



## Commentary

## Some comments on the scandal of rabies vaccine in China

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## 1. Vaccine background

Changchun Changsheng Biotechnology Co., Ltd. (Changsheng) was founded in 1992. It is a high-tech enterprise that concentrates on the research, development, production and application of human vaccine. It is an enterprise that developed their own influenza vaccine and human rabies vaccine. To date, its sales volume of rabies vaccine has occupied 23.19% of the national market and is the second largest producer in China.

In July 2018, Changsheng Scandal had caused a great sensation. Changsheng Scandal was exposed by one of his staffs. On July 11, 2018, China Food and Drug Administration (CFDA) conducted an unannounced inspection of the enterprise. On July 15, CFDA alleged that the enterprise deliberately forged its records of production data of rabies vaccine, required Jilin Medical Products Administration to revoke its GMP certificate (No. JL20180024), instructed the enterprise to stop producing rabies vaccine and demanded a recall of unused vaccines. On July 18, Jilin Medical Products Administration published that Changsheng was penalized with a fine for being found to produce defective DPT vaccine in October 2017. On July 23, President Xi Jinping issued an important directive and demanded a thorough investigation and severe punishment of violators. On July 24, local police detained 15 suspects including the chairwoman of board. As a result of the scandal, from July 16 on, the stock of the enterprise continued reaching decline limit for 32 trading days, with an evaporation of 80% of its market value. On October 16, 2018, CFDA confiscated the enterprise 9.1 billion yuan [1].

## 2. Price of rabies vaccine

The national Expanded Program on Immunization (EPI) provided 11 vaccines for children for free against 12 diseases [2]. Meanwhile, parents have the option to pay themselves for private-market vaccines, which include both domestically produced and imported vaccines [3]. Vaccine procurement in China is an open bidding process, both Chinese and foreign companies can participate in the procurement [4]. Vaccine procurement prices for Expanded Program on Immunization vaccines in China ranged

from 0.1 to 5.7 US dollars per dose, but prices for private-market vaccines ranged from 2.4 to 102.9 US dollars per dose - often higher than prices for comparable US vaccines<sup>1</sup>. However, higher prices didn't lead to safer vaccines [5].

According to Changsheng's financial statements, the sale fees have risen year after year since 2014–2017, reaching 583 million yuan and accounting for 60.27 percent of its total operating cost in 2017. Sale fees are referred as a variety of different fees including service fee, conference fee, transportation fee, market service fee and publicity expense. Among them, the service fee was 442 million yuan that accounted for 75.81% in 2017, which is the fee paid by Changsheng to the service companies. As a bridge of vaccines companies and CDCs, service companies play an important role after the reform of vaccine circulation and management regulations in 2016.

Fig. 1 is a comparison of sale fees of two companies, Liaoning Chengda Biotechnology Company and Changsheng, from 2014 to 2017.

Liaoning Chengda Biotechnology Company did have a leading position in rabies vaccine. But Changsheng took over the rabies vaccine market increasingly from 2015.

Fig. 2 is a comparison of lot release of two companies, Liaoning Chengda Biotechnology Company and Changsheng, from 2015 to 2017.

From the two figures above, we know that with the sale fees increasing, the rate of lot release is also increasing.

Since 2016, SDA required private-market vaccines to be bid by province-level Centers for Disease Control (CDC) and purchased by county-level CDC [6], and only province-level CDC and county-level CDC have regulatory involvement in procurement of vaccines. The new regulations have reformed the circulation of the private-market vaccines, improved the government's absolute control over vaccine purchasing. At the same time, it is easy to breed corruption among government officials.

## 3. Government regulations

This vaccine scandal exposed many weak links in the regulation system. Changsheng Scandal was exposed by one of his staffs instead of inspection supervision.

<sup>1</sup> The average annual exchange rate from 2013 to 2016 was used here.

