Delivering Mission Ready Medical Solutions to the Warfighter

Carrie Laurencot, Ph.D.
Senior Regulatory Affairs Advisor, OPAA/USAMMDA, MRMC

March 18, 2016

Disclaimer

- The views expressed in this presentation are those of the speaker and do not reflect the official policy of the Department of Army, Department of Defense, or the US Government. The speaker has no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the presentation.

US Army Medical Research and Materiel Command

Mission

Responsively and responsibly create, develop, deliver and sustain medical capabilities for the warfighter

Vision

Lead the advancement of military medicine

Why is Army Medicine Involved?

- Select, modify, and procure commercial medical materiel solutions when appropriate or we partner to develop.
- We take the lead in R&D when:
  - The issue is unique to the military
    - Blast injuries
  - Industry/academia lack interest
    - Endemic diseases in specific area of responsibility (AOR)
  - Military needs a timely solution
  - Directed by Congress

Threats to Service Member Health and Performance

Endemic Disease Threats
- Parasitic Diseases
- Bacterial Diseases
- Viral Diseases

Chemical/Biological Warfare Threats
- Bacterial Threats
- Viral Threats
- Toxin Threats
- Nerve Agents
- Vesicant Agents
- Blood Agents

Environmental Hazards
- Heat and Cold
- Altitude
- Toxic Industrial Chemicals & Materials

Battle Sequelae
- Loss of limbs
- Loss of tissue
- Loss of vision
- Pain

Combat Injuries
- Hemorrhage
- Head Trauma
- Blast Injury

Operational Stressors
- Sleep Deprivation
- Traumatic Stress and Situational Stressors
- Physical Work Load
- Cognitive Burden & Operational Complexity

Systems Hazards
- Laser
- Blast
- Biomechanical Insults and Stresses
- Noise

Army Medical Product Development

WE SAVE LIVES… by advancing military medicine through basic and translational research, responsive transitioning, comprehensive medical development, innovative solutions, and timely fielding

- Ensure Manufacturability, Sustainability, Usability, Validity
- Conduct Operational Test
- Obtain FDA Clearance/Approval

Army's Medical Lifecycle Manager

A full lifecycle command leveraging DoD, Federal, Academic, and Industry partners to advance military medicine

