

Biomedical E&I BMEI-2022

**Regulatory Affairs
Regulator Guidances
Preclinical and Clinical evidence**

November 29, 2022

Dmitry Kulish

Skoltech

BMEI STRUCTURE AND TOPICS

- MONDAY
 - mentoring by request
- TUESDAY
 - lecture of the topic of the week
 - Indication + MOA + POC
 - Patent
 - Formulation + Manuf + QC
 - Reg guidances + Preclin + Clin
 - Value chain + Value delivery
- THUR
 - mentoring by request
- FRIDAY
 - Team presentation
 - **Last course activity day: Wed Dec 16th**

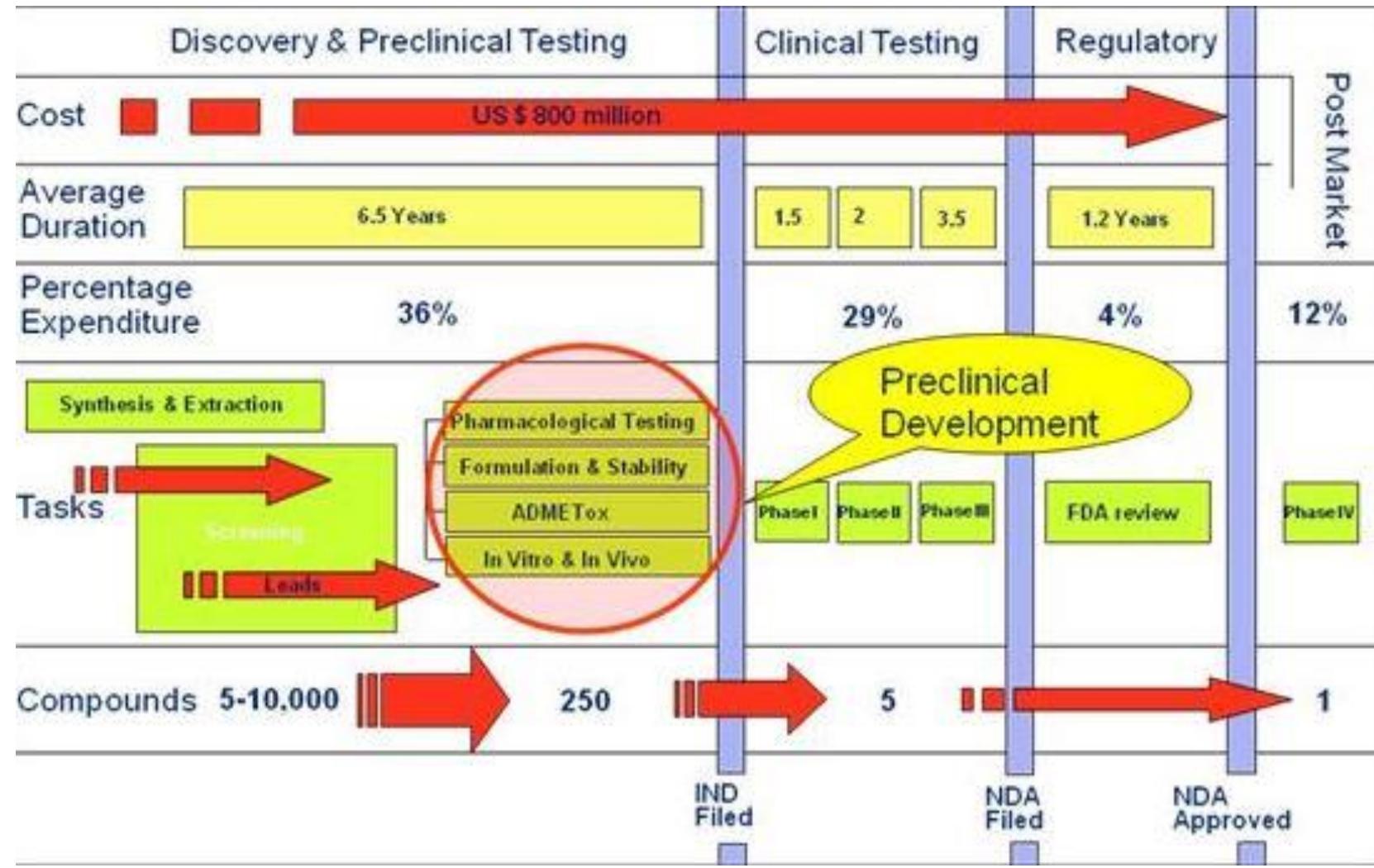
| TUE-FRI 9-12 | | | |
|--------------|----|---|-----------------|
| week 1 | 1 | Onco/Tobacco game + BMEI course intro | |
| | 4 | | |
| week 2 | 8 | ELP | |
| | 11 | LECT: Indication + POC experiment + charact | |
| week 3 | 15 | PRESO: Ind + POC experiment + valid QC | Michail Grubman |
| | 18 | LECT: Grubman | Michail Grubman |
| week 4 | 22 | LECT: PATENT | |
| | 25 | PRESO: PATENT three claims | |
| week 5 | 29 | LECT: Reg + Guidances + Preclin + Clin | |
| | 2 | PRESO: Reg + Guidances + Preclin + Clin | Sophia Yartseva |
| week 6 | 6 | LECT: Formulation + Manuf + QC release | Sophia Yartseva |
| | 9 | PRESO: Formulation + Manuf + QC release | |
| week 7 | 13 | LECT: BMEI career | |
| | 16 | FIN PRESOS | Michail Grubman |

