

2006-2007 Influenza Vaccine Production & Distribution

MARKET BRIEF



HEALTH INDUSTRY DISTRIBUTORS ASSOCIATION
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For more information about HIDA membership, products, or services, please contact HIDA at (703) 549-4432.

Health Industry Distributors Association (HIDA)
310 Montgomery Street
Alexandria, Virginia 22314-1516

Phone: (703) 549-4432 • Fax: (703) 549-6495 • www.HIDA.org

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I. Preface

During the last influenza season, despite a relatively strong overall supply, healthcare providers and patients expressed frustration with the process by which influenza vaccine travels through the supply chain.

The following trends emerged during the 2006-2007 influenza season:

- **Flu Vaccine Manufacturing Increased.** The Centers for Disease Control and Prevention (CDC) estimate 120.9 million doses of flu vaccine were produced. This exceeds average production in each season since 2000-2001 (88.3 million doses), and is more than any past season.
- **Delays in Vaccine Manufacturing.** Timing was a crucial issue this flu season—highlighting, as in past seasons, that the question of when influenza vaccine reaches the point of care is as important as how much vaccine is produced. As in several recent seasons, total projected production numbers were achieved by the conclusion of the 2006-2007 flu season. However, the supply came later than expected or arrived in several staggered and/or partial shipments during peak periods of demand.

This report by the Health Industry Distributors Association (HIDA)—the second in a series—explores the current dynamics involved in influenza vaccine production and distribution. For information on past seasons, or for further detail on influenza production and distribution information, visit www.HIDA.org.

II. Distribution's Role in Influenza Vaccination

The influenza vaccine supply chain is divided into two channels. In one channel, vaccine is sold directly by the manufacturer to a customer (a physician office, public agency, pharmacy, community vaccinator, etc.). In another channel, vaccine is sold by manufacturers to distributors, who in turn deliver vaccine to their customers; primarily physician offices [Figure 1]. During the 2006-2007 influenza season:

- Manufacturers shipped about 50% of the flu vaccine supply directly to their customers [Figure 2].
- Distributors committed to order and deliver approximately half (the remaining 50%) of the vaccine supply—an increase from the previous season when about 35% of vaccine went through distributors.

