Commercializing Medical Products – Development, Regulatory, and IP Considerations

UNCLASSIFIED

Disclaimer

The views expressed in this presentation are those of the author(s) and may not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government.

Agenda

- Developing Medical Products to Support the DoD – Dr. Tyler Bennett and Ms. Kathleen Berst
- Regulatory Pathways for Developing Medical Products
  - Introduction to the FDA – Dr. Robert Miller
  - Routes to Market: Key Regulatory Considerations for Drugs, Vaccines, and Biologics – Ms. Emily Badraslioglu
  - Routes to Market: Key Regulatory Considerations for Devices – Ms. Lisa Borek
- Intellectual Property Considerations – Mr. Jeremiah Kelly and Ms. Liz Arwine

Developing Medical Products to Support the DoD

UNCLASSIFIED

Dr. Tyler Bennett
Deputy for Acquisition
United States Army Medical Materiel Agency

Ms. Kathleen Berst
Deputy for Acquisition
United States Army Medical Materiel Development Activity

Why is Army Medicine Involved?

We 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
- Industry/academia lack interest
- Military needs require acceleration of solution
- Directed by Congress
- Available commercial product cannot be sustained in military environment

One Goal – *Translate Research Into Fielded Product*

- What constitutes a “fielded” product?
  - Safe and Effective (Key Performance Parameter)
    - Approved or cleared by the FDA for intended use
  - Militarily relevant
    - Environmentally suited
    - Acceptable to the user community
  - Affordable and Sustainable
    - Early manufacturability considerations addressed
    - Reimbursable
    - Commercially viable

USAMRMC Organization Chart

USAMRMC Actual Personnel – DEC 2016			
MILITARY	CIVILIAN	CONTRACTOR	TOTAL
1064	2268	3189	6521
16%	35%	49%	100%

Deputy Commander

Also DHA Director for R&D

Commanding General

Chief of Staff

Other Organizations
- Congressionally Directed Medical Research Programs (CDMRP)
- Telemedicine and Advanced Technology Research Center (TATRC)

Command Sergeant Major

Principal Assistant for Research and Technology

Principal Assistant for Acquisition

USAMRMC's Product Development and Regulatory Capability

US Army Aeromedical Research Laboratory (USAARL)

US Army Institute of Surgical Research (USAISR)

US Army Medical Research Institute of Chemical Defense (USAMRICD)

US Army Medical Research Institute of Infectious Diseases (USAMRIID)

US Army Research Institute of Environmental Medicine (USARIEM)

Walter Reed Army Institute of Research (WRAIR)

US Army Medical Materiel Development Activity (USAMMDA)

US Army Medical Materiel Agency (USAMMA)

6th Medical Logistics Management Center (6MLMC) (ADCON)

US Army Medical Materiel Center, Europe (USAMMCE)

US Army Medical Materiel Center, Korea (USAMMCK)

US Army Medical Research Acquisition Activity (USAMRAA)

Medical Research and Technology Laboratory Commands

Medical Advanced Development Commands

Strategic Medical Logistics Commands

Operational Medical Logistics Commands

Contracting Activity

USAMRMC's Medical Product Portfolio

Where Our Products Touch the Lives of Warfighters

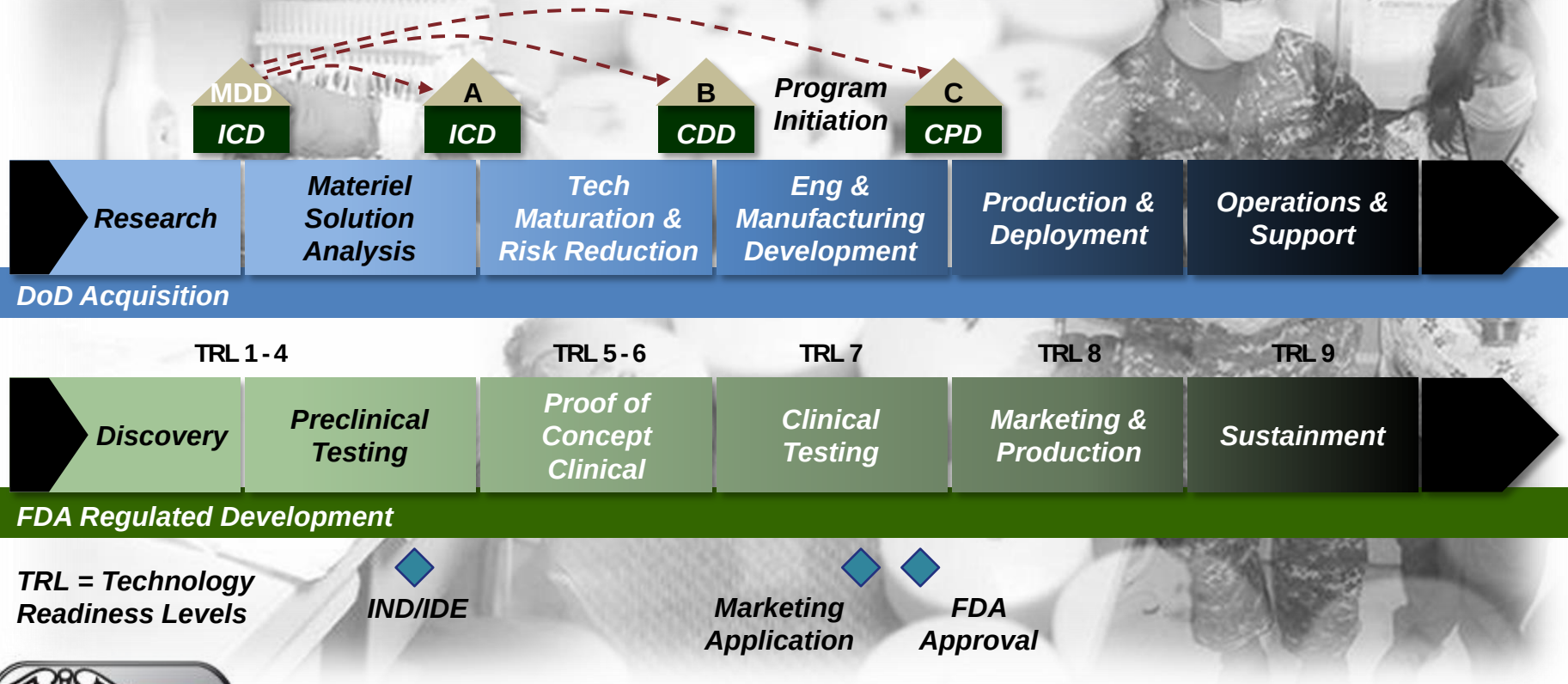
Prevention

Diagnose and Treat

Rehabilitate & Restore

Governing Processes

Integration of DoD 5000 and FDA Regulation Process

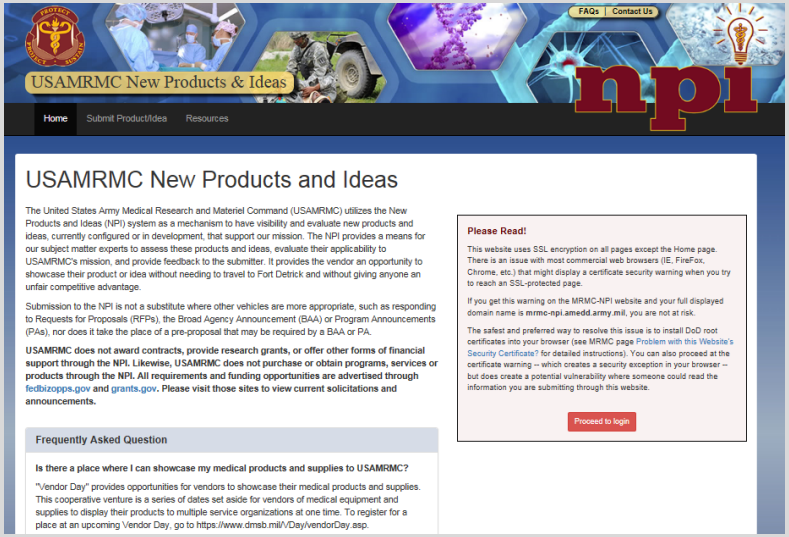


"Translate Research Into Products"

