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Blockchain & The Pharma Supply Chain - Beyond DSCSA Compliance

(Source: an edited excerpt from an article prepared by Maria Palombini, IEEE Standards Association, and published by Bioprocess Online)

Current pharmaceutical industry efforts to adopt blockchain for supply chain integrity tend to focus on compliance with the U.S. FDA's 2013 Drug Supply Chain Security Act (DSCSA), designed to protect patient safety through track-and-trace protocols.

While that is a positive development, investing significant resources to achieve mere compliance with a legislative mandate normaly does not drive the level of investment needed to solve a global problem. The DSCSA, whether by design or unintended consequences, does not adequately address the supply chain down to the consumer level. Thus, it leaves a gap that continues to plague all stakeholders in the supply chain.

A more holistic view of the value of blockchain to the pharmaceutical supply chain would take into account the magnitude of the global fake drug/counterfeit drug problem; the financial, economic, and social costs of fake drugs/counterfeit drugs; and the positive financial and economic benefits of moving beyond compliance to tackling the issue of fake drugs/counterfeit drugs head-on. There is, for the pharmaceutical industry, a potential ROI for adopting blockchain form end-to-end supply chain integrity and optimization. The ROI is could be enormous and would cover the cost of implementation as well as vastly reduce the financial, economic, and social impacts of fake drugs/counterfeit drugs. Patient safety would improve as a direct consequence.

Fake drugs/counterfeit drugs are a growing challenge to the industry not to mention the opioid crisis. The World Health Organization (WHO) estimates 10% of medicines worldwide are fake/counterfeit, and that category rises to 30% in emerging economies. This problem applies to both "lifestyle" medicines and lifesaving drugs. The rise of internet-based pharmacies has exacerbated the problem; WHO estimates a staggering 50% of medicines purchased online are fake. In Europe alone, the financial and economic impacts of fake drugs/counterfeit medicines are estimated by the EUs Intellectual Property Office (EUIPO) to result in annual losses of 10.2 billion euros (US$11.8 billion) and 90,000 direct and indirect jobs lost to manufacturers. The WHO estimates more than 120,000 lives are lost each year in Africa due to fake anti-malarial drugs alone.

Policy-based solutions tend to encourage compliance with legislative mandates. The FDA's DSCSA offers a step in the right direction, but it falls short in reaching the transfer of pharmaceuticals at the pharmacy/dispensary level to the patient. Yet addressing supply chain integrity and optimization has intrinsic challenges because it involves the various players in the supply chain - from source materials to manufacturers to distributors to wholesalers to retailers. Bilateral and multi-lateral agreements present daunting

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- U.S. wholesaler and distributor **Cardinal Health** reported revenues of US$34.2 billion for its first quarter of fiscal year 2019, an increase of 8% year -over-year. Quarterly GAAP diluted earnings per share increased 439% to US$1.94 and non-GAAP EPS increased 18% to US$1.29. Pharmaceutical Segment profit for the quarter decreased 12% to US$409 million, reflecting negative impact from the company's generic program performance, while Q1 revenue for the medical segment increased 2% to US$3.8 billion, primarily driven by new and existing customers, according to the company.
- Pharmaceutical manufacturer **Sanofi** (France) has begun plans to set up its first research institute in the city of Suzhou, China, further expanding its presence in the country. The facility will open in the third quarter of 2019. The company will invest US$22.8 million each year over the next five years, and will initially employ 30-50 staff.
- The effects and impact of obesity on the U.S. economy has surpassed US$1.7 trillion, an amount equal to 9.3 percent of the country's gross domestic product, according to the research firm **Milken Institute** in a new report. The estimate includes US$480.7 billion in direct healthcare costs and US$1.24 trillion in lost productivity. The study draws on research that demonstrates how obesity elevates the risk of diseases such as breast cancer, heart disease, and osteoarthritis.

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Five Strategies to Fight Fake Drugs

(Source: an edited excerpt from an article prepared by Michael Esposito, TrainReach Consulting, and published by Bioprocess Online)

Regulatory agencies in many countries are seriously understaffed to combat the many actors in the fake drug market and in some cases may even run into opposition due to political motives by the authorities. Fortunately, drug manufacturers of all sizes have developed solutions that provide good examples for other organization. Here are five of the most noteworthy ones:

1. Assign a dedicated individual or group in your organization to monitor the security of your supply chain. This includes preventing thefts that could occur at the manufacturing facilities, warehouses, the end customer, or while the product is being shipped. Because of the opioid epidemic, which has resulted in thefts at pharmacies and even by hospital employees, the supply chain should be intact up to the very point the drug is administered.

The strategy should include all your stakeholders, as there are many ways that product can be compromised. Also, ensure regularly compliance and share information, as the landscape is continuously evolving.

2. Work with regulatory agencies, industry organizations, international agencies such as the WHO, and law enforcement

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Blockchain (cont.)...

complexities, including a third-party, trusted arbiter. Adopting blockchain for supply chain integrity and optimization presents additional, significant challenges, so skepticism is understandable. Applying blockchain involves dollars invested, time spent, business process changes, and the potential risk of exposing intellectual property and proprietary business practices to competitors; so pharmaceutical industry players perceive it.

