MARKETS

PHARMACEUTICAL INDUSTRY WATER BUSINESS TRENDS

The technology and markets for high-purity water for use in pharmaceutical applications are dynamic. There are continuous technology improvements and the markets are growing faster in developing countries than in the developed ones.

The pharmaceutical industry is a major user of high-purity water systems and consumables. In 2014, the industry's high-purity water purchases will exceed $440 million. Table A shows the different major high-purity water treatment markets. This comparison also indicates how the pharmaceutical water business compares to the other markets.

These high-purity water markets have different treatment concerns. For example, the pharmaceutical industry is highly concerned with microbiological contamination, while the semiconductor industry pays greater attention to particle removal. Unique approaches are needed to minimize microbiological contamination at pharma plants. In addition, to the pharmaceutical industry, medical device manufacturing, hospital compounding, food and beverage, and animal research also need water with minimal microbiological contamination.

Pharmaceutical water treatment plants treat municipal water that meets U.S. Environmental Protection Agency drinking water standards to achieve United States Pharmacopeia (USP) standards required for different types of sterile compendial waters. The term compendial waters represents any water intended to be used for final drug dosage forms, including Purified Water (PW), Water for Injection (WFI), Bacteriostatic WFI, Water for Irrigation, and Water for Inhalation. The principal difference between PW and WFI is the allowable amount of bacterial contamination, which is measured by colony count and by endotoxin level.

PW and WFI, which are used in the production of various drugs, are required to meet conductivity, total organic carbon (TOC), and bacteria count limits. In addition, WFI must meet the USP endotoxin limit. Generally, several treatment steps use various water treatment technologies to produce PW or WFI from drinking-water quality feedwater. Uses for these pharmaceutical-grade waters include bottle washing, compounding (PW), laboratory, production, rinsing, steam sterilization (WFI), and tank cleanings (PW).

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Product Innovation

High-purity water treatment products, consumables, and instrumentation are being improved at a relatively rapid rate. Within the instrumentation and control category, there are improvements from smart sensors to enterprise management.

Dissolved oxygen (DO) monitoring is one example of the sensor improvement. There are two basic technologies for DO sensing: electrochemical and optical. Electrochemical is the traditional technology, and is comprised of polarographic sensors and galvanic sensors. Optical is the latest technology innovation in DO sensing. It is displacing electrochemical technology

Polarographic sensors operate as an electrochemical cell with a positive electrode (cathode) and a negative electrode (anode) connected by a salt bridge, which consists of a saturated

Figure 1. Aspects of the systems solution and the analytical solutions in a pharmaceutical water treatment plant.
Illustration courtesy of Yokogawa.

electrolyte solution such as potassium chloride (KCl).

Galvanic sensors operate as an electrochemical battery with a positive electrode (cathode) and a negative electrode (anode) connected by a salt bridge, consisting of a saturated electrolyte solution such as potassium hydroxide (KOH).

Optical DO sensors reflect a process wherein a dye-impregnated foil or membrane is made to fluoresce when stimulated by a specific wavelength of light such as from a light-emitting diode (LED). The fluorescence is subsequently "quenched" in terms of intensity and duration by oxygen diffused into the membrane. The degree and rate of quenching is proportional to the oxygen concentration. The quenching of the fluorescence is recorded by an optical detector and, after suitable algorithmic adjustments made by instrument software, is accurately correlated to the concentration of dissolved oxygen in the water sample.

Optical sensors offer the following advantages: no oxygen consumption, no requirement for flow past the sensor; infrequent calibrations, no electrolyte to replace or anodes to polish; and lower life time cost.

Possibly the most rapidly changing technology involves the high-purity water quality, physical, and other measured parameters of the entire plant information and laboratory management system. Several suppliers are supplying comprehensive and integrated software for treatment facilities. Figure 1 illustrates different aspects of a systems solution and analytical solution.

In treating water for the production of pharmaceuticals, the concentration of gases dissolved in the water plays an important role. In many cases the carbon dioxide (CO^2) content in the raw water has to be further reduced to obtain purified water with a conductivity of < 1.3 microsiemens per centimeter (µS/cm) (at a temperature of 25°C).

Historically, sodium hydroxide (NaOH) dosing has been used to control CO_2. With chemical dosing CO_2 is converted into a carbonate, which can be removed by the reverse osmosis (RO) system. The latest state-of-the-art technology for this task is membrane degasification where chemicals are not needed. Liqui-Cel® membrane contactors are an example of a membrane degasification system.

Market Dynamics

The high-purity water market with pharmaceutical applications is very dynamic. Growth is substantial, but geographically uneven. Estimates are that annual global spending on medicines will rise from $956 billion in 2011 to nearly $1.2 trillion in 2016, representing a compound annual growth rate of 3% to 6%.