How to Work with Us

- **Commercial Off The Shelf (COTS) items**
  - General Supply Schedules (i.e. E-CAT, E-MALL, GSA Advantage)
  - Direct Contract
- **Developmental Items**
  - Cooperative Research and Development Agreement (CRADA)
  - Broad Agency Announcement (BAA)
  - Small Business Innovation Research (SBIR)
  - Small Business Technology Transfer (STTR)
  - Other Transaction Authority (OTA)
  - Direct contract

Submit your ideas via the "New Products & Ideas" web portal
http://mrmc-npi.amedd.army.mil/



Sign up for Vendor Days
http://www.health.mil/VendorDay

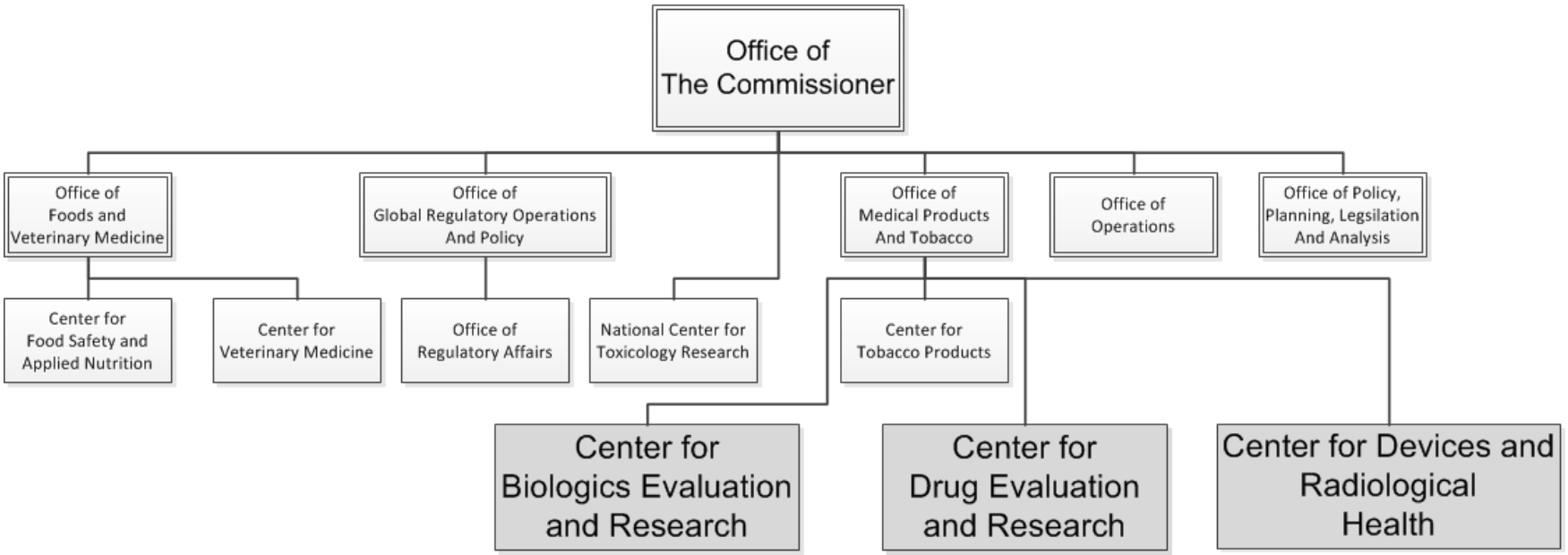
Introduction to the Food and Drug Administration

UNCLASSIFIED

Bob Miller, Ph.D.
Division of Regulated Activities and Compliance
US Army Medical Materiel Development Activity
US Army Medical Research and Materiel Command
6 March 2017

US Food and Drug Administration Overview

High Level US Food and Drug Administration
Organization Chart



Routes to Market: Key Regulatory Considerations for Drugs, Vaccines, and Biologics

UNCLASSIFIED

Emily Badraslioglu; Chief, Regulatory Science Branch
Division of Regulated Activities and Compliance, USAMMDA
US Army Medical Research and Materiel Command

6 March 2017

Why is regulatory so important?

All FDA regulated medical products in the Department of Defense (DoD) acquisition framework require approval

Regulatory is critical to reduce risk and ensure program success

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

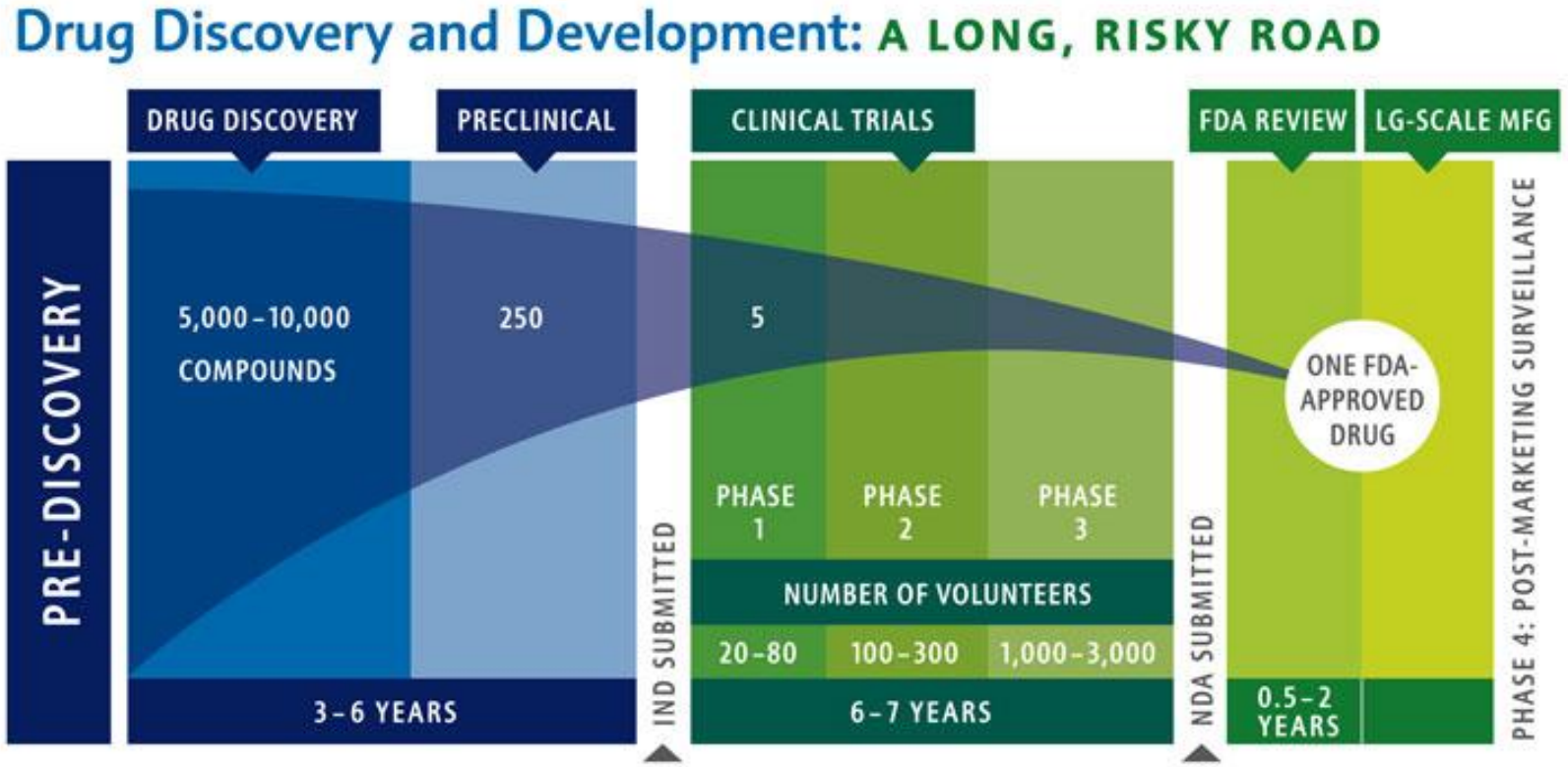
Navigating the Regulatory Pathway

FDA Approvals in 2016

In 2016, the FDA approved 28 new drugs with aggregate projected peak annual sales of US$35 billion

Nature Reviews Drug Discovery | Published online 2 Feb 2017; doi:10.1038/nrd.2017.14

Drug Development and Discovery



Source: Pharmaceutical Research and Manufacturers of America

What is our mission?