The first Pharma Supply Blockchain Forum, sponsored by the IEEE Standards Association (IEEE-SA), held in June 2017 at Johns Hopkins University, gathered scores of industry representatives from across the supply chain and stakeholders, including regulators. Seven participants revealed common concerns: Who will pay for a pharma blockchain? Who would own the data embedded in it? How would the industry get widespread buy-in to make it happen?

Without going into technical detail, several characteristics of blockchain recommend it as a solution to the challenge posed by the pharmaceutical supply chain. First, blockchain is autonomous and does not require trust, or arbiters, among participants. The method by which new blocks are added to the chain virtually guarantees the integrity of the data. A blockchain ledger records only the data a participant wishes or needs to share to make it effective. Intellectual property and competitive strategies can be shielded from data shared amongst trusted partners relevant to tracking and securing the supply chain.

Two specific use cases for blockchain in the pharmaceutical supply chain make sense. One is securing the supply chain - the answer to the massive, widespread growth in fake/counterfeit drugs and their associated costs. The other is optimization of the supply chain, which offers efficiencies, cost removals, and visibility into inventory as well as speed and accuracy in the event of a drug recall.

Currently, there is no real-time management of legitimate drug inventories and supplies equally visible to the key trading partners in the pharma supply chain, thereby making drug shortages a reactionary process. A survey conducted by Premier Healthcare Alliance in 2014 estimated drug shortages cost U.S. hospitals alone about US$230 million annually as they tum to higher-cost alternatives. A survey by the American Society of Health Pharmacists (ASHP) estimated annual, nationwide labor costs for managing shortages averages about US$216 million. So, an additional and financially rewarding benefit of using blockchain to secure the supply chain is real-time, enhanced visibility into inventory that also allows for reduction of spoilage and/or waste. This is particularly true in the case of cold chain logistics when sensor-equipped, temperature-sensitive drugs need to report and distribute real-time readings to all relevant parties. The coronary to inventory transparency is improved efficiency, speed, and accuracy in targeting drugs that have lost their efficacy in distribution, and/or implementing drug recalls.

A recently released IEEE-SA study, the State of Blockchain Adoption on the Pharmaceutical Supply Chain, found a direct correlation between "level of familiarity with blockchain technology" and an enterprise's likeliness to participate in various types of blockchain solutions. Similarly, the more respondents actively explored related solutions, the more value they found in applying the technology. The opposite was also established: the less known about blockchain's use in the supply chain, the less value perceived. Big Pharma cares about patient safety because it goes to the heart of its existence. From the available facts, it appears awareness, education, investments in, and explorations of blockchain-based solutions to the global supply chain would produce significant ROI, protect patient safety, and address long-standing, persistent challenges in the industry.

Five Strategies (cont.)...

(e.g., Interpol) to identify and combat fakes. The regulatory agencies in the markets that receive products usually have programs in place to combat counterfeits, with different requirements and levels of effectiveness. International organizations help both with developing effective strategies as well as resolving existing issues. As the number of countries participating in these initiatives increases, the reach of these programs likewise improves.

Many countries in Africa benefit from the USP's program for the improvement of medicines, Ghana being a standout among them. These initiatives help in a variety of ways: raising awareness for the need for increased law enforcement and stiffer penalties that go beyond copyright infringement, getting different parties to agree to a cross-national strategy, and allowing each country to keep up with new developments and adjust their practices accordingly.

3. Incorporate design elements into packaging to make counterfeiting more difficult. There is a surprising alignment between the U.S. FDA's requirements for product serialization and technological solutions that address counterfeiting. Bar coding and RFID tags are the best-known tools used in verifying the uniqueness of a product and package. Holographs and other detection elements can add layers of security to these already established technologies. Some companies specialize in applying unique identifiers that are difficult to mimic for each unit of use. A great source of information regarding the use of bar coding in healthcare packaging is the industry organization GSl, which holds webinars and conferences on subjects of interest to pharma and device companies, wholesalers/distributors, and other healthcare entities like hospitals and pharmacies.

4. Use verification methods at different points in the supply chain to ensure the integrity of a product. Because the potential for a compromised supply chain occurs at many different points, there is a need to establish product identity, quality, and purity throughout. A few of these key points include when raw materials such as APIs are received at a production facility, after they're blended, when the unit doses are filled (e.g., vials), when the units are packed into shipping cartons and pallets, and when they are received at the distribution centers. However, the vulnerability does not stop here. There may be a subsequent step in the supply chain when an electronic system cannot verify that a product's identity remains intact, such as customs at the port of entry or any step that relies on hard-copy documentation for verification.

Sometimes thefts occur when corrupt individuals working in the health ministry over order product and siphon some of it off for their own resale. An example of which occurred in Honduras. Those unscrupulous enough to engage in such practices will likely not be preoccupied with keeping a product at the correct storage temperature before reselling it.