LIFE CYCLE MEDICAL MATERIEL MANAGEMENT

Medical Knowledge and Materiel for the Warfighter

DoD and Service Medical Re

Medical Strategic and Operational Logistics

SUCCESSFUL LIFECYCLE MANAGEMENT COMMAND

Defense Acquisition Regulations Directorate

INTEGRATION OF DOD AND FDA REGULATIONS

C·D·R·H

FDA

CDER

CBER

COLLABORATIVE COMMAND

NIAID

ARMY MEDICINE

NATIONAL CANCER INSTITUTE

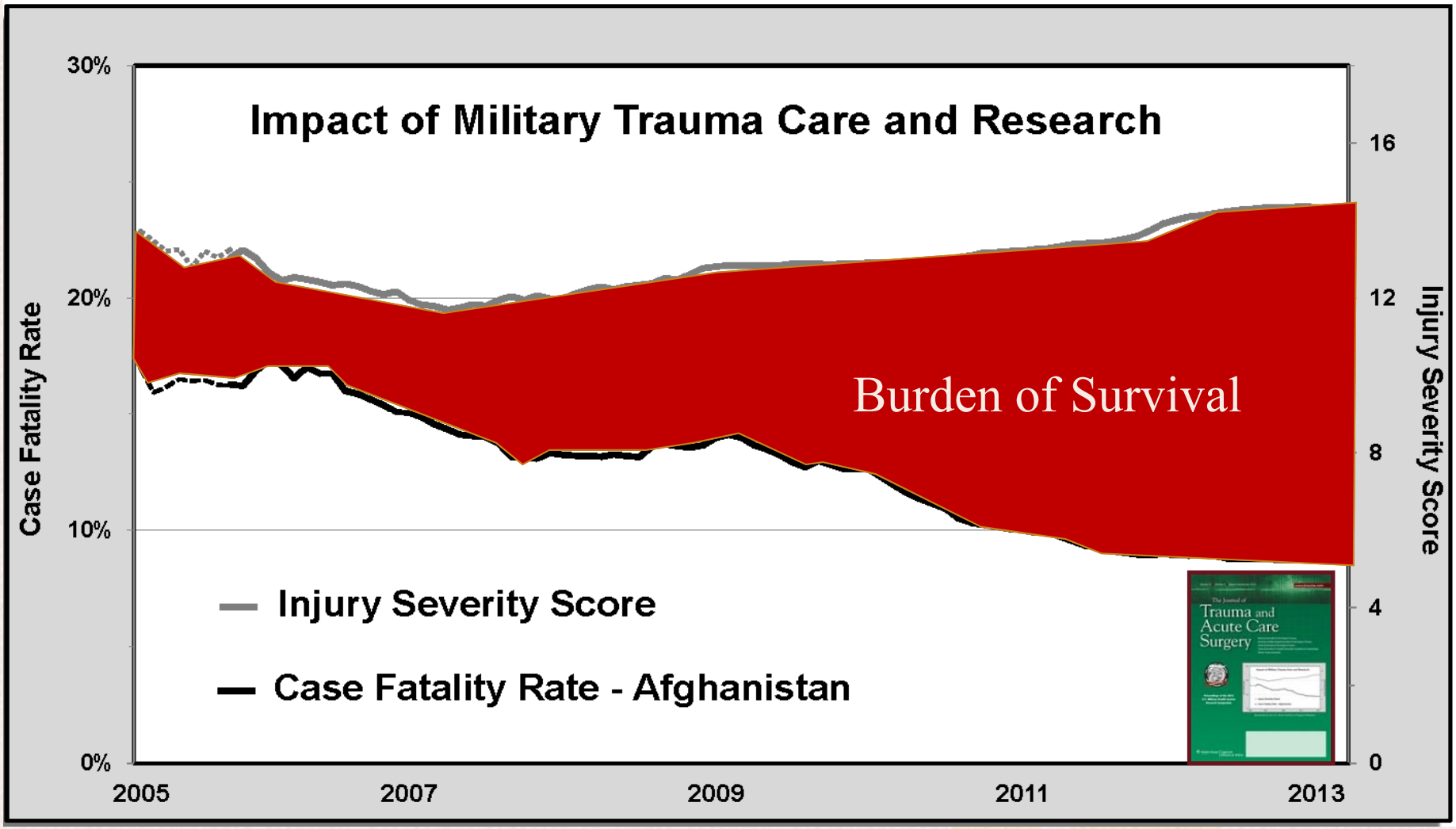
CDC

USDA

Health Affairs

DARPA

Injury Severity and Survival



Regenerative and Rehabilitative Medicine at MRMC

Clinical and Rehabilitative Medicine Research Program (CRMRP)

» Implement long-term strategies to develop knowledge and materiel products to reconstruct, rehabilitate, and provide definitive care for injured Service Members. The ultimate goal is to return the Service Member to duty and restore their quality of life.

Tissue Injury and Regenerative Medicine Project Management Office (TIRM)

» Develop innovative products to restore form, function, and appearance for wounded warriors who have suffered catastrophic injuries.

Portfolio represents >$240M DoD investment and ~$300M leveraged funding

- Over 200 projects
- Five Focus Areas: Extremity Injury Repair, Craniomaxillofacial Repair, Composite Tissue Allotransplantation (Hand and Face Transplants), Skin Injury Repair, Genitourinary / Lower Abdominal Repair
- 21 ongoing clinical trials; 23 pending clinical trials

There are many strategies . . .

. . . but only ONE goal.