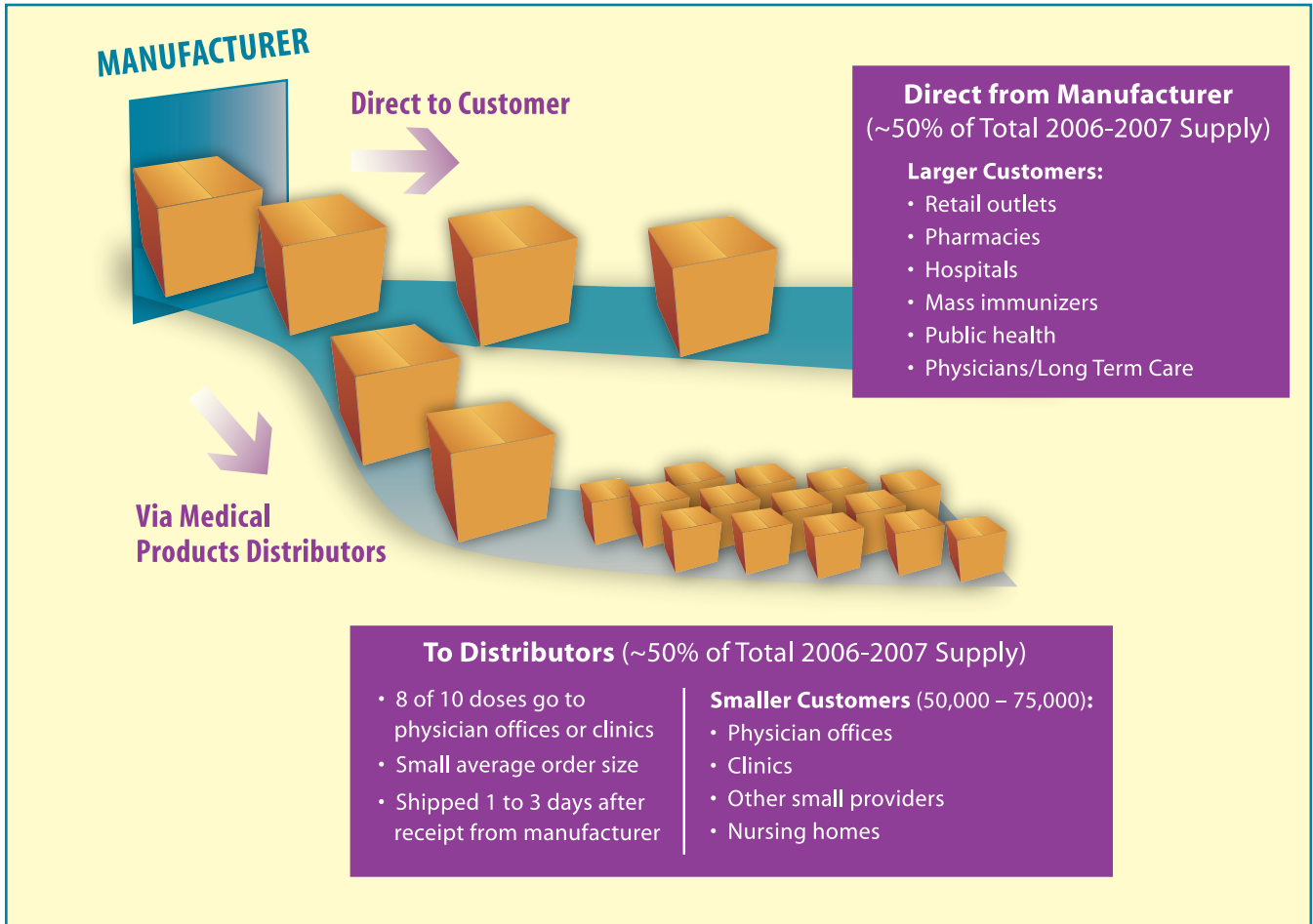
For the purposes of this report, “distribution” refers to how vaccine travels through the supply chain; i.e., the process of transferring vaccine to the end user. The term “distributor” refers to medical products distributors, who deliver vaccine (along with other products and services) across healthcare settings that include physician offices, hospitals, and nursing homes. The term “distributor” may also refer to wholesalers (firms that deliver to larger providers such as government agencies, hospital pharmacies, home health facilities, and others).

Distributor Facts

- Generally, 1 to 3 days pass between the arrival of flu vaccine at a distributor's loading dock and its delivery to the customer.
- Distributors are the primary channel for delivering influenza vaccine to physician offices, the preferred venue for vaccination.
- More than 600 distributors across the United States operate more than 800 distribution centers.
- The distribution system is designed to handle a range of delivery volumes to a wide variety of customers.
- Distributors serve more than 50,000 points of care across the country, and more than 12,000 U.S. medical practices with six or fewer physicians.¹

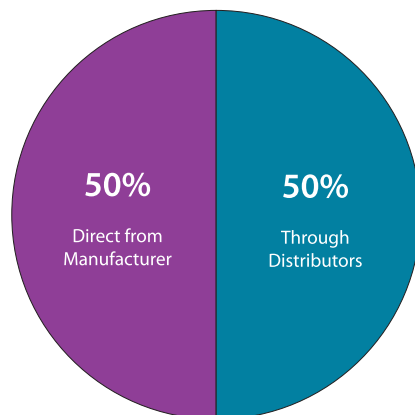
¹ HIDA 2005 Distribution Market Report; HIDA 2006 Physician Market Report.

