



A LIFE SCIENCES COMPANY LIFE CYCLE

**From concept to commercialization
and beyond**

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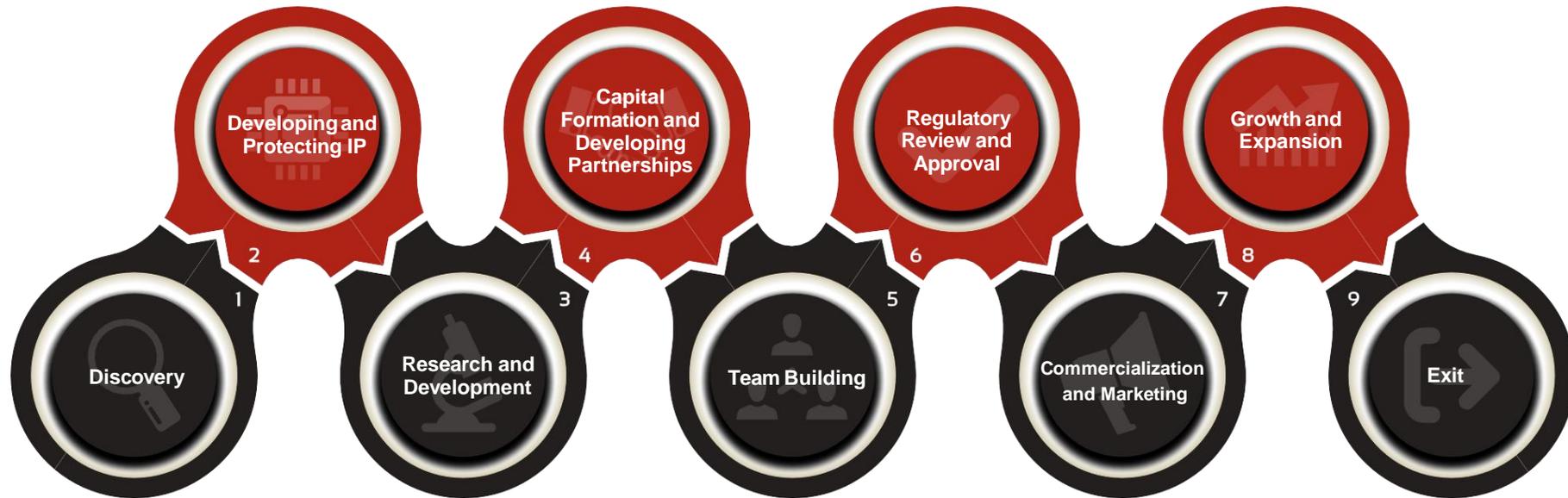
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Overview of the life sciences life cycle



Discovery

- Gain understanding of a particular disease or condition to provide best possible targeted treatments.
- Identify promising candidate or candidates (e.g., compounds/delivery mechanisms) for the diagnosis, cure, mitigation, treatment, or prevention of such disease or condition.
- **Key legal considerations:**
 - Acquisition of assets:
 - In-licensing of product/technology.
 - University spin-outs.
 - Use of platform technologies.
 - Patent prosecution:
 - Early patenting mitigates against competitors beating you to a claim, but delaying application allows for introduction of additional data to strengthen the patent and extend its expiration date.
 - Patent life is typically 20 years but could take 10-15 years to develop the product, leaving only 10 years to sell the product and recoup development costs.
 - Extensions available for drugs but not devices – need to consider how combination product will be regulated.

What is a combination product?

- Primary Mode of Action (PMOA) is the single mode of action of a combination product that provides the most important therapeutic action of the combination product.
 - Codified in FDC Act Section 503(g) and 21 C.F.R. Part 3.
 - Debate over PMOA definition.
 - 21st Century Cures Act attempts to clarify definition as “the single mode of action expected to make the greatest contribution to the overall intended therapeutic effects” of a combination product.
- Combination products include:
 - Two or more regulated components combined, e.g.:
 - Drug/device.
 - Biologic/device.
 - Drug/device/biologic.
 - Two or more separate products packaged together.
 - A drug, device, or biologic packaged separately but intended for use only with another type of product.



Examples of combination products

- Center for Devices and Radiological Health (CDRH) as lead agency for device PMOA
 - Skin bandages with antimicrobial agents.
 - Dental devices with fluoride.
- CDER as lead agency for drug PMOA
 - XHANCE® (Optinose)
 - Transdermal patch or chewing gum for drug delivery.
- CBER as lead agency for biologic PMOA
 - Allergan patches.
 - Syringes filled with RhoD immunoglobulin.

Initial regulatory considerations

- Combination products can be regulated as drugs, devices, or even biologics.
 - New Drug Application (NDA) (505(b)(1)), Abbreviated New Drug Application (ANDA), or 505(b)(2).
 - Premarket Approval (PMA), De Novo Request, or 510(k) Premarket Notification.
 - Review relevant FDA guidance documents for related submission type.
- Product's PMOA needs to be evaluated.
- Request for Designation can be reviewed by Office of Combination Products (OCP).
- Internal expertise may need to differ based on regulatory pathway.
- Timelines to approval differ for drug versus devices and for various submission types.

