Melamine-Tainted Milk: Progress in Impurity Detection

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Introduction

Recent reports of salmonella contaminated peanut butter, infant formula with melamine, and powder milk with perchlorate indicate serious lapses in quality control and regulation of food-production methods all over the world. This negligence in regulation, coupled with economics and greed have led many companies to add unsafe chemicals to food products to raise profit. The tainted infant-formula scandal in China is a prime example. More than 20 dairy companies, including Sanlu Dairy, one of the three largest dairy companies in China[1], were found to be producing tainted milk[2]. Tens of thousands of children developed urinary-tract problems, and at least six died due to consumption of contaminated milk[2]. These devastating cases are attracting new attention from society leading to stricter legislation, as well as to scientists, who are developing breakthrough screening procedures to regulate quality.

Background

1. *Chinese Tainted Pet Food*

   On March 15, 2007, the Food and Drug Administration (FDA) discovered that some pet foods were killing cats and dogs[3]. By the end of the month there were over 100 reported cases of pet deaths, and many more cases of kidney failure[4]. Investigation led to the discovery that numerous pet foods had been contaminated with melamine, prompting the recall of 5,300 pet foods in the United States[5].

   In China, food is priced according to quality, and the quality is determined by the protein content[6]. To obtain an indication of protein levels, regulators measure the amount of nitrogen in the food (rather than protein content directly), since protein is nitrogen-rich. Therefore, companies are tempted to add nitrogen-

rich compounds (melamine is 66% nitrogen by mass) to make their products seem higher in protein, allowing them to sell their products for more.

The source of the melamine was vegetable protein, including rice protein and wheat gluten imported from China[5]. The threat to the human food supply was immediately considered, prompting the FDA to impose limits on import of food ingredients from China[7]. Attempting to reassure the world, Wu Yongning, Deputy Director of the Chinese National Institute of Nutrition and Food Safety, said: "*I don't believe it has reached such a serious stage that human food is at risk*[5]." International scrutiny had already been heightened.

2. *Chinese Tainted Milk*

After increased incidence of kidney problems in children was reported by many Chinese hospitals, Sanlu, a state-owned dairy company, was prompted to conduct tests on its milk; results were released to state authorities August 1, 2008[8]. Fonterra, a dairy company in New Zealand that had a large stake in Sanlu, pushed for an immediate recall, but Sanlu acted only to pull baby-formula powder from distributors a few days later[9]. It was not until more than a month later, on September 11, 2008 that Sanlu publicly recalled 700 tons of baby formula[9].

There has been speculation that Sanlu waited so long due to pressure from the government because of the looming opening ceremony of the Olympics in Beijing[10]. Suspicion grew after Li Changjiang, head of the General Administration of Quality Supervision, Inspection and Quarantine (AQSIQ) said this about the Olympic food supply: *"All the food supply, including dairy, for the Olympics and Paralympics are safe…we took special quality management measures aimed at the food supply for the Games*"[11].

By mid-September, the Chinese government had stepped in, but the damage was done. Over 50,000 children were ill with 104 in serious condition; 22 powder-milk companies were determined to have produced tainted milk, including three of China's main producers. These companies, such as Sanlu Dairy would add water to the milk to increase its volume and then add melamine artificially to boost the protein content back to the levels of normal milk[6]. In some instances the milk had been watered down so much that the melamine content was 2563mg/kg[12]. Recalls had extended to 8,000 tons of baby formula, and the head of the Chinese product-quality agency stepped down[9].

Having been ordered to stop production, and facing heightened public scrutiny, Sanlu had no choice but to sell all assets and declare bankruptcy[13]. By November, Sanlu had announced the sale of its assets and some production facilities to a rival company, Sanyuan[14]. By December the company had received a loan to compensate the families of sickened children, which brought the company's total debt to 1.1 billion Yuan (U.S. $161 million)[14]. On December 23, Sanlu's application for bankruptcy was officially accepted[14].

Trials of four Sanlu executives began on December 31, 2008[15]. The four included Tian Wenhua, Hang Zhiqi and Wang Yuliang, all general managers, and Wu Jusheng, head of the milk division[15]. Ms. Wenhua testified that she had known of the tainted milk in May; she was sentenced to life in prison[16]. The other defendants received 5-15 years in prison[16]. In addition to these sentences, two death sentences were handed down, one to Zhang Yujun, who was convicted of selling 600 tons of contaminated protein powder to dairy companies. The Chinese government labeled him one of the "principal criminals"[17].

3. What is Melamine

Melamine is a white, crystalline powder derived as a trimer of cyanamide which is used extensively in agriculture[18]. Melamine is most commonly used to make durable plastics and resins. It is also commonly used in concrete production to reduce water content, strengthening the concrete. Melamine is toxic in humans[19], causing anything from irritation, to serious damage to the reproductive system as well as to the bladder and kidneys, and can result in bladder cancer[20]. Because the melamine in Chinese milk was thought to form a complex with uric acid, melamine was found in urine in the highest quantities in infants; melamine precipitates kidney stones[21].

4. FDA and Governmental Regulations

After the milk scandal broke, the World Health Organization (WHO) responded by reiterating the tolerable daily intake (TDI) limit of 0.2mg per kg of body weight and suggested some countries' limits were above this norm[22]. In October 2008, China set limits on melamine content in foods at 1mg per kg of infant formula and 2.5mg per kg of general dairy products[23]. Chinese health officials explained that melamine can leach from food packaging into food, making a zero-tolerance policy infeasible[23]. China is also considering setting melamine limits on animal feed after discovering 4.7ppm melamine in eggs from a Chinese producer[24].

