Overview of the Office of Vaccines Research and Review

SLIDE 1
This presentation describes the Office of Vaccines Research and Review, or OVRR, its mission, structure and functions, and the framework used by the FDA for regulating vaccines.

SLIDE 2
The mission of OVRR is to protect and enhance the public health by assuring the availability of safe and effective vaccines, allergenic extracts, and other related products. The Office has over 300 scientists and regulators dedicated to the mission of ensuring that vaccines are safe, effective, and accessible to the U.S. consumer to protect public health.

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The Office is led by an Office Director, supported by a Deputy Director and Associate Directors responsible for various functions in the Office. Program Management Staff and Senior Advisors provide additional support for resource management, including fiscal and personnel resources, information management, and communications.

Divisions under the Immediate Office of the Director include the Division of Bacterial, Parasitic and Allergenic Products; the Division of Viral Products; and the Division of Vaccines and Related Products Applications.

The Division of Bacterial, Parasitic and Allergenic Products, and the Division of Viral Products include regulatory scientists, medical officer, and research review scientists who provide the necessary scientific expertise to review sponsor submissions supporting the development of vaccines. These laboratory-based scientists not only review pre-licensure and post-market submissions, but also conduct research on the most scientifically challenging vaccine development problems facing FDA and vaccine developers. Regulatory scientists, medical officers, and administrative staff in the Division of Vaccines and Related Products Applications, support the managed review of sponsor submissions, conduct meetings with sponsors, and provide expert regulatory advice and guidance to sponsors and manufacturers of vaccines.

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The Office regulates all licensed and investigational vaccines for human use in the United States, and conducts laboratory-based research related to important regulatory problems. Authority to perform these functions is specified in Section 351 of the Public Health Service, or "PHS" Act, and specific sections of the Food, Drug and Cosmetic Act, or FD&C Act.

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Office activities consist of three dominant activities. First, it reviews, evaluates, and takes appropriate actions on investigational new drug applications or INDs, biologic license applications, or BLAs, amendments and supplements to these applications for vaccines and related products, conducts inspections, and other actions as necessary.

Secondly, OVRR develops policies and procedures governing the review of regulated products. Thirdly, OVRR conducts research related to the development, manufacture, and evaluation of vaccines and related products. All of these activities ensure the availability of safe and effective vaccines for the U.S. consumer.

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Every organization in the U.S. federal government has a legal framework for operating. Questions that federal employees must ask include, "Why are we doing what we're doing?" "What is the authority for us to do what we do?" and "Where does this authority come from?" In the United States, we have laws and statutes that are proposed and approved by representatives in Congress and by the President. Some of these laws include the Food and Drug Cosmetics Act, the Public Health Service Act, and the Food and Drug Administration Amendments Act of 2007. These laws establish the legal basis for all of FDA's activities and functions. Laws are interpreted and enforced in the United States by federal agencies through regulations published in the Federal Register. These regulations provide the approach and the requirements that the FDA will use to enforce or regulate products under the law. Regulations are consolidated in the Code of Federal Regulations. Regulations related to the FDA can be found on the web site www.FDA.gov, or through the U.S. Government Printing Office.

A third category of documents is called "guidance."

Guidance documents don't have the same force as law, but they represent FDA's current thinking, or current interpretation, and give sponsors and manufacturers practical advice on important aspects of vaccine development, including testing, manufacture and marketing of products.

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This slide lists the most important laws and regulations related to the development of vaccines.

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OVRR "Guidance for Industry" documents provide broad advice to sponsors on a variety of issues, including everything from how to schedule meetings with the FDA, to the amount and type of clinical data needed to support licensure of novel vaccines. "Guidance" documents provide FDA's current thinking concerning

regulatory issues. Vaccine sponsors and manufacturers may propose alternative methods and approaches and deviate from the
FDA guidance.

However, FDA will require that the sponsor provide a rationale for any deviations. Any deviations must not have a negative impact on the safety and efficacy of the product.

This slide lists some recent guidance documents published by the Office, which provide practical advice to the sponsors and the biopharmaceutical industry as they develop their vaccines.

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The U.S. currently has about 73 licensed vaccines, as of September 2010.

The formulations and delivery methods used for licensed products and investigational products are exceptionally diverse.

This slide shows some of those forms and vaccine technologies.

