WHITE PAPER

Limiting the Costs – the Multifarious Effects of Falsified and Substandard Medicines

Tackling the Global Problem of Substandard and Falsified Medicines

Introduction

There are ongoing global efforts to combat the dissemination of falsified and substandard medicines, which can pose a significant threat to public health and the product brand. Falsified medicines are those that have been deliberately and fraudulently tampered with and should be distinguished from substandard medicines, which are made legitimately but fail to meet either their quality standards or specifications, or both.

The WHO has estimated the cost to procure substandard and falsified medicines to be in the order of US$30.5 billion,[1] highlighting the urgent need to address this problem. "There is a huge economic cost to industry due to falsified and substandard medicines," confirmed Dr. Mansoor Amiji, University Distinguished Professor, Professor of Pharmaceutical Sciences and Professor of Chemical Engineering at Northeastern University (Boston., MA, U.S.A.). "However, the more important cost is the lives of those affected by these drugs." This is a concern that has recently come to light in the context of COVID-19, where vaccines and treatments are appearing on the market that have failed to meet the required quality standards.

Mansoor M. Amiji, PhD
University Distinguished Professor, Professor of Pharmaceutical Sciences and Professor of Chemical Engineering; Director, Laboratory of Biomaterials and Advanced Nano-Delivery Systems (BANDS) Northeastern University, Boston, MA, USA.

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Ensuring Quality Along the Supply Chain

Countering the problem of substandard medicines and adequately authenticating the end product presents numerous challenges for the regulators. "You have to consider the entire manufacturing chain to identify which potential places in the product development could be affected," said Dr. Amiji. "Anywhere along the pipeline can be impacted – everything from raw material quality to the manufacturing and distribution of the finished goods needs to be assessed. If you take the example of COVID-19 vaccines, the Pfizer vaccine requires a cold chain to be distributed. If the cold chain is not utilized, you are now dealing with a product in the clinic that is substandard because the requirements have not been followed."

One process that plays a key role in averting the production of substandard medicines is the current good manufacturing practice (GMP or cGMP), which is a system for ensuring that products are consistently produced and controlled according to quality standards. "The FDA, EMA, and other regulatory bodies have formulated requirements for GMP that have to be met when developing products for human use," said Dr. Amiji. "These guidelines cover the whole spectrum of production; for example, how raw ingredients are stored, whether vendors are legitimate, and the potential for contamination. Further along the continuum you need to consider storage of the finished product, as well as shipment and distribution. It is a complete cycle that runs from the start of the process to the product's expiry."

The Cost of Poor Quality

The effect of substandard medicines is not only monetary; there are additional reputational costs for companies to consider. "If a company produces a substandard product then people may have the assumption that every product produced by this company is going to be poor, and then consumer trust is lost," explained Dr. Amiji.

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The fake injectable contained cornstarch, acetone, and other chemicals, but no cancer-fighting ingredients. "In cases like this, where cornstarch was substituted for the actual therapy, the product will not provide the efficacy expected and maybe harmful," he said. "The people developing these products are not conducting quality control tests; they are there to make money out of vulnerable individuals."
In contrast, the driving force behind intentional falsification of medicines is the potential lucrative nature of the business. Dr. Amiji noted that falsified medicines aren't just a problem for developing nations, where the intentional distribution of falsified antibiotics and malaria therapeutics is widespread. "The extent of the problem is far-reaching and is being felt across the globe," he said. For example, in early 2012, the FDA warned 20 U.S. medical practices that they may have obtained counterfeit versions of Avastin, an injectable biopharmaceutical developed by Genentech to treat metastatic cancers.

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A more pressing concern relates to products that are dangerous to the consumer. A well-known example of this occurred in 1982 in Chicago, where a series of poisoning deaths resulted from drug tampering. The victims had all taken Tylenol-branded acetaminophen capsules that had been intentionally laced with potassium cyanide. "Almost overnight, Johnson & Johnson's subsidiary McNeil Pharmaceuticals, issued a nationwide recall of Tylenol products and subsequently eliminated the capsule formulation of Tylenol, instead developing a caplet that could not be tampered with," said Dr. Amiji. Johnson & Johnson's handling of the crisis was widely praised by the public and described as an 'exemplary public relations response'. "It was very rapid, very forceful, and it was certainly an effective way to mitigate the problem," noted Dr. Amiji, adding that it becomes problematic when companies do not react at such speed, or point the finger at someone else. "With substandard or falsified medicines there can be a lot of finger pointing, especially directed towards some of the African countries, India, or China. But this is no longer a third-world problem; it is a universal problem that affects everyone."

It should also be noted that falsification of biologics and genetic medicines also occurs, despite their complexity. "When it comes to intentionally creating these products the counterfeiters are not trying to develop anything complex, just something that looks like the final product," explained Dr. Amiji. "This might be as simple as a clear liquid in a vial, which the consumer won't be able to identify as a falsified product."

Authentication Measures

To protect against falsified and substandard medicines, various measures have been put in place by the regulatory agencies and drug companies to limit the potential risks. "The FDA website alerts consumers and patients on falsified and substandard medicines, and they are especially active right now around COVID-19 products – vaccines, therapeutics, and PPE – to ensure that they meet the

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regulatory standards and have the appropriate efficacy," said Dr. Amiji. "Drug companies are also establishing various ways to improve authentication, all the way from the manufacturing site to distribution." He added that while technologies are being developed to prevent tampering, it is a constant race against the counterfeiters.

Many countries are trying to validate pharmaceutical products at the borders; for instance, through chemical identification or tagging technologies. However, Dr. Amiji admitted that chemical identification, which involves using standard analytical methods to ensure the right drug is present in the correct amount, is a costly and time-consuming process. Other validation methods involve tagging products using bar or QR codes to ensure the product is authentic. There is also an emphasis on more covert technologies, such as watermarks or other markers that can be used to identify if a product is fake, as well as blockchain solutions.

Dr. Amiji concluded that pharmaceutical companies and regulators must continue to be vigilant and monitor activities to ensure that products are not compromised. "This is the most challenging aspect of quality control because you have to look at the entire manufacturing chain and not just the end product," he said.

About the Author

University Distinguished Professor, Professor of Pharmaceutical Sciences and Professor of Chemical Engineering; Director, Laboratory of Biomaterials and Advanced Nano-Delivery Systems (BANDS); Northeastern University, Boston, MA.

Dr. Amiji received his undergraduate degree in pharmacy from Northeastern University in 1988 and his PhD in pharmaceutics from Purdue University in 1992. Over the years, his research has received over $40m in sustained extramural funding from the National Institutes of Health (NIH), National Science Foundation (NSF), foundations, and biotech/pharma industries.

Dr. Amiji has supervised research efforts of over 120 post-doctoral associates and graduate students. He has also edited 10 books, along with over 70 published book chapters and over 360 peer-reviewed articles.

Dr. Amiji has received several awards including the 2006 NSTI Award for Outstanding Contributions towards the Advancement of Nanotechnology, Microtechnology, and Biotechnology, and the 2007 American Association of Pharmaceutical Scientist's (AAPS) Meritorious Manuscript Award. He is a Fellow of both AAPS and the Controlled Release Society. He has also received the Distinguished Alumni Awards from both Northeastern University School of Pharmacy and Purdue University College of Pharmacy.

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PerkinElmer, Inc.
940 Winter Street
Waltham, MA 02451 USA
P: (800) 762-4000 or
(+1) 203-925-4602
www.perkinelmer.com

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