated combination of pre-market regulatory specifications, appropriate sourcing of ingredients (active pharmaceutical ingredient (API), excipients, etc.), manufacturing processes, healthcare ecosystem communications, and regular and robust pharmacovigilance practices. A recent conference in Riyadh, sponsored by King Saud University, sought to discuss these issues and develop specific policy recommendations for the Saudi 2030 Vision plan. This and other efforts will require more and more creative educational programs for physicians, pharmacists, hospitals, and patients, and, most importantly evolving regulations on quality standards and oversight by Saudi health authorities.

1. Background

The increasing prevalence of low-quality medicines has become a global public health issue because of the dangerous therapeutic consequences associated with their use (Ten Ham, 2003). Low-quality medicines are either counterfeit or substandard products. The risks are high and global. Common examples are the growing number of counterfeit and substandard essential medicines such as antimicrobials (Kyriacos et al., 2008; Wondemagegnehu, 2011). That are expired, degraded because of improper storage or distribution. This unfortunate reality makes evolving quality guidelines and inspection protocols more urgent than ever. For example, new guidelines for industrial sampling have been developed to assess the quality of pharmaceutical products via inspection of random samples. However, since only small samples can be collected, the true prevalence of the low-quality medicines usually fails to be adequately determined (Reinke, 1991; Newton et al., 2009).

Substandard medicines also include drugs that are registered in a single country and approved by a local regulatory authority. However, these drugs often lack recognized levels of quality specification and often lack evidence of clinical safety and efficacy. Not surprisingly, many fail to provide the expected clinical outcome in patients. Several published articles have demonstrated poor patient outcomes when for instance cancer patients and patients on anti-psychotropic medications were switched from innovator drug to copy drugs which turned out to be of substandard quality or has decreased tolerability requiring close monitoring

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throughout brand-generic or generic-generic transition (Andermann et al., 2007; Desmarais et al., 2011).

According to Johnston and Holt in the British Journal of Clinical Pharmacology, "any formulation of a medication may be regarded as substandard if it has either too much or too little of the API compared with the formulation specifications (Johnston and Holt, 2014). Official national pharmacopoeias, such as the British Pharmacopoeia (BP) and United States Pharmacopeia (USP), publish the quality standards for medicinal substances and preparations manufactured or sold in the country". The information given specifies the acceptable limits for the amount of the API that should be present in a given formulation. However, many examples from a range of drug classes have been published of over/under-concentration of APIs in marketed drugs (Medina et al., 2016).

Inappropriate packaging can affect formulation content in certain storage conditions. For example, a study of generic versions of the antihypertensive medicine ramipril tablets found that, on initial inspection, quarter the sample inspected did not meet the label specifications for drug content. After three months of storage in temperature and relative humid-stressed conditions, further samples failed to meet the content specifications (Johnston and Holt, 2014; Medina et al., 2016). In other cases, a product may contain no API or the drug content may be completely different to that stated on the label. This may occur through deliberate falsification, but as the examples below demonstrate, accidental mislabeling which may also occur:

- One batch of the antibiotic (rifampicin) was mislabelled and bottles contained clonazepam (Health Canada, 2009).
- One lot of minocycline was mislabelled as amlodipine (Canada, 2013).
- One lot of finasteride was labelled as containing citalopram (Food and Drug Administration, 2011).
- Zopiclone was substituted for furosemide in a possible packaging mix-up (L'Agence nationale de sécurité du médicament et des produits de santé, 2017).

Moreover, Johnston and Holt has summarized that "in many other cases, contamination has clearly occurred due to poor manufacturing and/or quality-control processes, or unsuitable packaging. Contaminants have included the following: particulate matter in injectable cefotaxime; small glass particles in bottles of generic atorvastatin; tablet degradation products in docetaxel, streptokinase and clopidogrel; and potentially genotoxic impurities in batches of nelfinavir due to incomplete removal of ethanol following the cleaning of manufacturing equipment (Johnston and Holt, 2014). In addition to the official recall notices and studies published in peer-reviewed journals, there are numerous examples in the press of contamination in marketed drugs, such as the incidents described below" (Johnston and Holt, 2014).

- Paclitaxel formulation produced in India was found to contain excessive endotoxin levels and was withdrawn from the market (Herald, 2009).
- Batches of Tylenol, Motrin, Rolaids and Benadryl were recalled in the USA due to the presence of 2,4,6-tribromoanisole (Kavilanz, 2010).
- Generic formulations of clopidogrel marketed in India and Europe were found to contain methyl chloride, which can cause hepatic, renal and nervous system damage (Zoler, 2010).
- Methyldopa tablets produced in Cyprus were banned by the Tanzania Food and Drugs Authority as it was found that drug identification labels could be detached easily from the packaging, and there was 'vivid fungal growth' on the tablets (Ernest, 2011).

National regulatory bodies in Saudi Arabia such as the (SFDA) are responsible for assuring the safety, efficacy, and quality of food, drugs and medical devices for human and veterinary use. There is limited data on the size of medications quality in Saudi Arabia and the size of such problem. The list of essential medicines from the World Health Organization (WHO) is also considered essential in primary health care in Saudi Arabia. Yet, unfortunately, many medications from this list are among the most widely substandard and counterfeited (Caudron et al., 2008). For example, one study conducted in Saudi Arabia showed that amoxicillin has already been identified as substandard (Bin Abdulhak et al., 2011). Consequently, one of the central aims of advancing pharmaceuticals and patient care in Saudi Arabia is the "safe use" of quality medications (Comission, 2012).

One initiative of the Saudi 2030 vision plan should be to advance patient care through a more robust, safety/quality-centered culture together with a more collegial relationship between local and international drug manufacturers and Saudi regulatory authorities. Such an enhanced working relationship would result in a higher quality care to the public (Saudi, 2030). This concept of aggressive attention to better patient care through greater attention to quality and safety is only now emerging in developed and less developed countries.

2. Aim and Objectives of the scientific Meeting and workshop

To discuss regulatory science concepts related to advancing both the quality of medications and patient care in Saudi Arabia.

- Understand the complexity of the topic of drug quality and its importance relative to patient outcomes and as part of overall clinical practice
- Gain knowledge related to the many different aspects of quality, from drug manufacturing through registration, and improving both patient outcomes and pharmacovigilance reporting.

3. Methods

In November 2016, international experts in healthcare innovation and regulatory science joined Saudi academics and government representatives in Riyadh for a two-day conference, "Advancing Quality of Medications and Advancing Patient Care." Participants included representatives from government, academia and drug companies. Expert speakers shared their ideas with the audience with interactive discussions after each presentation and were recorded. Recommendations to advance the quality of healthcare and improve patient safety are summarized in the result section.

4. Results and discussion

Over two days, 30 experts from Riyadh region attended and enriched the discussion (Table 1).

Table 1
Baseline information of attendees (n = 30).

Characteristics	N, (%)
Gender	
Male	20 (66.7)
Area of experience[*]	
Academics	20 (66.7)
Regulators	2 (6.7)
Health Care Practitioners	13 (43.3)
Research centers	3 (10.0%)

[*] Total does not equal 100%.

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