Figure 1: Two Ways Vaccine Gets to Market



Source: HIDA research, industry sources

Figure 2: Percentage of Vaccine Sold by Channel in 2006–2007



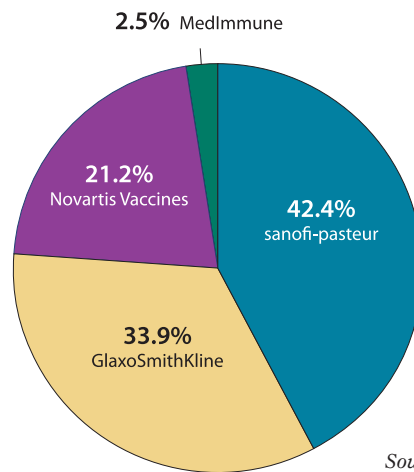
Source: HIDA research, CDC Flu Summit, industry sources

III. Historical Influenza Vaccine Production for the U.S. Market

Four manufacturers (GlaxoSmithKline, MedImmune, Novartis, and sanofi-pasteur) currently produce seasonal influenza vaccine for the U.S. market. During the 2006-2007 season, the largest share of production, approximately 42% of doses, was produced by sanofi-pasteur [Figure 3].

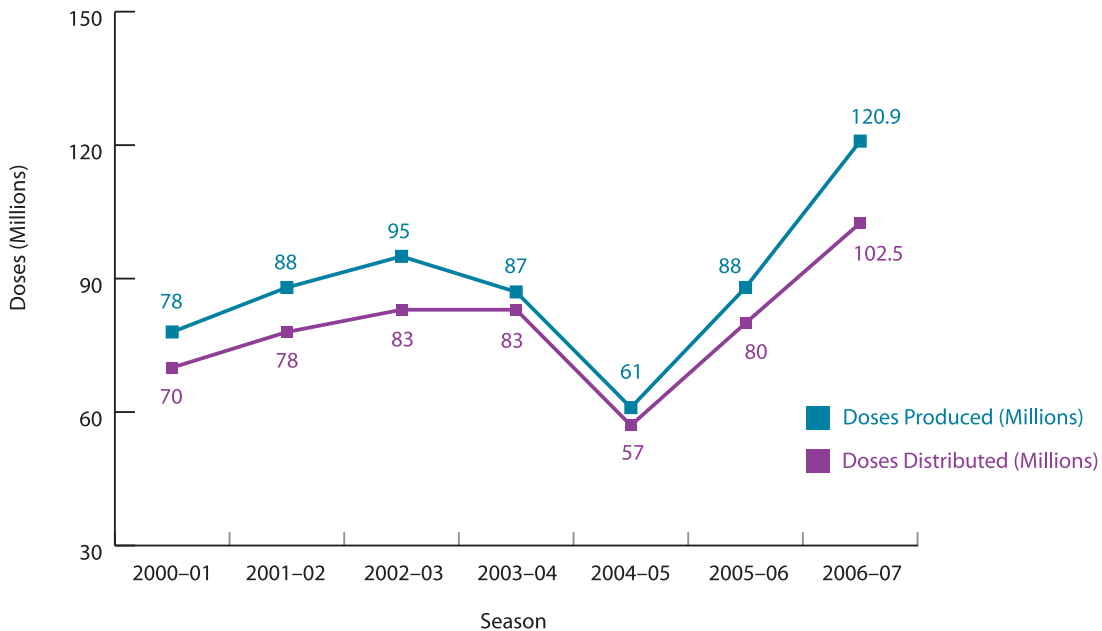
For the 2006-2007 season, approximately 120.9 million doses of flu vaccine were produced—the largest volume to date. The total number of doses distributed was estimated to be 102.5 million doses. Approximately 18.4 million doses were unsold. The number of distributed doses (i.e. ordered by/sent to a distributor or provider) may not reflect how many doses were administered to patients or demanded by patients [Figure 4].