Protect the Warfighter

More FDA approved products

Where do I start?

- Critical to identify if research is FDA-regulated
- Regulatory should be involved as early as possible
  - *BEFORE intended use and indications for use are being established*
  - *BEFORE manufacturing processes are established*

Maintaining good relationship and good standing with FDA is crucial to continued success

What is a drug?

- Any product (or component) that is intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man
- A product other than food (or component) that affects the structure or function of the human body
- A product that is recognized in the US Pharmacopoeia (USP), Homoeopathic Pharmacopoeia of the US (HPUS) or the National Formulary (NF) and their supplements

Center for Drug Evaluation and Research (CDER)

CDER regulates:

- *Prescription Drugs*. Prescription medicines include any drug product that requires a doctor's authorization to purchase.
- *Generic Drugs*. A generic drug is a drug product that is equivalent to brand name products in terms of quality and performance.
- *Over-the-Counter Drugs*. OTC drug products are available to consumers without a doctor's prescription including things like: toothpaste, dandruff shampoos and sunscreens.

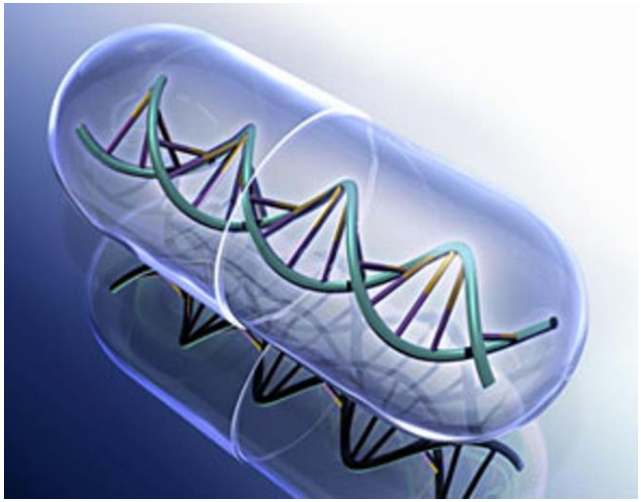
Center for Drug Evaluation and Research (CDER)

- CDER also regulates other categories of biological products mostly produced by biotechnology methods, including:
  - monoclonal antibodies designed as targeted therapies in cancer and other diseases
  - cytokines (types of proteins involved in immune response)
  - growth factors (proteins that affect the growth of a cell)
  - enzymes (types of proteins that speed up biochemical reactions), such as thrombolytics (used to dissolve blood clots)
  - immunomodulators (agents that affect immune response)

Biologics

Drug products derived from living sources, including humans, animals and microorganisms

- Virus
- Therapeutic serum
- Toxin and antitoxin
- Vaccine
- Protein
- Allergenic product
- Blood and blood component or derivative



Regulatory Strategy

- A clear and well planned strategy is essential for navigating the regulatory process and obtaining a timely and smooth approval for the product
- Plan of action for the approval process, linking the different activities and drug development phases, assessing the challenges along the way and formulating appropriate risk mitigation activities
- End goal: obtain FDA approval for the desired indication in the desired timeframe

Target Product Profile (TPP)

A TPP is a key tool to help ensure the eventual product meets all expectations

Begin with the end in mind

- What do I want on the product label?
- How will the product be utilized by the end user?
- What is my indication?
- What are the dosage and administration, adverse reactions, and contraindications?
- What human clinical studies will support the label claim?

Target Product Profile - A Strategic Development Process Tool, Guidance for Industry and Review Staff March 2007

Pre-Investigational New Drug Application (IND) Meeting

The pre-IND meeting can be very valuable in planning a drug development program:

- Early interactions with FDA staff can help to prevent clinical hold issues from arising
- A pre-IND meeting can also provide sponsors information that will assist them in preparing to submit complete investigational new drug applications.
- These questions and answers can be especially helpful to small businesses that may have limited experience interacting with the FDA, or are unfamiliar with pre-IND meetings.

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm069906.htm

Investigational New Drug Application (IND)

[21 CFR 312]

- Allows investigational new drugs to enter into interstate commerce
- Required for testing of investigational new drugs in human clinical trials unless otherwise exempt
- IND regulations require that human research studies be conducted under an IND if all of the following conditions exist:
  - The research involves a drug as defined in the FD&C Act
  - The research is a clinical investigation as defined in 21 CFR 312.3
  - The clinical investigation is not otherwise exempt from the IND requirements in 21 CFR 312.3

What do I include in my IND?

1. Form FDA 1571
2. Table of Contents
3. Introductory Statement and General Investigational Plan
4. Reserved
5. Investigator's Brochure
6. Clinical Protocol
7. Chemistry, Manufacturing and Controls
8. Pharmacology and Toxicology
9. Previous Human Experience
10. Additional Information

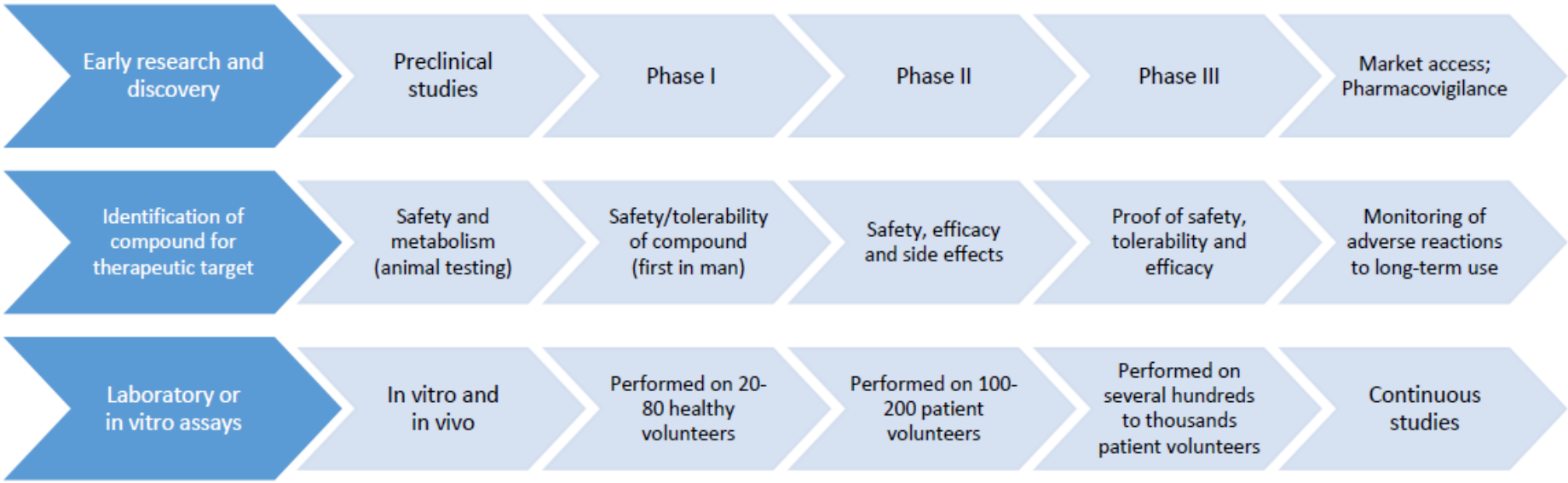
IND Filing Process

- Submit IND
- Wait 30 days per 21 CFR 312.40
  - Clinical hold (21 CFR 312.42)
    - Response to clinical hold
  - Authorization to proceed
- Non-hold comments

FDA Meetings

Type A	Type B	Type C
Meeting needed to help an otherwise stalled product development program proceed.	Meeting held for one of four specific reasons: (1) pre-IND meetings, (2) certain EOP 1 meetings, (3) EOP 2 and pre-phase 3 meetings, (4) pre-NDA/BLA meetings.	Any meeting other than a Type A or Type B meeting between CBER or CDER and a sponsor regarding the development and review of a product.
Scheduled to occur within 30 days of FDA receipt of the written meeting request.	Scheduled to occur within 60 days of FDA receipt of the written meeting request.	Scheduled to occur within 75 days of FDA receipt of the written meeting request.