The market for high-purity water systems and consumables is rising faster than total revenues because of the lower price per unit sale. This is caused by the penetration of generic drugs. Pfizer Inc. is the largest purchaser of high-purity water for pharmaceutical applications. It is also is the largest company judged by sales revenue. At present, Pfizer holds close to 7% of the world market. Table B lists the top 15 global pharmaceutical firms.

The lower price per dollar of revenue (and gallon of high-purity water) is reflected in lower expected revenues by the major companies because of generic drugs. Lilly is expected to see their sales erode 9.05% from 2014 through 2020. Pfizer and Bristol-Meyers Squibb are projected to see their sales erode at rates above 3% between 2014 and 2020. The average sales impact will be nearly 4%.

Generic medicines are making significant penetration worldwide. In the U.S., generics captured 25% of the 2012 market. In 2012, the combined pharmaceutical industry U.S. revenues were $209 billion. Of that amount, $156 billion came from companies offering brand name products, and $53 billion came from firms selling generic pharmaceuticals. Globally, the total number of pharmaceutical companies is 3,810, of which 2,707 make brand name products, and 1,103 compete with generic drugs.

There was a 7% negative impact on sales of the top 3 brand name companies in the U.S. in 2012. Merck was the largest brand name supplier in the U.S. in 2012 with sales of $24 billion. Other top players were Pfizer and AstraZeneca.

Merck leads with a 13% market share, followed by Pfizer and AstraZeneca with 10% market shares, respectively. Other market leaders in the U.S. include GlaxoSmithKline, Joynson and Johnson, and Eli Lily & Co. Figure 2 shows chart with estimates of the U.S. market place held by leading industry companies.

Teva Pharmaceutical and Watson Pharmaceuticals Inc. were the largest suppliers of generics in the U.S. in 2012 and each had a had a 5% market share. Sandoz Ltd. and Mylan Inc. are also leading providers of generic drugs.

International Markets

The leading industry growth markets are in Brazil, Russia, India, China, Mexico, and Turkey (also referred to as BRICMT). These nations have shown annual growth rates of 15%.

Pfizer experienced an overall growth rate of 16% in these countries between fiscal 2011 and 2012. The firm's two leading markets were Russia (34%) and China (32%). Pfizer's growth rates in the other nations were as follows: Brazil, 14%; India, 11%; Mexico, 4%; and Turkey, -7%.

Sandoz in 2012 experienced sales increases of 29% in Brazil, 27% in China, 15% in Russia, and 30% in Turkey.

More than 20% of Novartis revenues ($13 billion) were generated in Asia/Africa/Australia in 2012. Europe is the firm's leading market with sales of $20 billion (35%), followed by $19 billion in the U.S. (33%). Canada and Latin America contributed $5 billion (9%) of the company's sales.

Russia. The pharmaceutical industry in Russia has been witnessing double-digit growth rate recently. In October 2009, the Russian Ministry of Industry and Trade adopted the Pharma 2020 strategy, which encourages the local pharmaceutical companies to produce high-quality medications according to the good manufacturing practice (GMP) standards. It targets innovative conversion and competitiveness for boosting the Russian pharmaceutical sector, and to improve the production capacity.

According to the new regulations that will be enforced in Russia from 2014, it will be imperative for the pharmaceutical companies to pursue GMP-compliant production procedures.

The local industry is expected to develop about 50% of Russian-consumed drugs if the pharmaceutical industry in Russia grows at the same pace until 2020. The Russian pharmaceutical market is expected to reach $10.7 billion value by 2014.

By contrast with Japan, generic products account for more than 70% of use in Russia, where Sandoz, Novartis Pharmaceuticals, and Alcon, combined, rank as the country's largest pharmaceutical companies.

In December 2010, Novartis announced a 5-year, $500 million investment program in Russia, including construction of a state-of-the-art manufacturing plant in St. Petersburg. Commercial production at this new facility is scheduled to begin in 2014; generic products will account for the majority of output. The Novartis investment program in Russia also includes research and development collaborations, as well as public health initiatives.

Through a program called Pharma 2020, the Russian government is investing the equivalent of $4 billion to become more self-sufficient in producing prescription medicines.

China. Top players in the Chinese pharmaceutical industry are China National Pharmaceutical Group Corp. (Sinopharm), Shijiazhuang Pharma Group, Wuxi Pharmatech, and Harbin Pharmaceutical Group Co. Leading foreign players such as AstraZeneca, Pfizer, Bayer, and GSK, among others, have established themselves firmly in the market and are regularly expanding their services within the country. With the entry of foreign players in the industry, the quality of pharmaceutical manufacturing processes and use of high-purity water has increased.

Generic drug sales in Japan represent only 24% of overall consumption of prescription drugs in terms of volume. The comparable figure for the United States is approximately 80%,, and generic sales penetration exceeds 60% in Germany, Russia, and the United Kingdom.

Despite the growth in the developing countries, the production of high-purity water is still concentrated in the developed countries. Local production of pharmaceuticals is falling behind demand. The imports are still significant.