FDA review timelines

Submission type	FDA review timeline (goal)	Actual timeline
Drugs		
NDA	10 months	
505(b)(2)	10 months	
ANDA	10 months	
Devices		
PMA	180 days	12-18 months
De Novo Request	120-150 days	9-12 months
510(k) Premarket Notification	90 days	6-9 months

Research and development

- Development of a new product normally begins with non-clinical testing followed by different phases of human clinical trials to support regulatory approval of each candidate.
- **Preclinical/non-clinical studies:**
 - Designed to assess the potential therapeutics effects of a drug substance and/or medical device to demonstrate the reasonable safety of a candidate before it can move to human studies.
 - Conducted according to good laboratory practice guidelines, which regulate how laboratory studies are performed.
- **Key legal consideration** – Investigational New Drug Application (IND) or Investigational Device Exemption (IDE):
 - IND/IDE filing must be made prior to beginning human clinical trials.
 - FDA scrutinizes the results from the preclinical testing, looks at side effects and other safety features.
 - Interaction (i.e., pre-submissions) encouraged prior to conducting studies and filing submission.
 - If FDA approves the IND/IDE, then it can move on to human clinical trials.

Research and development (cont.)

- Clinical trials:
 - Designed to evaluate the safety and efficacy of a candidate in humans.
 - Conducted according to good clinical practice guidelines, which are internationally required quality and safety standards for designing, conducting, and reporting trials.
- Stages of clinical trials for combination product regulated as drug:
 - **Phase I – Human pharmacology stage:**
 - Used to evaluate pharmacokinetics parameters and tolerance, generally in healthy volunteers.
 - Studies may include single-dose studies, dose escalation, and short-term repeated-dose studies.
 - **Phase II – Therapeutic exploratory stage:**
 - Small-scale trials to evaluate a candidate's preliminary efficacy and side-effect profile in a limited number of patients.
 - **Phase III – Therapeutics confirmatory stage:**
 - Large-scale trials to evaluate safety and efficacy in large patient populations.
 - Preparations being made for submission of marketing applications based on positive phase III results.
- Stages of clinical trials for combination product regulated as device:
 - Not as structured as drug trial phases.
 - Pilot and pivotal studies usually completed.
 - Human factors testing could be required.

Research and development (cont.)

- **Key business/legal considerations:**
 - Cost of research and development (R&D).
 - Ownership of intellectual property and inventions.
 - Liabilities/indemnification (state/government entities).
- **Key clinical trial documents:**
 - Research organization contract agreements.
 - Sponsored research agreements.
 - Consulting arrangements.
 - Clinical trial agreements.
 - Manufacturing agreements (some details summarized in FDA filing).
 - Patient informed consents (submitted to FDA).
 - Investigator agreements (submitted to FDA).

Partnerships and collaborations

- Partnering with other stakeholders allows your organization to address scientific and technological challenges, create greater efficiencies in R&D, and accelerate discovery, production, and delivery of new treatments for patients.
- **Types of partnerships:**
 - In-licensing: Entity obtains licenses or rights for R&D, commercialization, or marketing of a drug or portfolio of drugs from another entity.
 - Out-licensing: Entity grants rights to research, develop, commercialize, or market a drug or portfolio of drugs to another entity.
 - Joint venture: Two or more entities enter a collaboration wherein all involved parties agree to achieve a specific objective. Typically involves joint governance and decision-making, and sharing of assets and liabilities.

Regulatory approval

- Upon successful completion of required clinical trials, the company can submit its application (NDA, PMA, etc.) for marketing approval.
- The application includes documentation of every stage of the development process to support approval of the candidate product (includes biocompatibility, chemistry, animal and clinical testing as well as manufacturing information, financial disclosures, etc.)
 - Prior (pre-submissions, informal, etc.) interactions before filing the NDA or PMA.
 - Right of references may be needed.
- FDA could take up to 12-18 months for review; however, in case of particularly high medical need or in areas lacking treatment, an expedited review can be granted – typically agreed upon in early interactions with FDA.
 - Review involves back and forth with FDA.
- If approved, the product can be marketed for sale in the United States.
- FDA can require post-approval studies to address any safety concerns (common with NDAs and higher risk devices) or determine suitability for underserved pediatric population (phase IV clinical trials).

Commercialization and marketing

- Marketing and sale of an approved product.
- But there's still a lot to be done first:
 - Obtain favorable pricing/reimbursement.
 - Enter into supply chain agreements (supply, manufacturing, distribution, etc.)
 - Build a sales force (or engage a contract sales organization).
 - Develop promotional materials (no off label promotion) and related standard operating procedures.
 - FDA reviews drug promotional materials but not device materials.
 - Competitors like to report each other.
 - Consider patient assistance programs.
 - Obtain state licenses to be able to sell in a particular jurisdiction.
 - Register and list with FDA.
 - Consider post-marketing FDA oversight (annual reporting requirements, post-approval studies, etc.)
 - Consider any device modifications following approval or clearance.
 - Compliance requirements (manufacturing QSR/GMP), federal/state reporting (Sunshine Act), FCPA, sanctioned countries, restricted parties.

Funding life cycle

- **Discovery stage:**
 - University research.
 - Government research/grants.
 - Nonprofit research/grants.
 - Corporate research.
 - Corporate-sponsored research.
 - Individual research.
 - Friends and family.
- **Development stage:**
 - Outside capital (angels, venture capital, private equity).
 - Structured financing (synthetic royalty financing).
 - Debt (public or private).
 - Initial public offering (capital raise).
- **Exit and growth strategy:**
 - Mergers and acquisitions.

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