product performance are opportunities that could improve the safety, purity and potency evaluations of vaccines.

Improved Disease Models

Better predictors of disease models are a major area where additional development is needed. In order to respond to bioterrorism threats, expanded resources are needed for large and small animal models that are suitable for ensuring that products being developed are likely to be safe and effective in humans. Development of models for bioterrorism threat agents such as smallpox, anthrax, as well as naturally occurring threats such as severe acute respiratory syndrome (SARS) and pandemic influenza would greatly facilitate the development of relevant counter measures. Similarly, development of better tissue culture systems for hepatitis C, West Nile, or SARS may improve the product development pipeline by providing more sustainable, screening tools for candidate products directed at those infectious agents.

FDA is uniquely positioned to identify these challenges in product development. CBER's strong research base allows for staff to generate data to support regulatory decisions and is instrumental in identifying and developing solutions for public health regulatory challenges. CBER research impacts a number of aspects of product development including product characterization, potency testing, adventitious agent testing, understanding and optimizing the immune response to vaccines or the disease pathogenesis of organisms, development of standards and methods, as well as developing better clinical data analysis tools. These research activities allow for CBER to be better aligned with the challenges of new technologies or public health questions, as well as to be a major contributor in addressing critical path questions.

CBER OUTREACH TO FACILITATE PRODUCT DEVELOPMENT

Although the CFR provides information on the requirements for investigational studies and licensing actions, CBER acknowledges the importance of providing additional guidance and information to vaccine developers on manufacturing, nonclinical testing, and clinical evaluation. Through the issuance of guidance documents, CBER provides its current thinking as to how the requirements of the CFR can be met and provides insight into possible methodologies and approaches to facilitate product development. Although guidance documents are nonbinding, the issuance of these documents allows for CBER to maintain flexibility in addressing specific regulatory challenges, such as cell substrate issues or licensure approaches for biodefense and pandemic influenza countermeasures, and is a key component in CBER outreach to industry. Specific examples of guidance documents that have been issued regarding vaccine manufacture and product development are found in Table 1. A complete list of guidance can be obtained through CBER's web page (10).

Another key component to outreach is CBER's participation in public workshops and pharmaceutical trade organization meetings to facilitate exchange of information and ideas. CBER staff presentations at these trade meetings have been a highly effective way of communicating new guidances and current thinking in an interactive forum, as well as provide open forums for addressing challenging topics. Examples of workshops in which CBER has been involved include workshops on assessing animal models of efficacy for anthrax and plague vaccines, toxicity testing approaches for vaccines, and most recently, post-marketing vaccine safety. More information on recent workshops can be found at (11).

Table 1 Key Guidance to Facilitate Vaccine Clinical Development

Title	Issue date
Draft guidance for industry: characterization and qualification of cell substrates and other biological starting materials used in the production of viral vaccines for the prevention and treatment of infectious diseases	9/28/2006
Guidance for industry: development of preventive HIV vaccines for use in pediatric populations	5/4/2006
Draft guidance for industry: clinical data needed to support the licensure of trivalent inactivated influenza vaccines	3/2/2006
Draft guidance for industry: clinical data needed to support the licensure of pandemic influenza vaccines	3/2/2006
Guidance for industry: considerations for developmental toxicity studies for preventive and therapeutic vaccines for infectious disease indications	2/13/2006
Draft guidance for industry: toxicity grading scale for healthy adult and adolescent volunteers enrolled in preventive vaccine clinical trials	4/29/2005
Draft guidance for industry: considerations for plasmid DNA vaccines for infectious disease indications	2/17/2005
Guidance for industry: FDA review of vaccine labeling requirements for warnings, use instructions, and precautionary information	10/1/2004
Draft guidance for industry: post marketing safety reporting for human drug and biological products including vaccines	3/12/2001
Guidance for industry: content and format of chemistry, manufacturing and controls information and establishment description information for a vaccine or related product	1/5/1999

Given the global nature of vaccine development, the ability of CBER to understand the issues facing our international stakeholders is critical so that international requirements and U.S. requirements could be met in the most efficient manner. CBER maintains international collaborations through representation at international organizations such as the International Conference on Harmonisation (ICH), the World Health Organization (WHO), Pan-American Health Organization (PAHO), and standards development organizations such as Health Level 7 (HL-7). In addition, CBER maintains relationships with other international regulatory authorities such as Health Canada and the European Medicines Authority (EMEA). CBER participation and exchange of information with the international community helps facilitate harmonization and standardization efforts on a more global level.

SUMMARY

Product development in the United States is conducted under the authority of the U.S. FDA from early states of investigational use through continued evaluation of product performance post-licensure. Critical to the success of product development is communication between the FDA science-based regulatory reviewers and industry. Outreach is an important aspect of how FDA shares current thinking with vaccine developers and