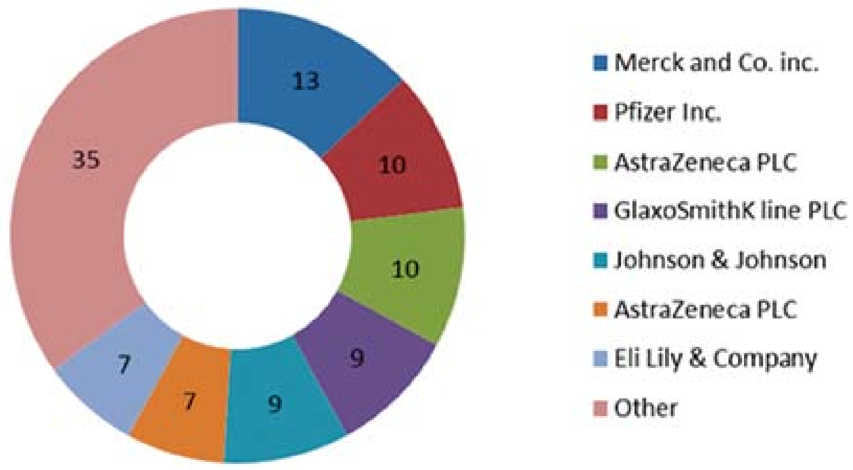

Figure 2. Market share of pharmaceutical industry leaders.

In the coming years the disparity between local supply and demand will be reduced. Table C provides examples of some of the pharmaceutical plant projects completed or under construction for the 2012-14 period in developing countries.

Closing Thought

The market for UPW systems and consumables will grow at close to double digit rates in the developing countries in the coming decade. Technology will also continue to involve at a rapid rate. Instrumentation and automation innovations will have the most significant impact on system performance.❑

Author Robert McIlvaine founded The Mcilvaine Company in 1974. Prior to beginning the company, he worked as an executive in the foundry, power, and pollution control industries. Among the areas focused on by the company are different aspects of water treatment, including pharmaceutical water treatment. He can be reached at rmcilvaine@mcilvainecompany.com.

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TABLE A
Key High-Purity Water System and Consumables Markets
($, millions)

Industry	*2014*
Coal-fired power	$1,237,082.23
Electronics	$1,472,607.61
Flat panel	$648,048.37
Gas turbines	$78,604.59
Industrial power	$372,615.40
Other industries	$198,459.93
Pharmaceutical	$440,751.56
Total	**$4,448,169.69**

TABLE B
Top World Pharmaceutical Corporations

Current Rank	*Corporation*	*Nationality*	*2012 Market Share (%)*
1	Pfizer	U.S.	7
2	Novartis	CH	6
3	Merck & Co.	U.S.	5
4	Sanofi	France	5
5	Astranazenca	Great Britain	4
6	Roche	Switzerland	4
7	GlaxoSmithKline	Great Britain	4
8	Johnson & Johnson	U.S.	3
9	Abbott	U.S.	3
10	Teva	Israel	3
11	Lilly	U.S.	3
12	Tadeka	Japan	2
13	Bristol-Myers Squibb	U.S.	2
14	Bayer Schering Pharma	Germany	2
15	Amgen	U.S.	2

TABLE C
Pharmaceutical Industry Projects Underway for 2012-2014

Location	*City*	*Project Title*	*SIC Description*	*Product*
Algeria	Saidal	Sanofi Aventis	pharmaceuticals	pharmaceuticals
Belarus	Minsk	National Academy of Sciences of Belarus (NASB)	biotechnology	genetics and R&D
Cameroon		Sandoz/Cinpharm/1A Pharma	pharmaceuticals	pharmaceutical ingredients
China	Hangzhou and Beijing	Sanofi-Aventis/BMP Sunstone	pharmaceuticals	pharmaceuticals and consumer health products
China	Shanghai	Newsummit	pharmaceuticals	drug development
China	Shanghai	Promega	biotechnology	biological products
Georgia	Tbilisi	Central Public Health Reference Library (CPHRL)		research on human health
India	Maharashtra	Omkar Specialty Chemicals (OSCL)	pharmaceuticals	active pharmaceutical ingredients
India	State in Western India	Helvoet Pharma-2	packaging	pharmaceutical packaging
India	Punjab	Nectar Lifesciences	pharmaceuticals	pharmaceutical ingredients
Malaysia	Nusajaya, Wilayah Iskandar	Malaysian Biotechnology	biotechnology	biotechnology
Uganda		Quality Chemicals Industries (QCI)-1	pharmaceuticals	pharmaceuticals
Russia	Yaroslavl	Takeda	pharmaceuticals	pharmaceuticals
Russia	Moscow, Podolsk District	Aurobindo/OJSC Diod/ Aurospharma	pharmaceuticals	generic and Over-the-Counter Drugs
Russia	Vorsino, Kaluga and St. Petersburg	AstraZeneca-12	pharmaceuticals	pharmaceuticals