As you can see, vaccine development is very complicated now. Vaccines may be live or inactivated. Novel vaccines may contain subunit antigens purified from infectious agents, or antigens made using recombinant techniques. Some vaccines are formulated with synthetic peptides. DNA vaccines represent a new frontier for molecular-based recombinant vaccines. Vaccines may be given by a traditional syringe, or by using a unique "delivery system" that may include a specialized cartridge, gold beads, latex beads, micro-droplet aerosols, micro needles, skin patches or electroporation for nucleic acids.

Some vaccines in development, especially those that rely on recombinants antigens, may require novel adjuvants to enhance the immune response. FDA has a continuing challenge to maintain scientific expertise in all of these areas of development.

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This slide provides a general scheme for clinical development, evaluation and licensure of novel vaccines and related products. Before a biologic product can be placed in clinical trials in the U.S., sponsors must submit an IND or investigational new drug application, for review by the FDA.

An IND application should detail how the product was prepared, important product specifications, how the product was evaluated for safety in pre-clinical toxicology studies, and provide a protocol and plan for clinical studies. Safety and the rights of subjects are the most important characteristics that the FDA evaluates in an IND application. Generally, products mature through three phases of clinical testing - Phase 1, 2, and 3.

Results from these clinical trials, along with data that demonstrate a consistent manufacturing process and efficacy of the product, are used to support a biologics license application, or a BLA.

FDA evaluates all of the data related to a product and submitted in the BLA, prior to approving a license for the product. Manufacturers may make changes in the product after licensure, by submitting a BLA supplement. Some changes may require additional clinical studies prior to approval. In some cases, FDA requires post-licensure clinical studies, that is, Phase 4 studies, to gain additional information concerning the safety and efficacy of the product. Not mentioned on this slide is the opportunity for the sponsor to ask the FDA to review their development plans in a pre-IND meeting. After submission of an IND, there are multiple opportunities for a sponsor to meet with the FDA and receive product-specific guidance. Formal meetings are usually planned after Phase 2 studies are complete. If the sponsor intends to submit a BLA, FDA will meet with the sponsor pre-BLA, to discuss submission requirements and regulatory issues.

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The OVRR research program contributes directly to the regulation of vaccines and related products, by addressing scientific aspects of critical regulatory issues. With the emergence of novel vaccine technologies, the FDA needs regulatory and review scientists familiar with state of the art technologies. The OVRR research program addresses all aspects of development and evaluation of vaccines and related products. These activities enhance FDA's ability to develop and maintain a sound scientific base for establishing methods and standards required to ensure the continued safety, purity, potency and effectiveness of vaccines and related products.

At the same time, FDA laboratories are the training ground for the next generation of scientists for the review and regulation of these products.

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The OVRR research program focuses upon improving the ability of the FDA to assess the safety, efficacy and availability of vaccines and related products. OVRR laboratories, as a priority, study factors affecting the safety of regulated products, create and validate appropriate methods and standards, identify new biomarkers, and introduce new methods and standards to evaluate and improve vaccine efficacy. They also develop new concepts and methods that open regulatory pathways to improve availability of vaccines and related products.

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The Influenza Research Program is just one of many research programs in OVRR. Its impact and success can be attributed to unique public-private partnerships that were formed to protect public health annually from seasonal influenza.

Each year, scientists at the FDA, the National Institutes of Health, the Centers for Disease Control and Prevention, the World Health Organization, other national regulatory authorities, and the biopharmaceutical industry, coordinate the selection of vaccine strains, the production of vaccine lots, and the development of laboratory standards that ensure the availability of safe and effective seasonal influenza vaccine. Using time-tested processes, this partnership has been crucial for the global response to emerging pandemic virus strains.

Laboratory activities at FDA have been focused upon developing new high-growth influenza virus strains for vaccines, improving methods for evaluating candidate virus strains prior to vaccine production, and preparing critical standards to determine purity and potency of the vaccines. Looking to the future, OVRR scientists are developing approaches that may improve the manufacture of vaccines, based upon cell culture and other methods. They are also evaluating new methods to assess the potency of the products, and investigating approaches to broaden protection against emerging viruses with pandemic potential. In summary, the Office of Vaccine Research and Review conducts the science-based review and the regulation of vaccines.

This unique research program serves to recruit, train and retain highly qualified scientists, who bring in-depth, state-of-the-art knowledge to the review of vaccine and related product applications. OVRR scientists, medical officers, and review staff are enhancing access to safe and effective vaccine, necessary to protect global public health.

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This concludes the presentation, "Overview of the Office of Vaccines Research and Review".

We would like to acknowledge those who contributed to its development.
Thank you.