Rehabilitation

Tissue Salvage

- O2 generating biomaterials
- Injury mitigation
- Control injury cascade

Restoration/Regeneration

- Bone Scaffolds
- Muscle regrowth
- Skin Substitutes
- Blood Vessels
- Nerves

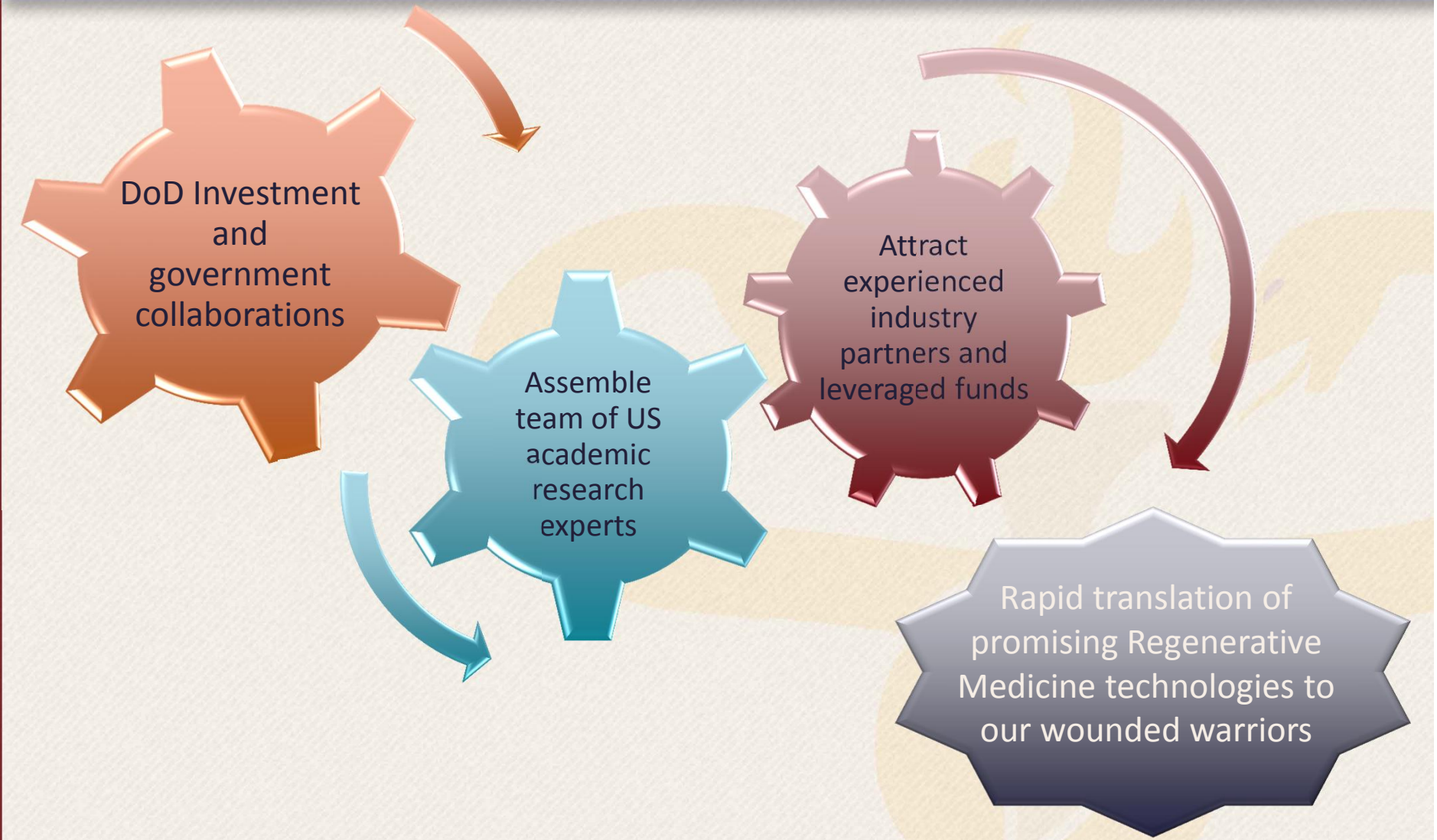
Assistive Technology

- Advanced prosthetics
- Robotics
- Sockets
- Orthotics

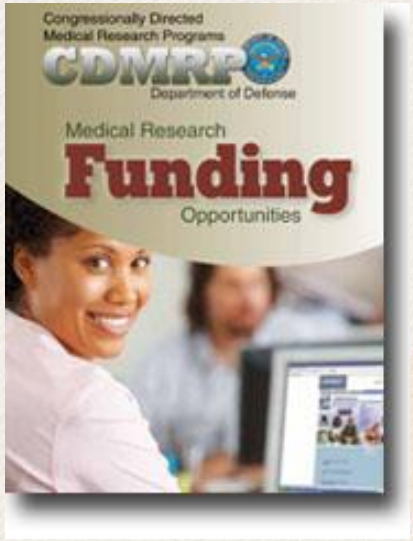
Transplantation

- Hand transplantation
- Arm transplantation
- Novel immunosuppression
- Biomarkers