Figure 3: Doses Produced in 2006-2007 (Projected: Total of 120.9 Million)



Source: Company press releases

Figure 4: Influenza Vaccine Production for the U.S. Market, 2000-2007



Source: U.S. Food and Drug Administration Center for Biologics Evaluation and Research; Centers for Disease Control and Prevention

The global market for influenza vaccine is expected to grow by 13.2% annually through 2012. By 2012, worldwide influenza vaccine sales are expected to exceed \$4 billion.²

By 2011, global demand for seasonal influenza vaccine is expected to be approximately 600 million doses, a 50% increase from 2006 demand (as indicated by global vaccination guidelines) and representing 8% annual growth.³ During 2006, the major manufacturers reported increased influenza vaccine revenues [Figure 5].

Figure 5: Change in Influenza Vaccine Revenues, 2006

Manufacturer	Increase in Influenza Vaccine Revenue (Percent)
Novartis	N/A
sanofi-pasteur	27.5%
GlaxoSmithKline	60%
MedImmune	71%

Source: Company press releases and financial reports

IV. Preferred Sites for Vaccination

Across all age groups, patients prefer to receive influenza vaccinations at a doctor's office [Figure 6]. Depending on age group, between 39% and 46% of patients actually receive their influenza vaccine in a physician office. For patients between the ages of 18 and 65, the workplace is also a popular vaccination site.

Figure 6: Sites for Flu Vaccination: Actual vs. Preferred

		18–49	50–64	65+
Doctor's office	Actual	46%	39%	45%
	Preferred	59%	46%	52%
Workplace	Actual	26%	18%	1%
	Preferred	25%	17%	0%
Clinic/community health center	Actual	4%	16%	18%
	Preferred	2%	13%	14%
Retail Store	Actual	10%	6%	11%
	Preferred	0%	2%	5%

Source: Centers for Disease Control and Prevention/Gallup Organization, courtesy of the American Academy of Family Physicians (2005-2006)

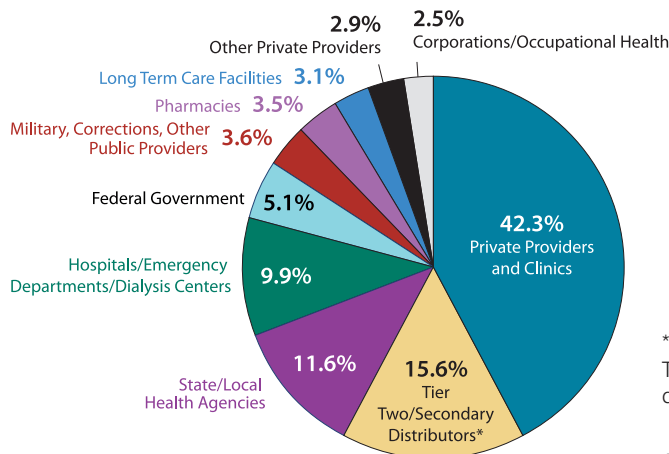
² Mitchell, Steve. "Analysis: Vaccine Market to Top \$23B." United Press International (February 9, 2007).

³ Reinhardt, Joerg. "Vaccines and Diagnostics—A New Strategic Growth Platform." Novartis Vaccines and Diagnostics (Jan. 18, 2007).

V. U.S. Influenza Vaccine Sales by Provider Type

While only 42% of vaccine produced (including that sold directly and through distributors) was sold to physician offices [Figure 7], 80% of vaccine doses sold by distributors were provided to physicians. Of all doses, 3.1% were sold to long-term care facilities, 10% were sold to hospitals, and about 19% went to pharmacies and tier two (or secondary) distributors, according to the CDC.