Clinical Trial Phases



Marketing Applications

- NDA: New Drug Application; 21 CFR 314
- BLA: Biologic License Application; 21 CFR 314 and 21 CFR 601
- Allows new drugs (biologics) to be marketed and distributed

What's in a BLA/NDA?

- Applicant information
- Product/Manufacturing information
- Pre-clinical studies
- Clinical studies
- Labeling

BLA/NDA Filing Proccess

- Pre-NDA/BLA Meeting
- Submit NDA/BLA
- Wait 60 days per 21 CFR 314
  - Day 74 Letter: FDA accepts the NDA/BLA for review, provides an action date and identifies the review class
  - Refuse-to-file (RTF) Letter: NDA/BLA has significant deficiencies

FDA Review

- Primary review: Reviews performed by individual disciplinary groups
  - FDA may request additional information; respond by filing requested information as NDA amendments
- Secondary review: Review by the division director
- Tertiary review: Review by the office director, who issues either an Approval Letter or a Complete Response Letter

FDA Review Timelines

- ***Standard Review*** is applied to a drug that offers at most, only minor improvement over existing marketed therapies. The 2002 amendments to the Prescription Drug User Fee Act (PDUFA) set a 10 month goal for a standard review.
- ***Priority Review*** designation is given to drugs that offer major advances in treatment, or provide a treatment where none existed. The goal for completing a Priority Review is six months.

http://www.fda.gov/Drugs/ResourcesForYou/SpecialFeatures/ucm279676.htm#

Expedited Programs for Serious Conditions

Fast Track	Breakthrough Therapy	Accelerated Approval	Priority Review
Intended to treat serious condition AND non-clinical or clinical data demonstrate potential to address unmet need OR designated as qualified infectious disease product	Intended to treat serious condition AND preliminary clinical data indicates drug may demonstrate improvement on a clinically significant endpoint over available therapies	Treat serious condition AND provides meaningful advantage over available therapies AND demonstrates and effect on a surrogate endpoint that is likely to predict clinical benefit	Application for treating a serious condition AND would provide significant improvement in safety or effectiveness OR supplement proposing labeling change due to a pediatric study OR application for drug designated as qualified disease product OR application/supplement submitted with priority review voucher
Submit designation request with IND or after but NLT pre-BLA/NDA meeting	Submit designation request with IND or after but NLT EOP2 meeting	Discuss pathway with review division during development	Submit designation request with BLA/NDA or efficacy supplement
FDA responds within 60 days	FDA responds within 60 days	FDA timeline not specified	FDA responds within 60 days Review takes 6 months instead of 10

Animal Rule

Regulations: 21 CFR 314.600 (drugs) or 21 CFR 601.90 (biological products)

Regulatory pathway to approval intended for drugs developed to ameliorate or prevent serious or life-threatening conditions caused by chemical, biological, radiological, or nuclear substances provided that human efficacy studies are not ethical and field trials to study effectiveness of the drug are not feasible.

Guidance for Industry, Product Development Under the Animal Rule, October 2015

When to use the Animal Rule?

FDA will rely on evidence from animal studies to provide substantial evidence of effectiveness only when all of the following four criteria are met:

1. There is a reasonably well-understood pathophysiological mechanism of the toxicity of the substance and its prevention or substantial reduction by the product;
2. The effect is demonstrated in more than one animal species expected to react with a response predictive for humans, unless the effect is demonstrated in a single animal species that represents a sufficiently well-characterized animal model for predicting the response in humans;
3. The animal study endpoint is clearly related to the desired benefit in humans, generally the enhancement of survival or prevention of major morbidity; and
4. The data or information on the kinetics and pharmacodynamics of the product or other relevant data or information, in animals and humans, allows selection of an effective dose in humans.

Guidance for Industry, Product Development Under the Animal Rule, October 2015

Orphan Drug Program

- **Orphan drugs** are developed for a disease or condition that:
  - Affects < 200,000 people in the US
    - For vaccines and blood products, applies to patients receiving the product annually
  - Affects >200,000 people in the US and offers no reasonable expectation that costs would be recovered from sales
- An Orphan product must:
  - Have a sponsor
  - Not have been approved previously under an application for the disease/condition for which orphan status is requested
  - Not be the subject of a marketing application submitted prior to the filing of the orphan status request

Begin with the end in mind…..

Medical Devices Regulatory Overview

UNCLASSIFIED

M. Lisa Borek, Chief, Medical Devices and Diagnostics Branch

USAMMDA

US Army Medical Research and Materiel Command

06 March 2017

Medical Device Regulatory Team

The Medical Device and Diagnostics (MD&D) Branch is within the Division of Regulated Activities and Compliance at USAMMDA

MD&D Branch – Who We Are

- **4 Professional Regulatory Staff Members and an Air Force Regulatory Fellow**– Regulatory and Quality subject matter experts in medical devices
- **35+ Combined Years of Experience** in Regulatory Affairs and Quality Assurance
- **Certifications -** Regulatory Affairs (RAC US); MT ASCP
- **Diverse Backgrounds:** Quality, Equipment Validation, Manufacturing, Animal Model Development, Imaging, Drug Discovery and Development, Clinical Research, Medical Device Submissions, Medical Technologist, Clinical Laboratory Science, Biology, Microbiology, Molecular Biology, Chemical Biology, Virology, Cancer Biology, Cell Biology

What We Do

- Act as regulatory affairs subject matter experts for medical devices. Provide regulatory guidance and advice to medical device development teams and participate on working groups and IPTs

- Track and analyze regulatory risks to the project and provide assessments of progression/milestones along the regulatory pathway

- Support and guide FDA interactions: Assist with preparation for FDA meetings; Attend key FDA meetings with contractors; Interpret FDA comments

- Consult with CDRH on topics that are relevant to all device developments

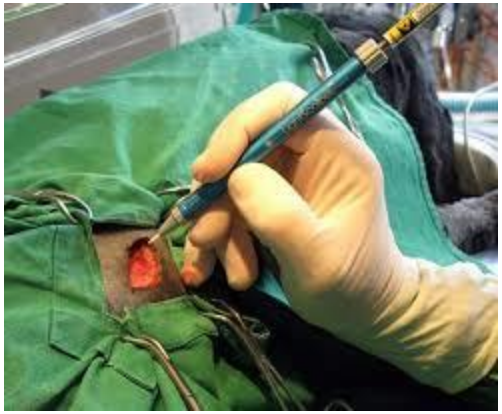
Medical Device Definition

Section 201(h) of the Federal Food Drug & Cosmetic (FD&C) Act:

"an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

- Recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
- Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- Intended to affect the structure or any function of the body of man or other animals
- **And which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."**

Many Types of Medical Devices



Medical Device Regulations

- **Title 21 CFR Parts 800-1299**
  - cover design, clinical evaluation, manufacturing, packaging, and post market surveillance of medical devices

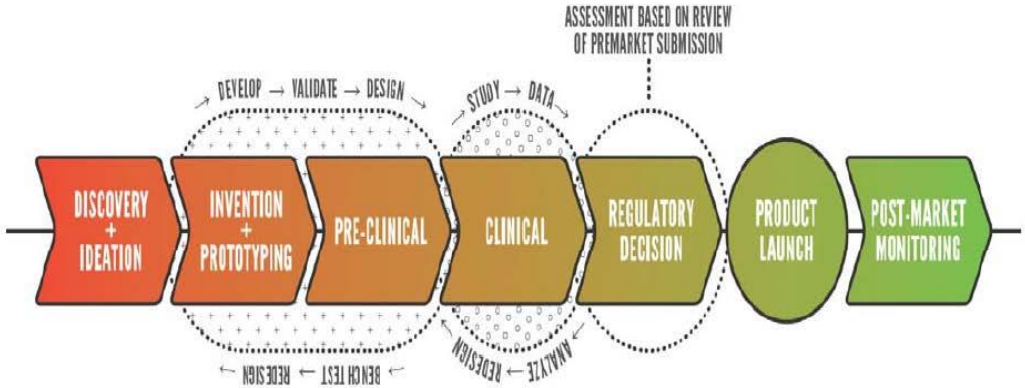
- **FDA - Center for Devices and Radiological Health (CDRH)**
  - responsible for regulating firms who manufacture, repackage, relabel, and/or import medical devices sold in the United States