Strategic Collaboration



Funding Opportunities



http://cdmrp.army.mil/funding/

W81XWH-16-R-BAA1
DoD USAMRMC
FY16 Broad Agency Announcement for
Extramural Medical Research
Department of Defense
Dept. of the Army -- USAMRAA

http://www.grants.gov/web/grants/search-grants.html?keywords=W81XWH-16-R-BAA1

Medical Technology Enterprise Consortium SM

http://www.mtec-sc.org

Fielding Medical Solutions

Lifecycle

- Focus on getting products “fielded”
  - Approved by FDA for intended use
  - Environmentally suited
  - Acceptable to the user community
  - Translatable into clinical practice
  - Reimbursable

FDA Regulated Medical Product Development

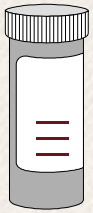
- FDA's regulatory decisions in the pre-market and post-market review process are based on a benefit-risk assessment.
  - Every regulatory decision involves a unique risk/benefit assessment for the disease, patient population, and agent(s) being evaluated.
    - **"One Size Fits All" fits No One!**
- This assessment is informed by science, medicine, policy, and judgment.
  - **Data driven decision making**
- The applicable law, regulations, and Agency policy provide the boundaries within which FDA makes regulatory decisions (i.e Food, Drug and Cosmetic Act, Public Health Service Act)

The Scheme of Things... (the basics)

FDA

Good Manufacturing Practices (GMPs)

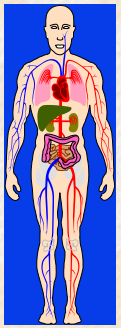
Regulations for manufacturers of Foods, Drugs, Cosmetics to assure the purity, quality and consistency of their product. (Quality Systems for devices)



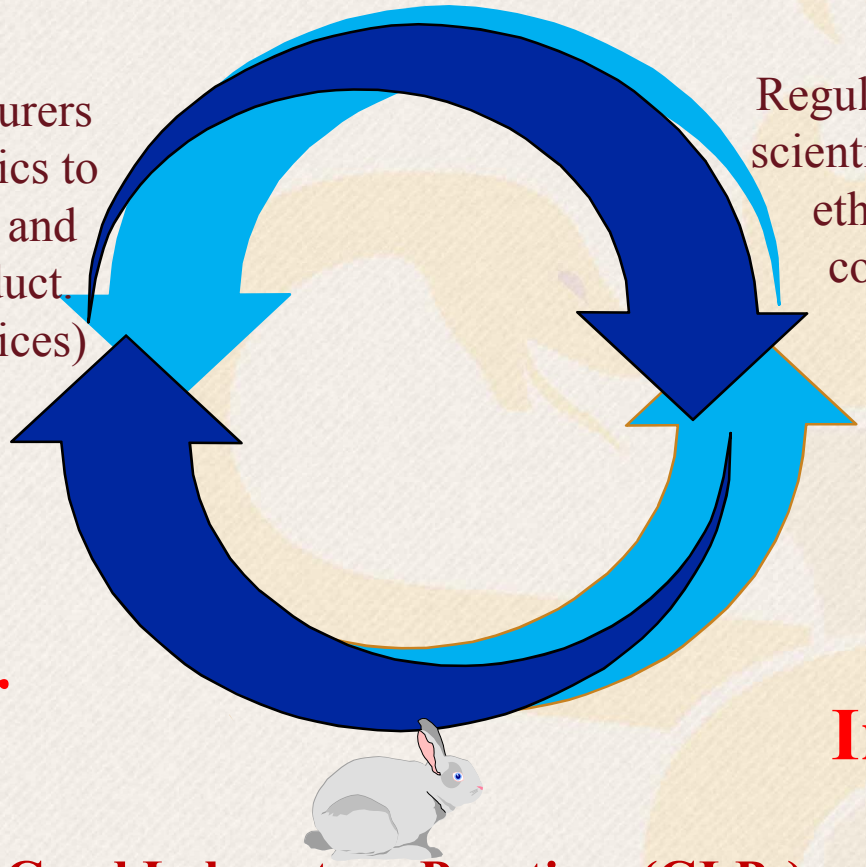
Manufacturer

Good Clinical Practices (GCPs)

Regulations to help assure the scientific quality, integrity and ethics of clinical studies conducted on humans.