Figure 7: 2006-2007 Vaccine Sales by Customer Type



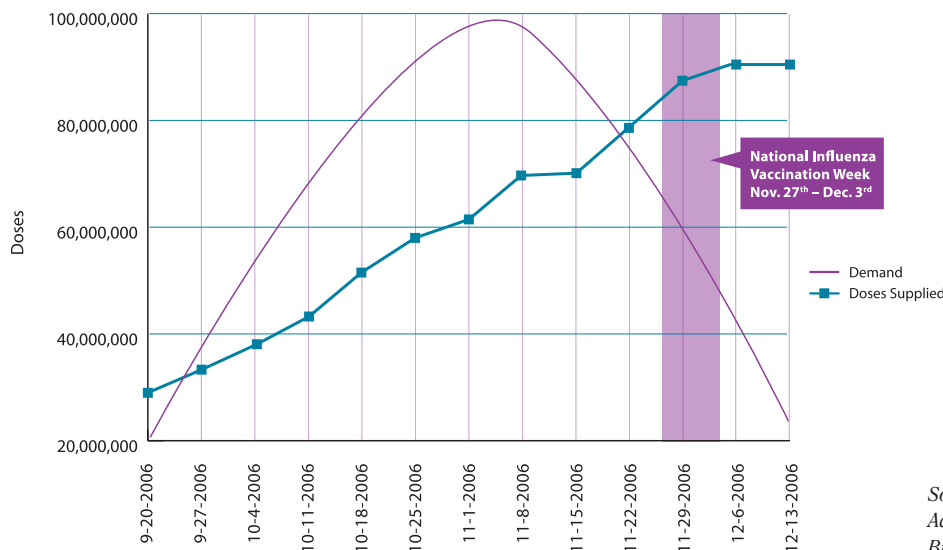
*Tier two/secondary distributors are not end users. They are distributors that purchase vaccine from other distributors and deliver to providers.

Source: Centers for Disease Control and Prevention

VI. U.S. Influenza Vaccine Demand Peaks Before Supply

Healthcare advocates worked to broaden the vaccination season into November and December (e.g., National Influenza Vaccination Week from Nov. 27 to Dec. 3, 2006). However, demand for flu shots remained at its highest levels in September and October. As is typically the case, vaccine delivery to distributors was staggered. As a result, some providers did not receive their expected order before the period of peak demand [Figure 8].

Figure 8: Cumulative Vaccine Releases, 2006-2007 Season

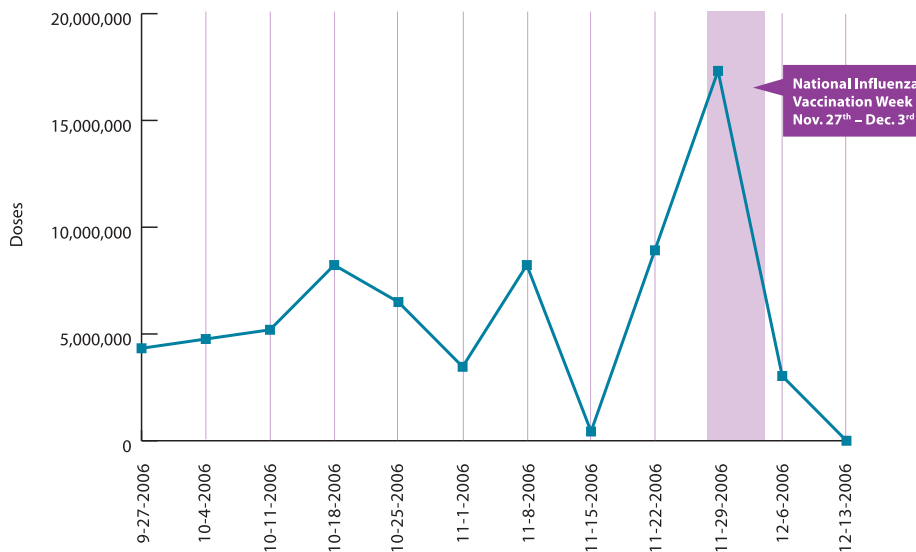


Source: U.S. Food and Drug Administration, Center for Biologics Evaluation and Research

VII. Number of Doses Varies Weekly

The number of doses released into the supply chain by manufacturers varied weekly, from several hundred thousand doses in one week to more than 15 million doses in another. This variability made it difficult for distributors and their customers to predict and plan for when they would receive their vaccine [Figure 9].