The U.S. also updated its standards in early October due to the pet-food incident as well as the tainted milk in China. The FDA declared that 2.5mg of melamine per kg of dairy would not harm humans, but stated that any infant formula imported to the U.S. must be melamine-free[22]. Later, the FDA said they were unable to set standards for infant formula because it was impossible to determine health effects in infants[25], but eventually settled upon a level of 1ppm,

as set by Chinese authorities[22]. The FDA also opened three offices in China to work with local officials to improve food-and-drug quality[21].

Detection Methods

1. *Previous Methods*

In the U.S., dairy producers are held to stringent standards. Enforcement begins at farms that are regularly inspected by National Milk Producers Federation (NMPF) inspectors who look for any sort of illegal activity, and for unsanitary conditions[26]. In addition to these inspections, company representatives from the manufacturers who buy a farm's milk regularly come to oversee farm conditions. Also, because a farm's production is relatively constant, if milk was watered down as it was in China, this increased volume would be noticed by regulators[26]. In addition to these heuristic checks, U.S. milk is also analyzed for nitrogen, protein and butterfat content, and the freezing point of the milk is also determined to see if it is depressed, which would indicate the presence of impurities. Strict production standards are set by the U.S. Department of Agriculture, Marketing Service[27].

2. *New Methods*

There had previously been no method for melamine detection in food or tissue samples but the tainted pet-food and milk scandals have spurred development of new detection methods. The first new technique, developed by the FDA, combines gas chromatography and mass spectrometry to detect melamine, ammeline, the hydrolysis product of melamine, ammelide, the hydrolysis product of ammeline, and cyanuric acid, the hydrolysis product of ammelide, down to 10μg/g [28]. The sample is first wetted in acetonitrile, or other solvent. This effluent is filtered, collected, and evaporated. The remaining solids are suspended in pyridine or other solvents, run through a gas chromatograph, and

fed to a mass spectrometer. This method can provide semi-quantitative measurements of the amounts of adulterators[28].

The FDA has also developed additional methods utilizing liquid chromatography, triple quadrupole tandem mass spectrometry for detection in liquid infant formulas[29] as well as in solid foods[30]. The detection methods in liquid formula can go as low as 0.25μg/g [29] but is more prone to interference from other components in the sample[21]. The method for solid foods separates melamine and other adulterators from the sample, minimizing interference, allowing for detection of concentrations as low as 0.1μg/g [21]. The downside to these methods is that they are relatively labor-intensive, requiring between 35-75 minutes per sample[21].

Researchers at Purdue University have also been working on methods using near- and mid-infrared spectroscopy[31]. This method allows detection down to 1ppm and a confidence level of 99.99%[31]. It also requires little sample preparation, and detection times are only two minutes or less, both necessary qualities of any method that would be used to safeguard the food supply. The downside to this method is that the statistical methods used to correlate the spectra to melamine content need to be recalibrated for every sample[31].

In addition, methods under development use extractive electrospray ionization in conjunction with mass spectroscopy. Extractive electrospray ionization (EESI) is a process for converting a liquid sample to a fine spray, and spraying it through a second spray of charged microdroplets of solvent[32]. Then, because the compounds of interest prefer to be dispersed in the spray of charged solvent droplets, they transfer into that spray, which is then fed into the mass-spectrometer. This method requires the least amount of sample preparation[32].

Detection limits using this method are as low as 500ppb, and sample-run time is only 30 seconds[21].

Significance Now

1. *Victims*

China's Ministry of Health has estimated the number of victims at approximately 290,000 where 51,900 had to be hospitalized[33]. In addition, 11 cases of death had been reported, although the government only confirmed three[33]. Outrage intensified over the government's mishandling of the incident[34]. Any victims who became sick prior to September 12 were not offered free medical attention by the government, forcing many families to spend their savings on medical bills[35]. Families who hired lawyers to file lawsuits now say their lawyers are facing pressure to drop the cases[36], leaving many families completely devastated by this scandal and with no one to turn to. One deceased child's parents appeared on New Zealand TV and said the people involved in the tainted-milk deserved to "*die a thousand deaths*"[37], highlighting the anguish that this case has brought.

2. *Dairy Farmers*

Victims and their families are not the only ones to suffer. Dairy farmers, those who supplied fresh milk to dairy companies such as Sanlu, are also hit hard by the world's new lack of trust in Chinese dairy. Farmer Yang Lianying, for example, is forced to dump his fresh milk every day because no one buys it[38]. The lack of sales, coupled with the rising price of feed for their herds are making it increasingly hard for many village farmers to put food on their own tables. One farmer exclaimed: "*It is the small farmers like us who helped make Sanlu the big company that it is. But now, if Sanlu falls, who will help us?*"[38]. Many farmers are forced to sell their cows because they cannot continue to feed them[38]. At the end

of the day, China's problem is stated by Yanzhong Huang, a professor at Seton Hall University: "…*But the deeper and more fundamental challenge China faces is a systematic lack of business ethics.*"[39].

Conclusion

The Chinese tainted-milk scandal left hundreds of thousands of families devastated emotionally and financially. Many will never be recognized or reimbursed for their losses. The company at the heart of it all, the Sanlu Group, was forced to shut down and declare bankruptcy. Its executives were tried, and sentenced to jail, and rightfully so, for, as one testified, they knew about the tainted milk early on. In addition, the dairy farmers who once supplied these large companies with their raw milk are now left with large herds and no one to buy their milk.

There is, however, some good news. This scandal has spurred scientific research toward new impurity-detection methods. These methods mostly utilize mass spectrometry for detection, but couple various methods for sample preparation such as gas and liquid chromatography and extractive electrospray ionization. In the end, this is a game of cat and mouse; for every impurity violator that regulators catch, other law breakers will devise new schemes to maximize profits at the cost of their fellow man.

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