Investigator



Good Laboratory Practices (GLPs)

Regulations to help assure the scientific quality and integrity of data from non-clinical (animal) laboratory studies.

From: Dr. Pilaro, CBER, FDA

But wait, there may be more…..

- **Good Tissue Practices (GTPs)**
  - Tiered, risk-based approach to regulation of human cells, tissues, and cellular and tissue-based products (HCT/Ps)
  - Regulations will increase the safety of HCT/Ps by preventing the introduction, transmission and spread of communicable disease.

- **Combination Products**
  - A product composed of any combination of a drug and a device; a biological product and a device; a drug and a biological product; or a drug, device, and a biological product.
    - Can be a single entity (components are physically, chemically or otherwise combined) – i.e. Skin substitutes with cellular components; orthopedic implant with growth factors.
    - May be separate products packaged together; or separate products packaged separately where both are required to achieve the intended use, indication, or effect.

PLAN with the GOAL in MIND

- **GOAL = FDA licensure/clearance**
  - Develop a draft package insert (PI)/target product profile
  - Need to understand the info needed for PI to properly label the product **prior** to initiating the clinical studies.
  - Consider reimbursement issues

- **Risk Mitigation**
  - Develop a regulatory strategy
  - Employ quality systems in all aspects of product development (i.e. GMPs, GLPS, GCPs, etc.)
  - Engage with the FDA early and often
    - For your product
    - For your field – be an active player in regulatory science
  - Establish an experienced product development team and communicate with all members of the team regularly.
    - **LISTEN TO YOUR REGULATORY EXPERTS**

Integrated Product Teams – Key Tool For Success

Broad expertise is needed to develop and field products

Managing FDA Regulated Products

FDA Regulatory Management includes:

- Experienced personnel, tools, standards, approaches to assess safety, efficacy, quality & performance of FDA regulated products with the goal of expediting product licensure in compliance with FDA laws, regulations and requirements.
- What it encompasses: Development of drugs, biologics, devices and combination products for human use
- What it does not encompass: Institutional Review Board responsibilities.

- Regulatory management is critical to successful medical product development.

- Program delays due to unacknowledged FDA requirements increase cost, lengthen schedule, waste manpower, and increase risk.