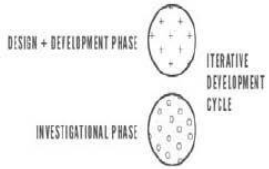
Regulatory Keystones

- **Medical Devices cannot be:**
  - Adulterated - (e.g., contaminated)
  - Misbranded - (e.g., wrong labeling**)**
- **Medical Devices must be reasonably:**
  - Safe and Effective

Medical Device Development Pathway

The regulatory process affects a significant portion of the device development pathway from discovery to product launch and post market





Basic Regulatory Requirements

For medical devices distributed in the U.S:

- Premarket Notification- 510k (unless exempt) or Premarket Approval (PMA)
- Investigational Device Exemption (IDE) for clinical studies
- Quality System Regulation (QSR)
- Labeling Requirements
- Establishment registration
- Medical Device Listing
- Medical Device Reporting

Device Classification

Classification defines the level of regulatory control necessary to assure the safety and effectiveness of the device and is based on the risk the device poses to the patient and/or the user

Class I - **Lowest Risk** – Least amount of regulatory control. Minimal potential harm to the user; Simple in design, manufacture, history of safe use

- Examples: Tongue Depressor, Adhesive Bandage ('Band-Aid')

Class II – **Moderate Risk** – Typically require pre-market notification by submission and FDA review

- Examples: Infusion Pumps, Absorbable Suture

Class III – **Highest Risk** – Most stringent regulatory controls. Devices that support or sustain life. Present a potential for unreasonable risk of injury or illness

- Examples: Pacemaker, Heart Valve

Investigational Device Exemption

21 CFR Part 812 - IDE Regulations - Allows the investigational device to be used in a clinical study to collect safety and effectiveness data. Most clinical studies are conducted to support a PMA, smaller percentage of 510ks require clinical data

- Sponsor must determine if their device is significant risk (SR) or non-significant risk (NSR**)**
- BOTH NSR and SR studies subject to informed consent and IRB review
  - **SR Device -** Sponsor must submit IDE application to CDRH. Investigational plan approved by IRB and IDE must be approved by FDA prior to study start
  - **NSR Device -** Sponsor need not submit IDE application to FDA before initiating clinical investigation of the NSR device. IRB approval for study to commence
- Sponsors of IDE's are exempt from Quality System Regulation except for Design Controls
- GCP requirements must be complied with during clinical studies of devices

Premarket Submissions

- **PMA – Premarket Approval** – Most stringent type of submission FDA approves
- **510(k) – Premarket Notification** – Sponsor demonstrates new device is **substantially equivalent** (at least as safe and effective) to a predicate (already marketed) device in terms of intended use, technological characteristics, and performance testing
- **De Novo** – Provides a way for a new device that has no predicate device to be classified into Class I or II upon meeting certain criteria. Novel devices of low-moderate risk
- **HDE - Humanitarian Device Exemption** – Regulatory path for devices intended to benefit patients with rare diseases or conditions that affect fewer than 8,000 individuals per year. Requires safety, but not efficacy

Sharing Lessons Learned

Conducted Informal Survey –

Regulatory Scientists, Ex - FDA reviewers

Diverse experience from different agencies

Question – If you could share some lessons you have learned with potential partners, what would you share?

Answers were very consistent, identifying the same issues

Lesson 1- Intended Use

1. Who is the user and what is the use environment? If it's for the warfighter in the field, what does that mean to the regulatory strategy and pathway?
2. Understand how the product must meet the military requirements and the capability gap – these feed into the regulatory requirements and help develop a regulatory path
3. Draft An Intended Use Statement early

Draft Intended Use Statement Early

Pathway to Approval Depends the Intended Use

Intended Use – Know how the product will be used

Indications for Use –

- Who will be the target patient population?
- What clinical benefit, claims will be made?

Intended User

- Who will use the product? (doctor, medic, nurse, medic, lab technician, EMT) Highly trained or less trained user?

Use Environment

- What is the use environment – Stateside hospital, field hospital, battlefield, doctor office, home, at the point of care

Current Route from Injury to Definitive Care

Role of Care 1
Point of Injury
(Prolonged Field Care)

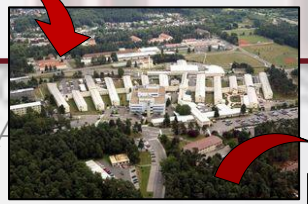
TACTICAL MEDEVAC

Role of Care 2
Forward Surgical Teams

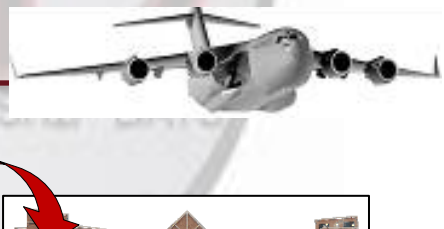
INTRATHEATER TRANSPORT

Role of Care 3
CSH, EMEDS, EMF

INTERTHEATER TRANSPORT



Role of Care 4
Definitive Care



Full Range of Care

Post Acute Care

VA

MEDEVAC = medical evacuation
CSH = combat support hospital
EMEDS = expeditionary medical support
EMF = emergency medical facility
VA = Veteran's Administration

Lessons 2- Submission Quality

1. We rarely see written regulatory strategy developed as a formal project document that aligns the regulatory activities to bring a new or modified product to market with the business end of things. In all cases a clearly developed regulatory strategy would help create quality submissions
2. A lot of companies just state that they comply with standards and it's obvious they didn't even read the standard. What tests did you perform? What was the methodology? What was the acceptance criteria?
3. The devil is in the details – a good quality submission with sufficient detail will get you good quality comments from FDA review groups

Use Regulatory Tools

Regulatory Strategy

- Provides overall definition and direction to the project team
- Identifies important regulatory elements to be addressed
- Living document, updated through the development process

Regulatory Plan

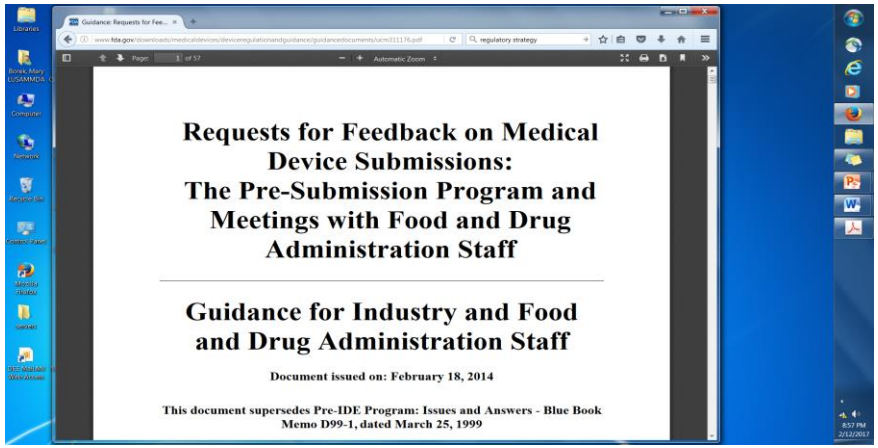
- Describes specific steps, actions required to successfully meet objectives of the regulatory strategy
- Contains the specific elements required to assemble the regulatory submission

✓ **Utilizing both reduces regulatory and quality risk and increases chance of regulatory success**