Talk with the supply chain professionals at every step in the process, as well as regulatory authorities and customers, to create a method that works for the organization.

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Five Strategies (cont.)...

5. Take advantage of new technologies. Blockchain is an area that large pharma companies and wholesalers/distributors have been exploring for a number of years, although its potential has not yet been fully realized. The attractiveness of block chain is its ability to maintain data integrity, which makes it especially useful to ensure the necessary verification at different points in the supply chain.

In addition, smartphone applications have been developed for consumers in some markets to identify legitimate product. While this is not a substitute for a diligent regulatory body, it gives the consumer an additional tool to ensure that what they're ingesting is authentic. By searching the internet regularly, it's possible to gauge the wide variety of new initiatives that exist.

Pharma companies ignore the issue of fake drugs and drug diversion at their own peril. If anything, problems will tend to multiply as transnational clandestine operations continue to be involved in the highly lucrative fake drug market. The ongoing battle between real and fake meds has been recognized as a major healthcare crisis and as such, there is a wealth of information available to combat this epidemic. There are plenty of best practices to draw upon, with new information being revealed on a regular basis, whereby organizations may implement as detailed as budget and time allow.

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FIGHT THE FAKES WEEK
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For more information and social media messaging for your organization, please visit www.fightthefakes.org/Week

YOUR VOICE WILL MAKE A POSITIVE IMPACT IN SPREADING THE WORD ABOUT THE DANGERS OF FAKE MEDICINES!

Operating Profits Increase by 46.1% for Japan's 4-Major Wholesalers

(Source: Pharma Japan)

The top four Japanese drug wholesalers (Alfresa, Medipal, Suzuken and Toho) saw their combined operating profit rise 46.1% in April-September 2018 although combined sales fell slightly, according to a Jiho tally. Their average operating margin exceeded the 1% mark, which is seen as a threshold for "reasonable profit rates."

Based on distribution improvement guidelines introduced in April, the four companies appear to have succeeded in reducing yakkasa (difference between NHI and market prices) to some degree. In addition, new businesses being developed to reduce SGA costs and bring in profits apparently had some success as well.

Suzuken, which reported the biggest increase in operating profit of the four companies in the first half of FY2018, reduced its SGA expense ratio more than the other companies by reducing personnel expenses through an early retirement program it offered last fiscal year. Alfresa Holdings saw the second-highest operating profit growth due mainly to a roughly 16 billion yen (US$124 million) increase in sales, year on year, and a reduction in its SGA cost ratio. Though the four companies had an average operating margin of 1.02%, only Alfresa reported a rate of over 1% at 1.52%.

Despite the NHI price revision in April, combined sales for the four companies were virtually unchanged, resulting from growth in sales of the hepatitis C treatment and anticancer drugs. The combined growth rate in sales by the four wholesalers is on par with Crecon Research & Consulting's estimate of -0.1% average market growth for ethical drugs in the April-September period.

The four wholesalers' prediction, for the balance of the fiscal year, vary on how far they will be obliged to renegotiate prices with their customer medical institutions and pharmacies. Medipal Holdings said, "We expect more deals to be renegotiated than last year," while a Toho Holdings said, "Long-term agreements have been reached in many cases."

All four wholesalers will try to maintain prices settled in accordance with agreements they reached by September. Nevertheless, with dispensing pharmacies experiencing financial difficulties due to significant dispensing fee reforms, the prospects for renegotiation remain unpredictable.

In Brief (cont.)...

For more information visit https://www.milkeninstitute.com/publications/view/944.

- **AstraZeneca** has agreed to divest the prescription medicine rights to *Nexium (esomeprazole)* in Europe, as well as the global rights (excluding the U.S. and Japan) to *Vimovo* (naproxen/esomeprazole) to **Grunenthal**. The drugs fall outside AstraZeneca's three main therapy areas. Additionally, *Nexium* has lost compound patent protection in the majority of global markets. *Vimovo* will receive patent protection in most European markets until 2025.
- **Biogen** CEO *Michel Vounatsos* stated that Japan remains a top priority strategic market for the company as it fits the big biotech's priority focus on neuroscience, emphasizing that the rapidly-aging country is included "very early" in its global clinical development. "Needless to say, Japan is at the top of the list in terms of priorities," Vounatsos stated at a Tokyo press conference on November 9th marking the company's 40th anniversary of its inception in 1978. "It's the third pharma market with an epidemiology that meets very well the portfolio of clinical development programs that we have as an organization."
- China' top market regulator is threatening to hand down harsh penalties with substantial fines for a wide range of violations, under a new draft law culminating from a major quality control scandal earlier in the year. Violations under scrutiny include falsifying manufacturing records and failing to recall products sold after quality issues and other potential safety risks. The draft was released by the State Administration for Market Regulation on its website and is solicited public feedback through November 25th.

(Sources: Drug Store News, Nikkei Asian Review, PharmaJapan and World Pharma News)