FDA Regulatory Management

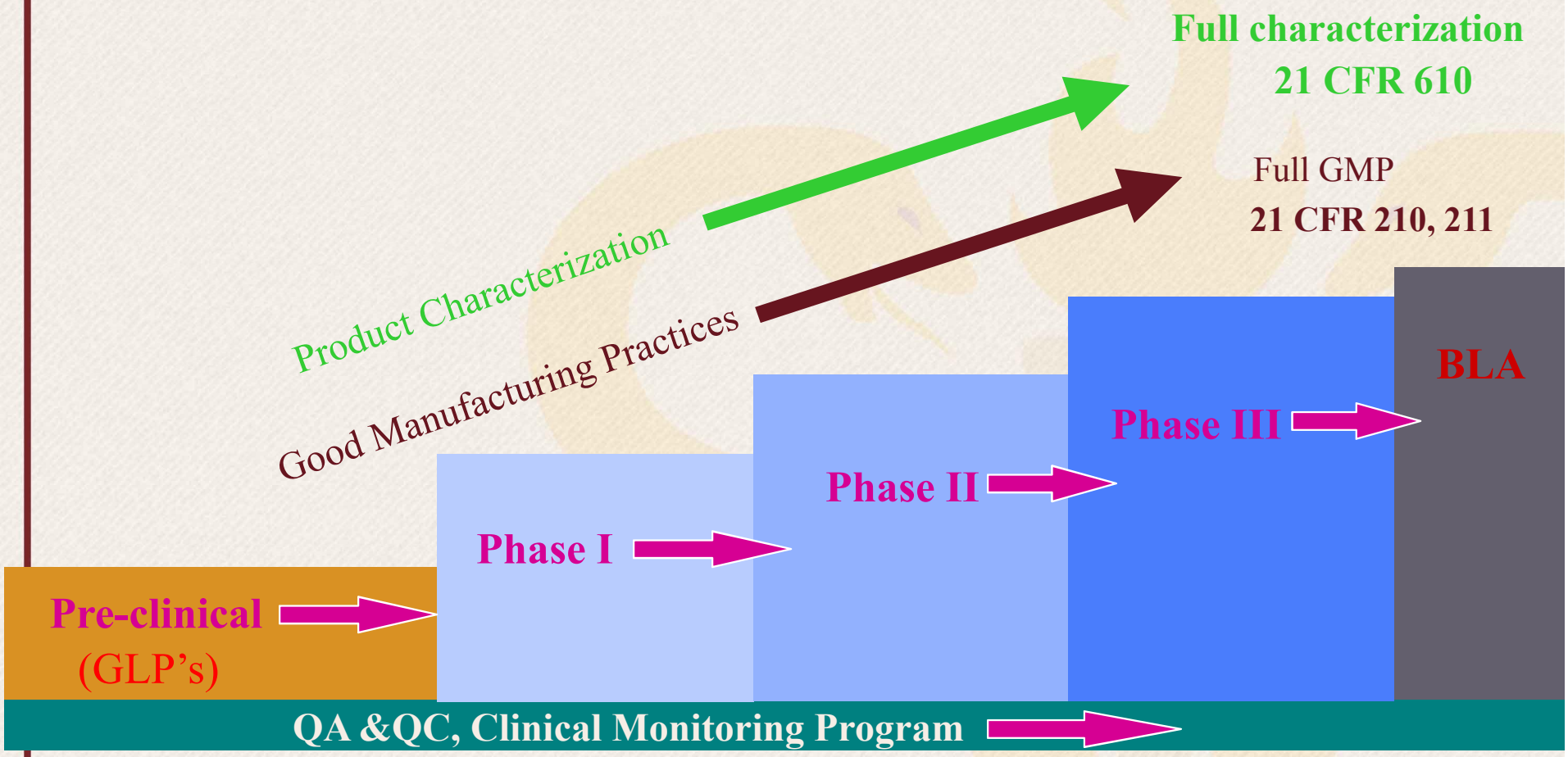
Regulatory team should be involved as **early as possible, even as intended use and indications for use are being established and before GMP manufacturing**

- Critical to identify how product will be regulated by the FDA.
- FDA medical product regulations are complex and explicitly required.
- Scientific and regulatory development input must be up-to-date.
- Maintaining good relationship and good standing with FDA is crucial to continued success.
- Regulatory oversight of contracted activities reduces product development risk.

When do cGMP Requirements first apply?

- With the very 1st material used in making the medical product
  - Starting material
    - Raw material, intermediate, or API used in the production of API
    - Examples – Donor cells, Cell Banks

Step-wise Approach to Application of Manufacturing Regulatory Requirements



Prior to Phase I : need product safety testing and basic characterization info

Developing a Regulatory Strategy

(Adapted from "Developing an Effective Regulatory Strategy", Mark D. Kramer, *Regulatory Focus, December 2010, courtesy of Lisa Borek)*

Step 1. Ask Question: What is your product? What data is necessary to support desired claims? Lifecycle issues? Plans for Manufacture and GMP compliance? What will help assemble a complete picture of the scope of testing required to gain approval?

Step 2. Gather Regulatory Info: Gather regulatory information and available data. Evaluate what could impact your strategy. Understand the regulatory landscape.

Step 3: Create Draft Strategy Document: Define objectives, Identify potential regulatory pathway, Outline plans for preclinical testing and clinical investigations, Lay out strategy for communicating with FDA.

Step 4: Present and confirm strategy: Obtain input among cross functional project team and obtain feedback. Sound strategy informs expectations, evaluates potential hurdles and proposes proactive plans to address them.