Lesson 3– Use Pre-Submissions

- Most contractors seem to want to avoid early interactions with FDA when they should not. We have seen varied reasons: they don't want to, they strongly believe that they don't need to, they feel talking to FDA will add more to their timeline, cost
- Get early FDA feedback, utilize the FDA Pre-Submission program fully. Not taking advantage of the FDA pre-submission process can potentially impact development process

FDA - Early and Often



- Early interaction with CDRH allows FDA to become familiar with your device, particularly important for novel devices

- Important to fully understand the regulatory requirements to develop the product that is desired/required
  - Regulatory requirements affect contract/agreements, schedules, cost, logistics

Lesson 4– Quality Is Important

- The biggest issue among small companies and start-ups is not having a Quality Management System in place
- Small companies often have processes that are inadequate which can quickly snowball as you move into product development.
- Don’t forget Design Controls during development. The FDA will need to see the total history of how the device was designed, built and tested
- Have quality agreements in place with all subcontractors
- Site visits can be helpful for both sides, don’t think of them as something you’d like to avoid. Site visits can help the government team understand your products and processes better and help identify/address regulatory or quality issues before they affect progress

Medical Device Quality

Compliance to Quality System Regulation (QSR, 21 CFR Part 820) is a requirement for non-exempt devices

Design Controls (21 CRF Part 820.30) - Quality practices/procedures incorporated into the design and development process for medical devices

- ✓ Applies prior to market approval for all Class II and Class III Medical Devices and certain Class I Medical Devices. This includes software medical devices

Lesson 5– Regulatory

- Having the appropriate regulatory competencies available is important for your success

- Contractors need to hire a competent regulatory affairs scientist. You cannot develop a regulated product without this competency in-house or available through contracted services

- CEOs and business interests should not overrule the in-house regulatory direction/advice when it comes to responding to FDA

Lesson 6– Listen to FDA

- Think about the quality of the information you are providing to reviewers relative to the quality of the comments you'd like to get back. You're the expert in your device
- Poor quality info means the FDA review team won't be able to review fully and will need to ask for clarifications
- Don't use a strategy' of 'pushing back' at FDA during the review process. I had experience with a company that 'pushed back' and after two years finally had to do what FDA had asked them to do all along. It really doesn't save $$ because of the time wasted
- **Take FDA's advice**

Thank You!

FDA-Regulated Medical Product Development & Intellectual Property at the U.S. Army Medical Research & Materiel Command (USAMRMC)

UNCLASSIFIED

UNCLASSIFIED

Jeremiah J. Kelly, Esq., M.P.P.
Chief, FDA Regulatory Law Division
Office of the Staff Judge Advocate, USAMRMC

6 March 2017

Understanding the Risks

- Product development and Tech Transfer collaborations require strategic thinking regarding:
  - Proper evaluation of the FDA-regulatory landscape (allocation of sponsor responsibilities, unique approval mechanisms, marketing exclusivity)
  - Correct selection of legal instrument (assistance agreement, contract, CRADA, OTA or a combination)
  - Including proper terms/clauses in our legal agreements to ensure protection of intellectual property (patents, technical data, etc.), equities of the parties.
- Hallmark of our approach: flexibility
- Failure in any one of these areas creates risk to the product development effort or the tech transfer mission.

Choosing the Correct Legal Vehicle

- USAMRMC utilizes five (5) types of legal instruments to accomplish its product development mission:
  - Assistance Agreements (grants and cooperative agreements)
  - Contracts
  - Cooperative Research and Development Agreements (CRADAs)
  - Other Transaction Authority (OTAs)
  - License of Federal Technology
  - Agreements Differ on:
    - Purpose and use of funds
    - Patent rights flexibility
    - Allocation of Technical Data Rights
      - Restricted
      - Federal or Government Purpose
      - Unlimited

Marketing Exclusivity

- Marketing Exclusivity for Drugs
  - New Chemical Entity (NCE) – 5 years (21 CFR 314.108)
  - New Clinical Information Change or "Other" – 3 years
  - Pediatric (PED) – 6 months add-on exclusivity
  - Orphan Drug – 7 years (21 CFR 316.31)
  - Qualified Infectious Disease Product (QIDP) – 5 years add-on exclusivity (*NEW*)
  - Generic Drug Exclusivity (available for 505(j) applicant only) – 6 months
- Marketing Exclusivity for Biologics
  - New Biologic – 12 years
  - Interchangeable Biosimilar – 1 year
- No Marketing Exclusivity for Devices

Special Review Designations

- Priority Review Vouchers (PRVs)
  - Tropical Disease PRV
    - Applications for drugs for the treatment or prevention of certain tropical diseases under §524(a)(3) and (4) of the FD&C Act
    - Example: filovirus (e.g., ebola) added 12/16/13
  - Rare Pediatric PRV
    - Applications for drugs to treat of rare pediatric diseases as defined under 529(a)(3) of the FD&C Act
  - Material Threat Countermeasure PRV
    - "material threat medical countermeasure application," as defined under Section 319 of the Public Health Service Act
    - §3086 added by the 21st Century Cures Act on 12/13/16
  - General Features
    - Applicable to both 505(b)(1) NDAs or 351 BLAs
    - Not applicable to any active ingredient approved under 505(b)(1) NDA or 351 (BLA).
    - Transferable option by contract; 1 year notice before use
    - Value: several PRVs sold; value ranges from $67.5 million to $350 million

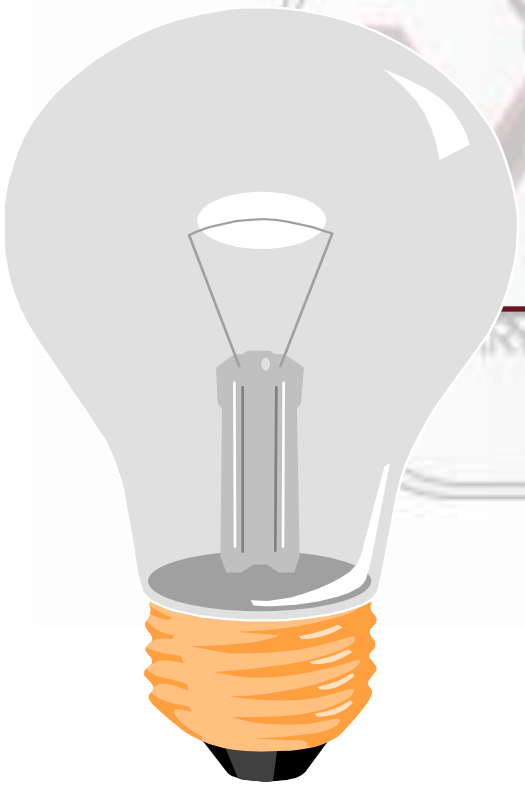
Special Approval Pathways

- Animal Rule
  - Where: 21 CFR §314.600 (Subpart I)
  - Qualifying Criteria:
    - new drug or biologic that intended to "treat or prevent serious or life threatening conditions causes by exposure to lethal or permanently disabling toxic biological, chemical, radiological, or nuclear substances" and where "human efficacy studies cannot be conducted because it would be unethical….and field trials…have not been feasible." 21 CFR 314.600
  - Discuss w/ review division as early as possible
  - Features:
    - FDA will rely on animal studies to show efficacy when, *inter-alia*, effect is demonstrated in more than 1 animal species predictive of the response in humans; Animal study endpoint is related to the desired endpoint in humans ,
    - Post-market studies when exigency emerges. *See* 21 CFR 314.610.(b)(1)

Special Approval Pathways

- Emergency Use Authorization (EUA)
  - Where: §564 of the FD&C Act (21 USC §360bbb-3)
  - Qualifying Criteria:
    - Secretary of DoD must declare that there is a (or potential for) military emergency involving heightened risk to U.S. military forces of attach with CBRN agent(s); or
    - Secretary of DHHS must declare that there is (or potential for) a public health emergency that affects national security, or health and security of U.S. citizens living abroad that involves as CBRN agent(s) or disease attributable to such agent.
    - FDA's analysis based on totality of evidence, known benefits outweigh known risks when used for indication, and no adequate, approved alternatives exist)
  - FDA Guidance on Pre-EUA Filings
  - Features:
    - Not product approval, but authorization to use an unapproved drug, biologic or medical device during or in anticipation of a CBRN emergency (including emerging infectious disease threats)
    - Labeling requirements
    - Adverse Event Reporting required
    - Effective until declaration terminated