Figure 9: Weekly Releases, 2006-2007 Season



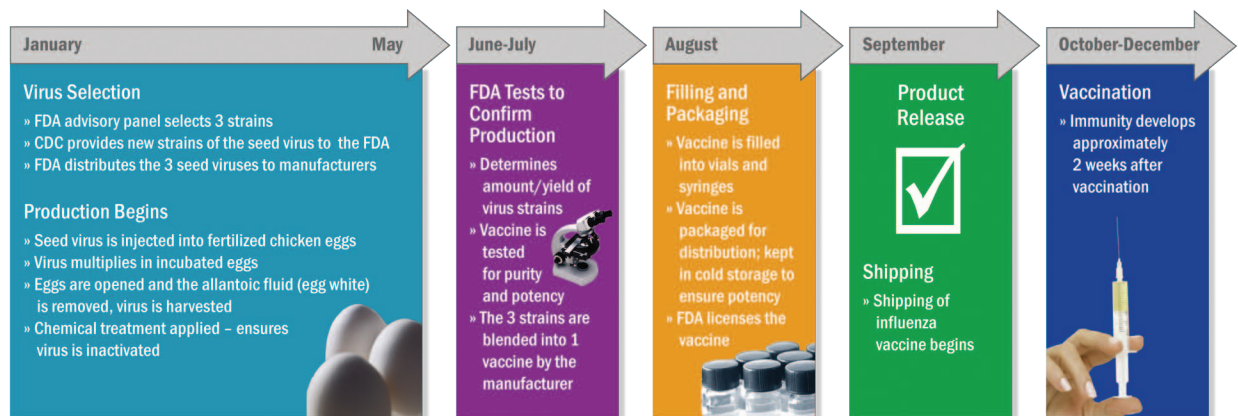
Source: U.S. Food and Drug Administration, Center for Biologics Evaluation and Research

Note: The above figure, timeline, and data capture the FDA approval and release of already-manufactured vaccine. Approved and released vaccine has not necessarily reached physicians, hospitals, other providers, or patients—there is a delay between the conclusion of the approval and release process and the delivery and administration of the vaccine.

VIII. Influenza Vaccine Manufacturing Process

The manufacturing process is typically five to eight months long. It is subject to delays depending on the results of virus selection and incubation processes [Figure 10]. Vaccine manufacturers are currently exploring new ways of producing vaccine that eliminate the long lead times required for current egg-based manufacturing. Those methods have not yet been approved for mass production.