Developing a Regulatory Strategy: Final Point

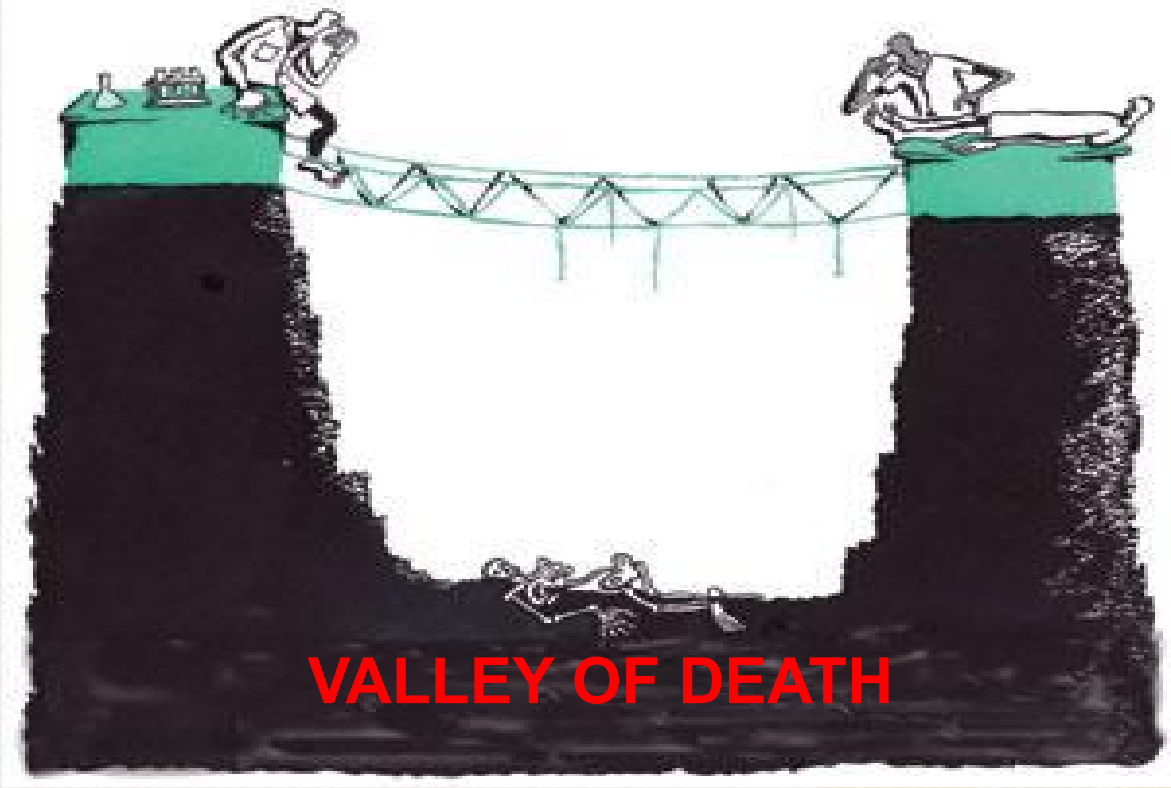
Step 5: Strategy document is a LIVING document! Set schedule for periodic review of Regulatory Strategy Document and update as necessary to reflect current status of development. Serves as a tracking, planning, and risk management tool.

Expect change and plan for it!

It is ALL about the DATA!

- Goal of product development is for generation of evidence to support product licensure **and** commercialization in order to bring new medical products to the public.
- **Evidence generation should begin in Phase I** and be considered a 'living' process that can be updated throughout the product lifecycle to reflect new internal data in addition to the latest external demands.
- Medical product manufacturers need to satisfy the sometimes divergent needs of both licensing authorities and payers.
- **Time to market does not mean time to FDA licensing but time to reimbursement**. Plan accordingly!
  - Relative efficacy needs to be evaluated pre-market.

Ignore business, logistics, regulatory, etc…



and your research could wind up here!

“The maturation of 3D printing within the biomedical industry will ultimately be dependent on the ongoing evolution and synthesis of regulation and technology”.

Morrison, RJ , Kashlan KN, Flanangan CL, Wright JK, Green GE, Hollister SJ, Weatherwax KJ. Regulatory Considerations in the Design and Manufacturing of Implantable 3D-Printed Medical Devices. Clin Transl Sci. 2015 Oct;8(5):594-600