

Assuring Vaccine Supply

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Assuring Dependable Vaccine Supply

- Crucial to use all available expertise in immunization policies
- Vaccine industry should be brought back to table as full participant in formulating and implementing policies
 - Currently industry expertise is significantly underutilized

Vaccine Development

- Pool of vaccine manufacturers is small
- Vaccines involve the growth of living organisms, which adds to complexity of development and production

Industry Participation in Policymaking

- Manufacturers are best able to determine timeframes for implementing policy changes
- Manufacturers have direct contact with health care providers and understand responses to policy changes
 - Particularly in private sector



Industry Participation in Policymaking

- Vaccines and Related Biological Products Advisory Committee (VRBPAC) includes manufacturers
- National Vaccine Advisory Committee (NVAC) has historically included industry although there is currently no representation
- CDC's Advisory Committee on Immunization Practices (ACIP) does not include manufacturers as full participants in working groups



Where Dialogue Has Worked

- Dialogue is greatly improved on influenza vaccines regarding production and distribution
 - Manufacturers advise CDC how many doses of influenza vaccine they plan to produce
 - When there was unprecedented demand in 2003, Aventis Pasteur set aside 250,000 doses and worked with CDC to ensure that these doses would reach those at greatest need
 - The Influenza Summit is a good example of all sectors coming together to resolve issues



Communications, Coordination and Cooperation with U.S. Government

- Aventis' goals include ensuring that manufacturing capability, capacity and new product launches are in harmony with government guidelines
- Industry must understand how government agencies interpret guidelines and recommendations
 - Some rules and regulations are clear, but others are subject to interpretation
 - Requirements occasionally change after studies are underway



Challenges for Clinical Development

- Challenges exist in pre- and post-licensing phases
- FDA is making parameters stricter and requesting large sample populations to fulfill parameters
- In post-licensure, there is also the requirement for increasingly larger studies
 - Has unintended effect of saturating clinical study sites that can handle large population sample sizes
 - Increases product development timelines and data

Knowledge of Industry Process

- Despite enormous talent within regulatory agencies, staff does not always have insight into day-to-day aspects of manufacturing process
 - Product development and manufacturing processes are very specific
- It takes years to understand specific challenges in vaccine production even for industry engineers, R&D and manufacturing teams
- To remedy this, Aventis is urging that Congress expand funding for FDA's Center for Biologics Evaluation and Research (CBER)
 - To keep CBER scientists up to date in vaccine technology
 - The more informed regulatory authorities are, the higher will be the comfort level in accelerating important vaccine development; thereby, reducing potential supply problems



Impact of Government Decisions

Example 1

- In 1999, CDC issued a joint statement with the U.S. Public Health Service, FDA, AAP and AAFP to reduce preservatives in all childhood vaccines
- Policy guidance was issued with relatively short notice
 - Manufacturers had to move away from preservatives and to single-dose packaging from multidose vials
- Due to lack of industry consultation, government agencies did not fully understand the dramatically impact on product development and vaccine supply
 - Reformulation of DTaP took approximately two years and reduced total vaccine output by approximately 25%



Impact of Government Decisions

Example 1

- In absence of evidence of a safety issue, regulatory changes that require production alterations should allow ramp-up time for producers to meet new guidelines without disrupting product supply

Impact of Government Decisions

Example 2

- Request for proposal (RFP) issued for clinical studies for pandemic influenza and biodefense procurement requested that vaccines be produced in preservative-free, single-dose vial presentations
- This would necessitate clinical study and stability data only relevant to single-dose vials, but an actual global pandemic would require use of multidose vials
- A more pragmatic approach would consider what would be needed in real-life scenario
 - Globally, there is insufficient capacity to produce enough pandemic vaccine in single-dose vials



Good Manufacturing Practices and Emerging Regulatory Environment

- It is critical that industry works collaboratively with government regarding cGMPs to streamline and accelerate validation requirement process
 - Will further expedite licensing of manufacturing facilities
 - Will avoid manufacturers building factories after receiving promising results and prior to receiving a license
 - Current methods may necessitate different factory specs and processes
 - Cannot compromise quality and safety



Good Manufacturing Practices and Emerging Regulatory Environment

- Vaccine production and launch could be delayed pending validation of the process, buildings and equipment
 - The sooner validation occurs, the faster manufacturers can respond to recommendations for launch
- There needs to be more extensive consultation about cGMPs when they are on the drawing board
 - Should include more public/private dialogue
 - This has started to occur over the past year with the FDA GMP reform initiative

Good Manufacturing Practices and Emerging Regulatory Environment

- Aventis recognizes the important of cGMPs in vaccine product, especially as they relate to safety and effectiveness
 - Yet, what may appear to be a minor policy change regarding vaccine manufacturing can result in incomplete or overly complex solutions that delay vaccine production
- Government, health care providers and general public should understand that vaccine development involving increased emphasis by the FDA on cGMPs requires:
 - Ongoing investment in facilities
 - Process validation
 - Hiring and training of personnel with specialized expertise



How to Improve Validation Process

- Improve facilities
 - On average, validation for a new building can take 1-2 years
- Accelerate validation processes
 - Without creating supply interruptions
- Accelerate clinical development of processes
 - Improve efficiency to expedite availability of new products to patients

Ensuring Adequate Vaccine Stockpiles

- Government, health care community and industry agree that it is essential to establish stockpiles for routine vaccines
- Manufacturers are blocked in completing task due to recent SEC accounting regulations that determine timing for stockpile revenue recognition
- To resolve this issue, there must be engagement between industry and government
 - SEC issue demonstrates importance of communication among government agencies
 - Must resolve problems like this promptly in the interest of public health



Summary

- As industry is underutilized in policymaking, manufacturers need to again be an active participant in the immunization enterprise
 - Greater industry participation ensures more informed policy development and effective implementation
 - Industry should have opportunities to engage in substantive dialogue and provide input
 - Not delegated to the role of information supplier
 - There should be an industry role in NVAC and ACIP working groups
- Government and industry must recognize and address concerns about actual or potential conflicts of interest
- Manufacturers should accept responsibility for proposing an industry code of conduct