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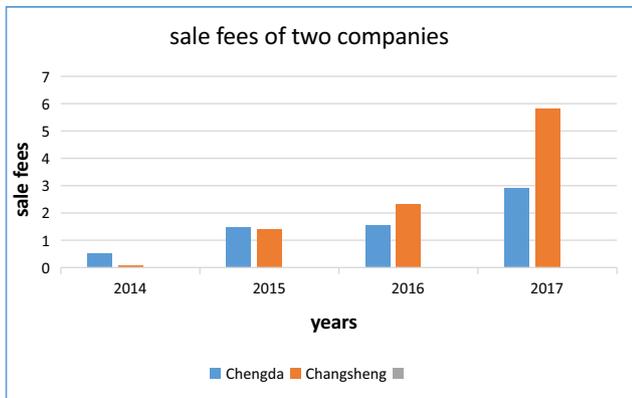


Fig. 1. Sale fees of two companies.

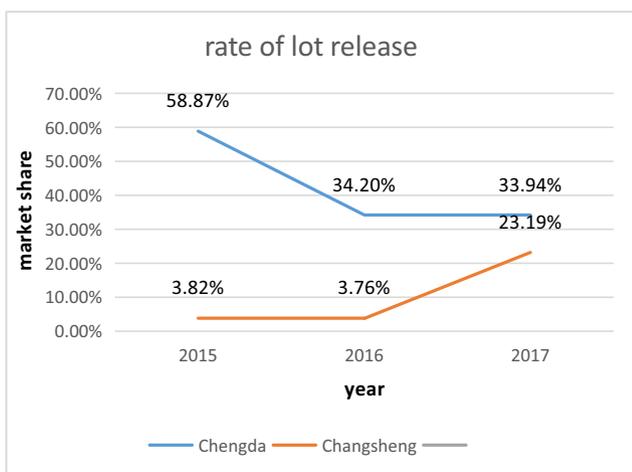


Fig. 2. Rate of lot release of two companies.

Before putting into the market, the vaccine companies have to send the vaccine samples to the National Institutes for Food and Drug Control for quality testing. It will not be approved if the samples under the national standard. The vaccine manufacturers blind the inspection departments with qualified samples, but provide unqualified products in the market.

Without adequate inspection, the vaccine incidents happens regularly.

The company was accused of a series of forgeries by SDA, such as fabricating batch numbers and production date and using expired raw liquid [1]. All the fraudulent activities Changsheng did was to reduce cost.

Lack of supervision of the regulators during manufacturing process allows the production of the sub-standard rabies vaccines. Thus, the supervision system needs continuous improvement to assure the safety of total supply chain from producing to distributing. However, it is difficult to ensure the neutrality and fairness of the supervision by SDA since it is responsible for both the approval and regulation of vaccines production. Furthermore, the regulatory agencies exercise complete control over the procurement of private-market vaccines, which weakens the market competition through administrative monopoly [7]. Take the private-market vaccines as an example, successful bid companies always with high sale fees.

#### 4. Comment

The SDA imposed severe administrative penalties on Changsheng and revoked its pharmaceutical trading license. Meanwhile the involved persons, no matter in Changsheng or in regulation agencies were investigated thoroughly and punished severely. Forty-eight government employees were penalized because of failing to fulfill their regulatory responsibility in February 2019.

However, the Chinese regulation system of private-market vaccines still needs improving. First, strengthen the supervision of manufacturing process to ultimately ensure the safety and compliance of vaccines. Not only inspecting the vaccines before putting into the market, but also conducting sampling inspection during the production process. Second, increase the transparency of government procurement. Anyhow regulation should enhance the effectiveness of vaccines markets, not impede them. Third, establish an independent system to inspect the circulation of vaccines.

Delivering vaccines without approved cold storage conditions in 2016, Changsheng sub-standard rabies vaccine in 2018 and expired vaccine in 2019, the repeated occurrences of scandals are also related to the unclear and asymmetry information of vaccine manufacturing and circulating. Therefore, it is imperative to establish a traceability mechanism [8]. Traceability system monitors and records the information of producing, circulating and testing in each link of supply chain. Then the information can be shared by regulatory authorities, CDC, manufacturing enterprises and vaccine consumers. So abnormal vaccine can be traced back quickly and precisely to prevent serious consequences and avoid damages to the personal health and better yet, help prevent corruption as well.

#### Compliance with ethical standards

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#### Declaration of Competing Interest

Zaidi Guo, Li Bai and Shunlong Gong have no conflicts of interest that are directly relevant to the content of this article.

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