MILITARY MEDICINE PARTNERSHIP DAYS



UNCLASSIFIED

Elizabeth Arwine
Patent Attorney
USAMRMC
6 March 2017

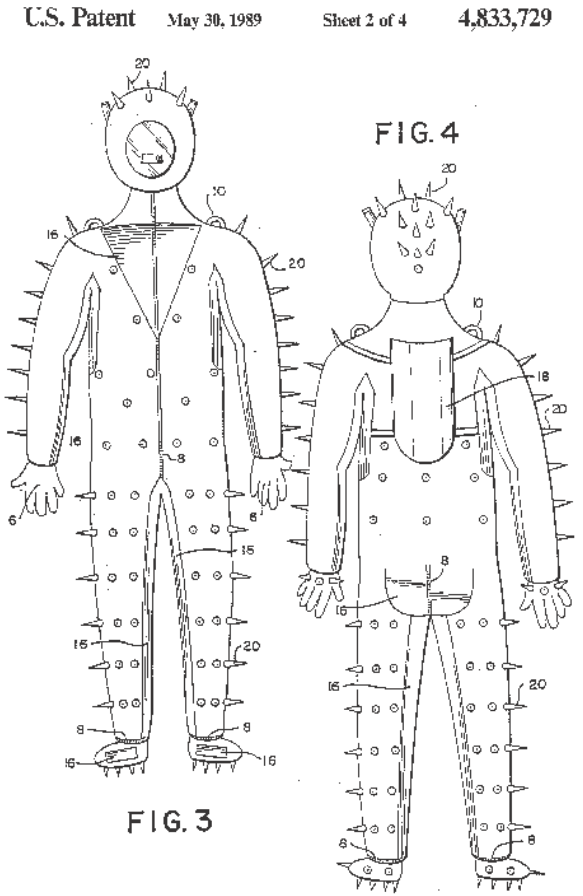
- THE CREATING SPACE
  - Contracts, Grants & Cooperative Agreements
  - Cooperative Research & Development Agreements (CRADAs)
- PROTECTION MECHANISMS
  - Patents
  - Copyrights
  - Trademarks
- T2 & COMMERCIALIZING
  - Licensing

CREATING

- Inventions arise from:
  - Intramural organizations:
    - Government laboratory or organization
  - Extramural organzations:
    - Contracts
    - Public Assistance Agreements
      - Grants & Cooperative Agreements
  - Joint Efforts:
    - CRADAs & Undocumented Research

INTELLECTUAL PROPERTY

- Patents
- Trademarks
- Copyright
- Trade Secrets



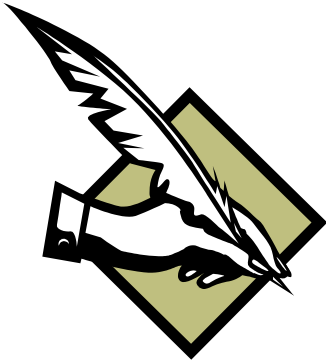
TRADEMARK

- A name, symbol, logo, combination or other device that indicates the source and quality of goods and services and distinguishes those goods and services from those of the competition.

- Also includes servicemarks, collective marks, certification marks.

COPYRIGHT

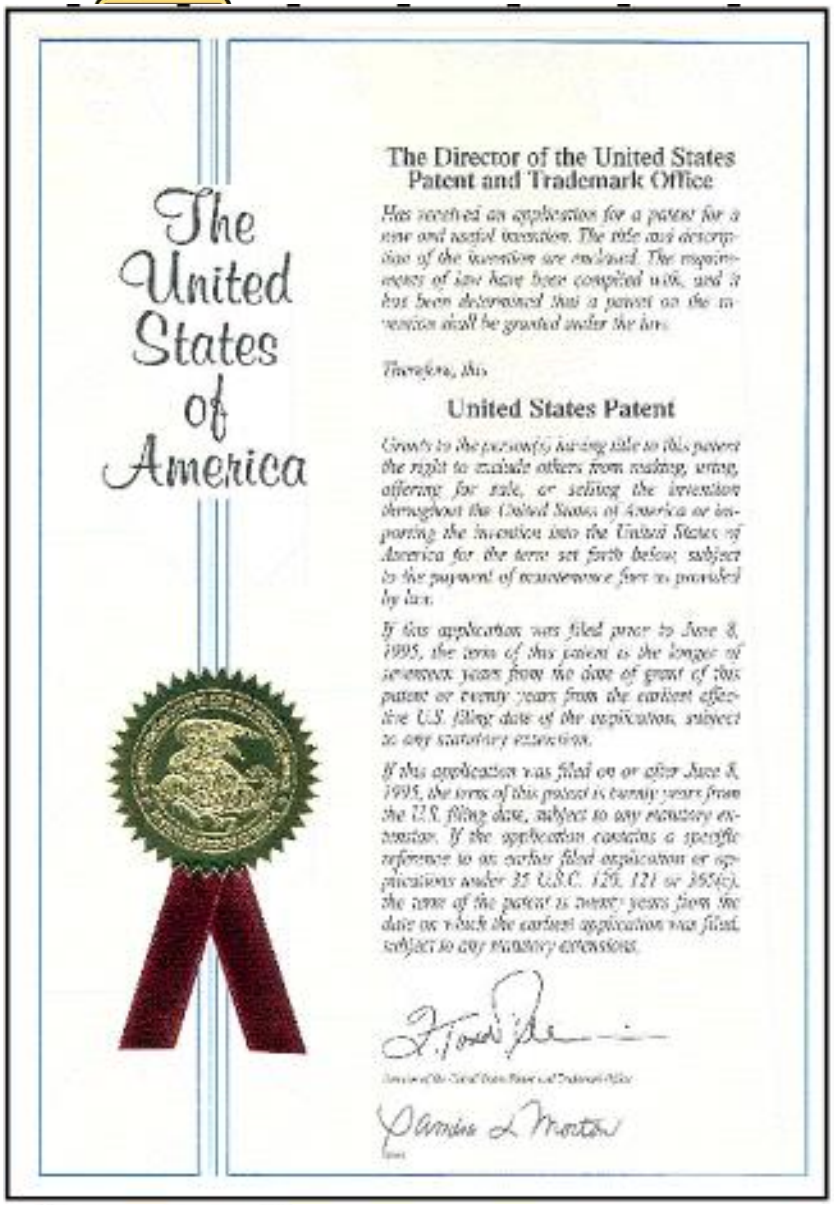
- An exclusive right to reproduce, distribute, perform, display or prepare derivative works of copyrightable material.
- Examples:
  - Literary & Graphic Works
  - Audiovisual Works
  - Music
  - Databases & Software



PATENT

- A grant from the U.S. Government for a limited time during which the owner can exclude others from making, using, offering to sell, or selling the invention that is claimed in the patent document.
- Authorized in U.S. Constitution, Article I, Section 8
- Grant is Territorial--Protection Only in U.S.

EXAMPLE


The United States of America

The Director of the United States Patent and Trademark Office

Has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this

United States Patent

Grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America for the term set forth below, subject to the payment of maintenance fees as provided by law.

If this application was filed prior to June 8, 1995, the term of this patent is the longer of seventeen years from the date of grant of this patent or twenty years from the earliest effective U.S. filing date of the application, subject to any statutory extension.

If this application was filed on or after June 8, 1995, the term of this patent is twenty years from the U.S. filing date, subject to any statutory extension. If the application contains a specific reference to an earlier filed application or applications under 35 U.S.C. 120, 121 or 365(c), the term of the patent is twenty years from the date on which the earliest application was filed, subject to any statutory extensions.

