Life Cycle Product Development
and the Decision Gate Process

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Introduction
The U.S. Army Medical Research and Materiel Command (USAMRMC) manages and executes research and development, production, and fielding of new medical systems. Their product line includes vaccines, pharmaceuticals, and medical devices, all of which need to meet both DoD-specific and FDA requirements before fielded to DoD service members. USAMRMC has implemented a process called Decision Gate in order to effectively meet these requirements during medical product development. During the Decision Gate Process the product’s readiness/feasibility is evaluated before advancement to the successive developmental stage. What follows is a brief summary of this very complex medical acquisition process.
For each stage, a set of entrance and exit criteria are established based on the capabilities that the product must demonstrate to meet military requirements. Specific documents (required by the DoD 5000 Series) are created during each developmental phase and are used during milestone decisions to assess if exit criteria are met. As a product moves through the developmental stages, the required documents evolve and Key Performance Parameters (KPPs) are developed. KPPs must be testable since this is the only way to ensure a product delivers the desired capability.

The Decision Gate process applies proven business practices, conserves resources, and speeds medical products to all U.S. Armed Forces. It integrates the DoD life cycle acquisition process with the FDA product development requirements and assures that at each decision point, the movement of the product to the next developmental stage is conducted in accordance with product-specific requirements. The table on the next page compares the Acquisition and FDA life cycle developmental stages for medical products and summarizes the major transitions (milestones) that a product must go through for continued development. The entire process, from discovery to disposal, is often referred to as “cradle-to-grave” product life cycle development.

Table 1: Comparison of Acquisition and FDA Life Cycle Stages

<table>
<thead>
<tr>
<th>Acquisition Life Cycle Stages</th>
<th>FDA Life Cycle Stages</th>
<th>Decision Gate Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Materiel Solution Analysis</td>
<td>Discovery and Research</td>
<td>Materiel Development Decision (MDD)</td>
</tr>
<tr>
<td>Technology Development</td>
<td>Preclinical/Clinical Development</td>
<td>Milestone A: Prior to first-in-man studies</td>
</tr>
<tr>
<td>Engineering and Manufacturing Development</td>
<td>Clinical Development</td>
<td>Milestone B: Prior to transition to USAMMDA and commitment to continued clinical studies</td>
</tr>
<tr>
<td>Production and Deployment</td>
<td>Regulatory Submission</td>
<td>Milestone C: Prior to submission of NDA, BLA for FDA for licensure</td>
</tr>
<tr>
<td>Operations and Support</td>
<td>Post Licensure</td>
<td></td>
</tr>
</tbody>
</table>
The first milestone in the Decision Gate process is the Materiel Development Decision (MDD). It is the formal entry into the Defense Acquisition Management System. At this phase, funds are provided to USAMRMC laboratories to conduct basic research to develop vaccines, pharmaceuticals, and device prototypes that meet military needs. There may be more than one product in development for the need defined in the MDD, and this is encouraged so that alternative products can be compared during the discovery phase. The process is explained below and will describe how Milestones A, B, and C function to move a product, such as a vaccine, through the developmental stages.

Lab-scale vaccines are first tested in animal studies and if safety and efficacy are demonstrated then pilot production lots under Good Manufacturing Practices (GMP) may be manufactured (depending on funding or if the laboratory has partnered via a Cooperative Research and Development Agreement (CRADA) with a commercial or nonprofit entity who provides funding). Essential assays or tests that will measure the safety and efficacy of the product are also developed. Animal studies are repeated using the GMP-product. If safety and efficacy are demonstrated in two animal models, and a reproducible GMP manufacturing process developed, the laboratory Product Manager (PM), along with the tech-based Integrated Product Team (IPT), requests a Milestone A Review. During this review, a team of multi-discipline and oversight committees critically evaluate the product before the laboratory Milestone Decision Authority (MDA). If the candidate meets the established exit criteria, then the MDA approves transition of the vaccine to the next developmental stage that will allow early clinical development (Milestone A).