Figure 10: Influenza Vaccine Production Timeline



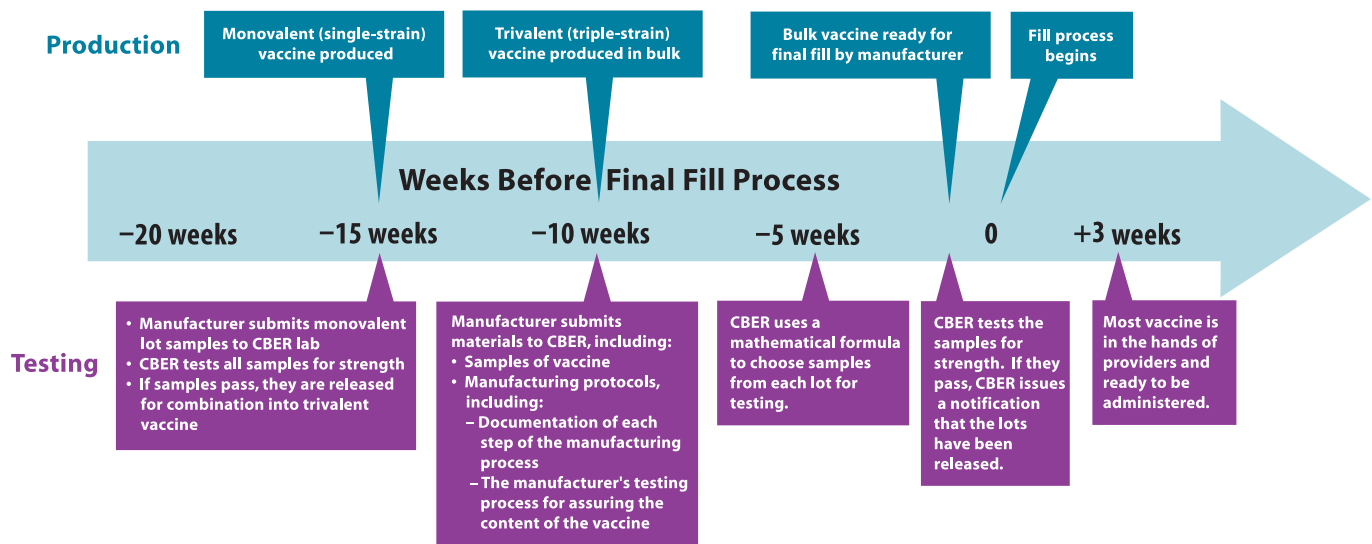
Source: www.flusupplynews.com

IX. 15+ Week Lot Release and Testing Process

Manufacturers are required to submit samples of vaccine to the U.S. Food and Drug Administration's (FDA) Center for Biologics Evaluation and Research (CBER) to ensure their effectiveness and safety. These analyses are conducted by CBER scientists at the monovalent stage (when vaccine is developed for a single strain of influenza) and at the trivalent stage (three monovalent vaccines are combined into a final vaccine targeted toward three virus strains) [Figure 11].

The lot release process must be repeated for each lot of vaccine that the manufacturer produces. Over the course of the most recent influenza season, the release process ranged from 21 lots (for MedImmune) to 85 lots (for sanofi-pasteur).

Figure 11: Influenza Vaccine Lot Release Process



Source: U.S. Food and Drug Administration, Center for Biologics Evaluation and Research; HIDA independent research

Vaccine manufacturers are required by law to submit samples of each manufacturing lot of vaccine to CBER to ensure that they meet FDA standards for effectiveness. Once the lots are approved, they are officially released by CBER and are ready to be packaged and sold by the manufacturer. The guidelines for the lot release process appear in the Combined Federal Regulations (CFR):

- **610.1 Tests prior to release required for each lot.**
No lot of any licensed product shall be released by the manufacturer prior to the completion of tests for conformity with standards applicable for such product. Each applicable test shall be made on each lot after completion of all processes of manufacture which may affect compliance with the standard to which the test applies. The results of all tests performed shall be considered in determining whether or not the test results meet the test objective, except that a test result may be disregarded when it is established that the test is invalid due to causes unrelated to the product.
- **610.2 Requests for samples and protocols; official release.**
(a) *Licensed biological products regulated by CBER.* Samples of any lot of any licensed product together with the protocols showing results of applicable tests, may at any time be required to be sent to the Director, Center for Biologics Evaluation and Research. Upon notification by the Director, Center for Biologics Evaluation and Research, a manufacturer shall not distribute a lot of a product until the lot is released by the Director, Center for Biologics Evaluation and Research, provided that the Director, Center for Biologics Evaluation and Research, shall not issue such notification except when deemed necessary for the safety, purity, or potency of the product.

Acronyms

Centers for Disease Control and Prevention (CDC)
U.S. Food and Drug Administration (FDA)
Center for Biologics Evaluation and Research (CBER)
Combined Federal Regulations (CFR)

Sources

- Centers for Disease Control and Prevention (www.cdc.gov)
- U.S. Food and Drug Administration, Center for Biologics Evaluation and Research (<http://www.fda.gov/cber/flu/flu.htm>)
- American Academy of Family Physicians (www.aafp.org)
- Flu Supply News (www.flusupplynews.com)

About HIDA

The Health Industry Distributors Association (HIDA) is the international trade association representing medical products distributors. Since 1902, HIDA has provided leadership in the healthcare distribution industry.

HIDA also works closely with the manufacturing community through the HIDA Educational Foundation. This outreach

serves to build strong manufacturer/distributor relationships as well to communicate the value of distribution in the healthcare supply chain.

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