- Term: 20 years calculated from the date of filing the patent application
- Example: Application filed 1 April 2002, term expires 1 April 2022, but patent not awarded until 1 April 2008
- Effective patent term is 14 years beginning 1 April 2008

TYPES OF PATENTS

- Utility
  - For Functionality
- Design
  - For Ornamentality
- Plant
  - For Asexually Reproducible Plants

UTILITY PATENT

- PROCESS
- MACHINE
- ARTICLE OF MANUFACTURE
- COMPOSITION OF MATTER
- IMPROVEMENTS THEREOF

- Term: 20 Yrs From Filing Date—Global Harmonization

GENERAL IP FRAMEWORK

The Bayh-Dole Act:

Contractor generally may retain title to any invention made while performing under a government contract, grant, or cooperative agreement.

Government retains a non-exclusive license to use or make the invention.

CONTRACT/GRANT/CA REQUIREMENTS

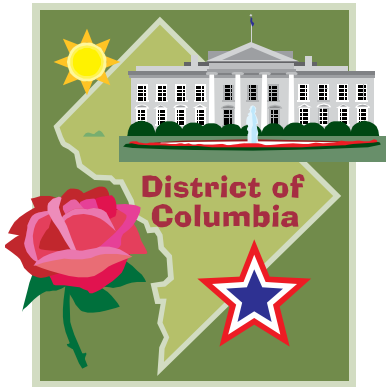
- To retain title to invention, contractor must do 3 things!

  - **DISCLOSE** *INVENTION TO GOVT*
  - **ELECT** *TO RETAIN TITLE*
  - **FILE** *PATENT APPLICATION*

- And do these 3 things in a timely fashion!

PATENT LICENSE AGREEMENTS (PLA) TYPES

- Nonexclusive
- Exclusive
- Partially Exclusive
  - field of use
  - geographic
  - duration

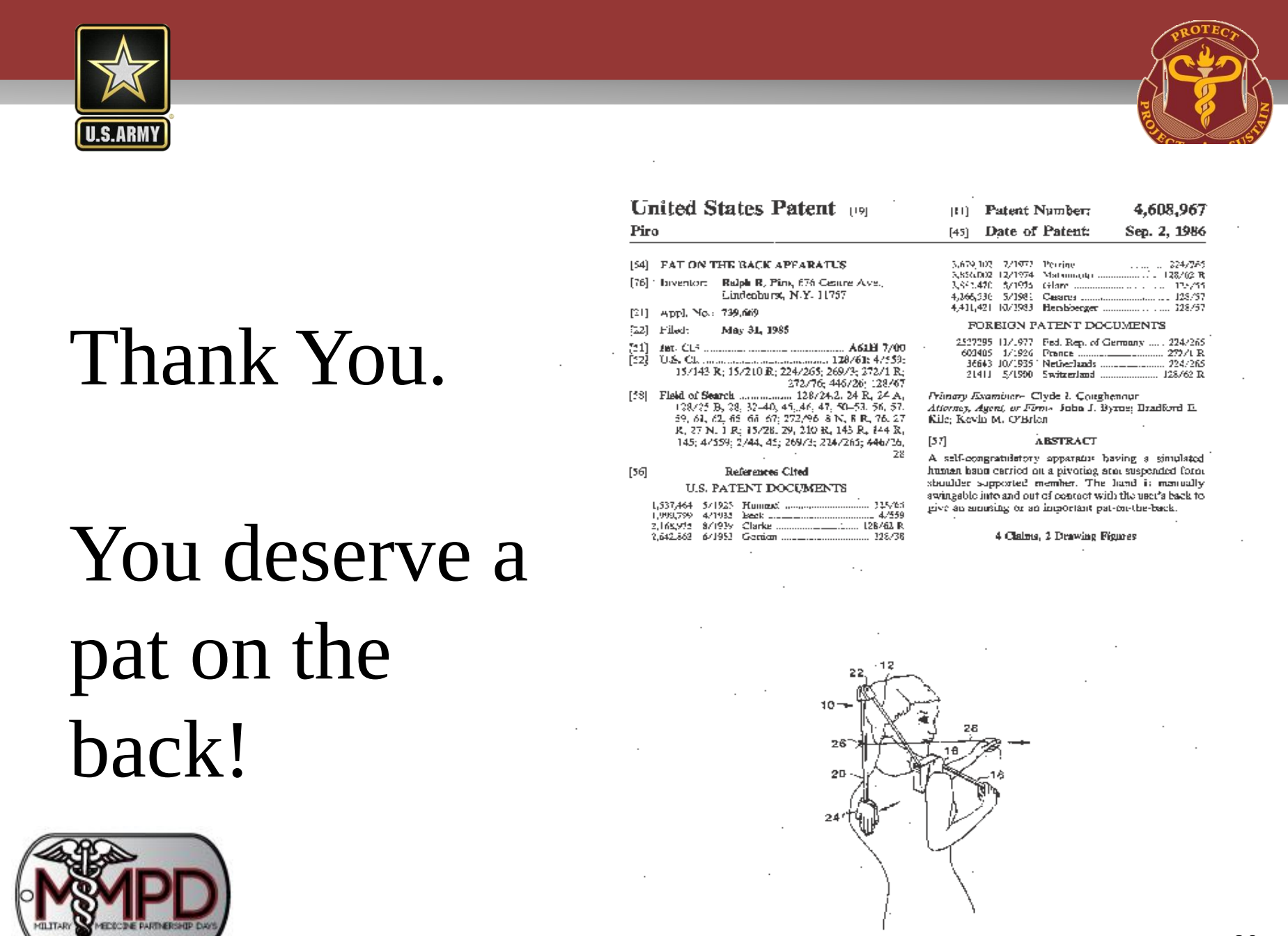


IP GENERATION, REPORTING, OWNERSHIP & LICENSING

- 4 SCENARIOS:
  - Contracts
  - Grants & Cooperative Agreements
  - Small Business Innovative Research (SBIR)
  - Cooperative Research & Development Agreement (CRADA)

Thank You.

You deserve a pat on the back!



United States Patent [19]
Piro

[11] Patent Number: 4,608,967
[45] Date of Patent: Sep. 2, 1986

[54] PAT ON THE BACK APPARATUS

[76] Inventor: Ralph R. Piro, 676 Centre Ave., Lindenhurst, N.Y. 11757

[21] Appl. No.: 739,669

[22] Filed: May 31, 1985

[51] Int. Cl.[4] A61H 7/00
[52] U.S. Cl. ..... 128/63; 4/559; 15/143 R; 15/210 R; 224/265; 269/3; 272/1 R; 272/76; 446/26; 128/67
[58] Field of Search ..... 128/24.2, 24 R, 24 A, 128/25 B, 28, 32–40, 45, 46, 47, 50–53, 56, 57, 59, 61, 62, 65, 66, 67; 272/96, 8 N, 8 R, 76, 27 R, 27 N, 1 R; 15/28, 29, 210 R, 143 R, 144 R, 145; 4/559; 2/44, 45; 269/3; 224/265; 446/26, 28

[56] References Cited

U.S. PATENT DOCUMENTS

1,537,464	5/1925	Hummel	135/63
1,998,599	4/1935	Isaak	4/559
2,165,975	8/1939	Clarke	128/63 R
2,642,862	6/1953	Gordon	128/38
3,679,102	7/1972	Perrine	224/265
3,850,002	12/1974	Matsumoto	128/62 R
3,851,470	5/1955	Glare	72/93
4,366,330	5/1981	Casarez	128/57
4,431,421	10/1983	Hershberger	128/57

FOREIGN PATENT DOCUMENTS

2527295	11/1977	Fed. Rep. of Germany	224/265
603405	1/1926	France	272/1 R
36643	10/1935	Netherlands	224/265
21411	5/1890	Switzerland	128/62 R

Primary Examiner—Clyde I. Coughenour
Attorney, Agent, or Firm—John J. Byrne; Bradford E. Kile; Kevin M. O'Brien

[57] ABSTRACT

A self-congratulatory apparatus having a simulated human hand carried on a pivoting arm suspended from a shoulder supported member. The hand is manually swingable into and out of contact with the user's back to give an assuring or an important pat-on-the-back.

4 Claims, 2 Drawing Figures

Questions?

For additional questions after the conclusion of the conference, send an email message to usarmy.detrick.medcom-usamrmc.mbx.mmpd@mail.mil