Early clinical development depends on available funding or a CRADA partner who can provide funding. At this phase, the product is still under management of the laboratory, but USAMMDA (U.S. Army Medical and Materiel Development Activity – the advanced product developer of medical products) plays a key role in working with the laboratory to write, organize, and submit the IND application to the FDA. USAMMDA is also the Sponsor for the first-in-man studies even though the product still has not yet formally transitioned to USAMMDA (Milestone B).

IPT members from the laboratory and USAMMDA (as well as the nongovernment partner, if applicable) regularly assess data from early clinical studies to assure that the product meets both the defined acquisition exit criteria and regulatory requirements. If a vaccine meets these requirements, a Milestone B Review is requested before the advanced development MDA. When a successful Milestone B Review is achieved via Decision Gate, the MDA approves continued development of the product. The product at this stage has demonstrated “proof of concept” in early human studies. It is transitioned from tech base to advanced development, and is now under the management of a USAMMDA Life Cycle Product Manager (PM).

The USAMMDA Life Cycle PM is accountable and responsible for the development of the
medical product to FDA licensure and follow-on sustainment. Movement of the product through clinical development and regulatory submission (see table) involves development of a clear regulatory strategy that will also meet established exit criteria. A multi-disciplinary IPT and oversight committees establish a baseline plan for cost, schedule, and performance for the medical product that includes the following: manufacturing, clinical studies, transition to a nongovernment partner for production, sustainment, and regulatory considerations. A risk analysis of the plan is completed to ensure minimal risk or establish ways to mitigate risk. This plan is presented to the MDA for approval. Meetings for review and comment by the FDA are requested for portions of the plan that will involve submission of the BLA/NDA.

At this phase, the IPT assigned regulatory scientist establishes an on-going work relationship with the FDA, and assures all FDA comments are reviewed and addressed by the IPT. The IPT and oversight committees are all working on specific aspects of the plan under management of the PM. The PM is like the conductor of a symphony orchestra, assuring all parts work in harmony to produce one final product that meets acquisition and regulatory criteria. Upon completion of the clinical phase of the plan, the goal to submit the BLA/NDA to the FDA is based on a Milestone C decision. All data obtained during this phase are reviewed before the MDA, as per previous milestone decisions. Approval by the MDA results in submission of the BLA/NDA to the FDA.

Following licensure of the product by the FDA, it is necessary for the USAMMDA PM to establish contracts for procurement and assure that quantities that meet DoD requirements are obtained. The PM is also responsible for release of product from stockpile and assures that FDA regulations for product compliance and post-marketing drug surveillance are met. The USAMMDA PM orchestrates the post licensure stage until the product is no longer needed or is replaced by a newer product that meets the same requirement. At this stage the product is disposed and the life cycle process completed. Few products developed in the laboratory will succeed in making it through all developmental stages, but all products that enter the acquisition process at the MDD will be evaluated using the same process with decision gates and milestone transitions. This process ensures the performance of the product is developed in line with the capability requirements.
About Clinical Research Management, Inc.
Clinical Research Management (ClinicalRM) is not only involved in the testing of new antibiotics in Phase I, II, III studies, monitoring protocol development, site selection, and assistance with FDA approvals, but is also involved in responding to the challenges of antimicrobial resistance. Our epidemiologists track resistance patterns around the globe and they evaluate how the observed resistance appears, where it emanates from, and how we can best contain the spread of the new resistance factors.

Our scientists work with the Government and academia to develop new responses to the ever-growing threat of multiple-resistant superbugs. They use in silico techniques, as well as information from genomics, to determine sites on, or in, these organisms that are most likely to be vulnerable to engineered antimicrobials. ClinicalRM is committed to developing new responses to disease and the challenges presented by these super-bugs. If you feel ClinicalRM can add value to your research efforts, we are interested in speaking with you. Call toll free at (800) 431-9640 or visit www.clinicalrm.com

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Currently a Technical Writer for ClinicalRM, Ms. Golenda has spent over 25 years in designing, implementing and managing diverse biomedical research projects. She is an experienced manager, researcher and teacher with strengths in mammalian/parasite and bacterial cell culture, drug screening, preclinical and clinical protocols, resource management, federal grant procedures, government management policies, technology transfer, technical writing and federal government acquisition policies.

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