NEXT DAYS

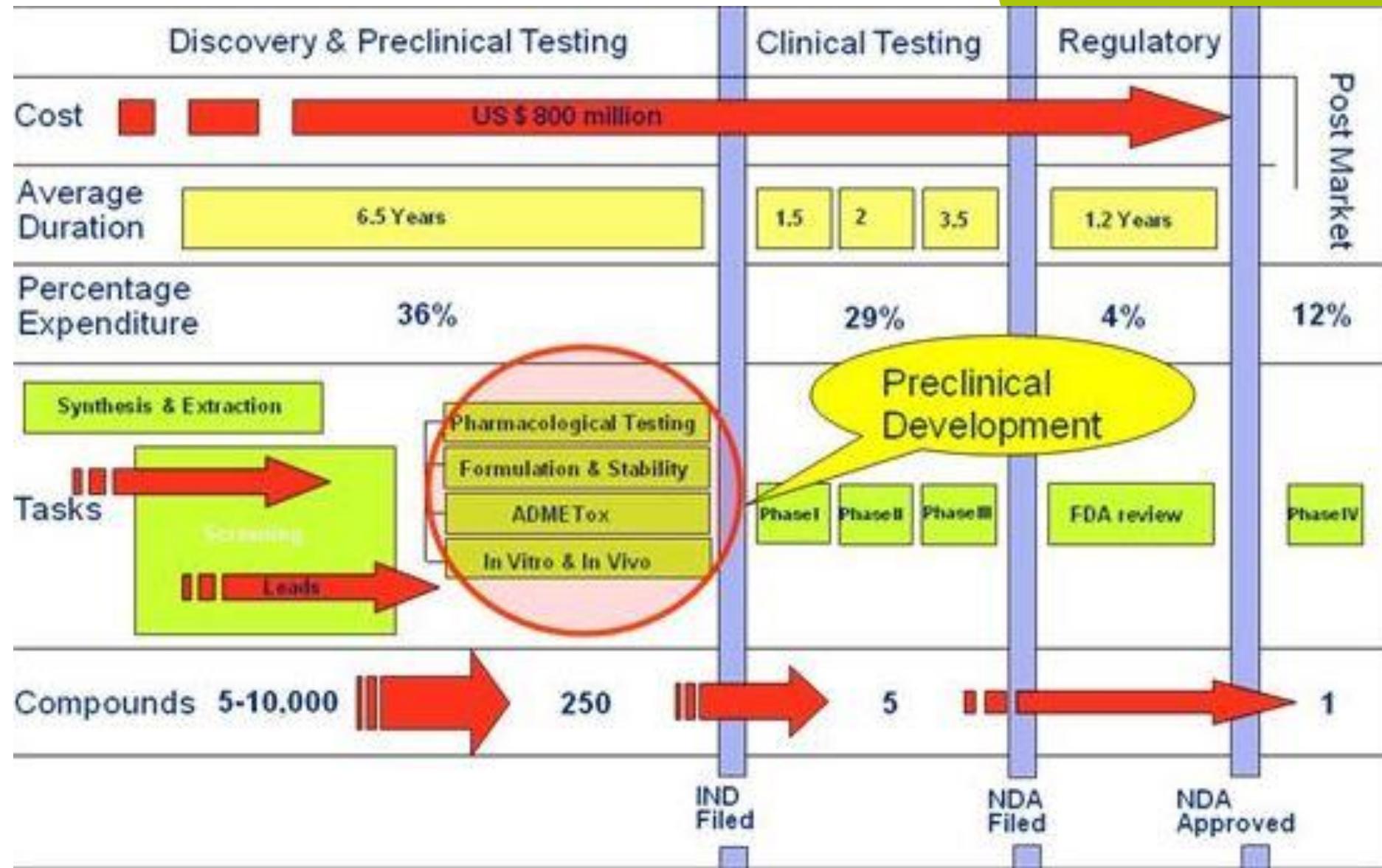
- Friday Dec 02: Reg presentation
 - graded submission in Canvas: Monday Dec 05
- **Monday Dec 05, 11pm:**
 - **Graded submission of the team IP presentation in Canvas**
- Tuesday Dec 06: Sophia Yartseva lecture
 - as well as “Manuf + QS”
- Friday Dec 09: “MANUF + QC” presentation
 - graded submission in Canvas: Monday Dec 12

| PROJECT | ICD+MOA+POC | NOVELTY | NON OBVIOUSNESS UTILITY | CLAIMS |
|----------------------------|---------------------------|------------------------------------|----------------------------|---|
| HYPER TENSION | great update ! way to go! | cant believe no CADD patents outth | good update | Great update, but still non patent language |
| HER+ CELL CYCLE CMB | good | good | good | SUPERGOOD! Structure + TECH descriptors |
| BRCA PLGA | good | good | good update | better structure but senseless “immunogen” and “buffer” |
| GLIO SCAN DIAG | good | good | good update | great structure, but lack tech descriptors |
| GLIO CAR MPh | good | good | good | SUPERGOOD! Structure + TECH descriptors |
| GULLAINE BARRE | good | good | good | SUPERGOOD! Structure + TECH descriptors |
| PARK DIAG | good | good | good update | great structure, but lack tech descriptors |

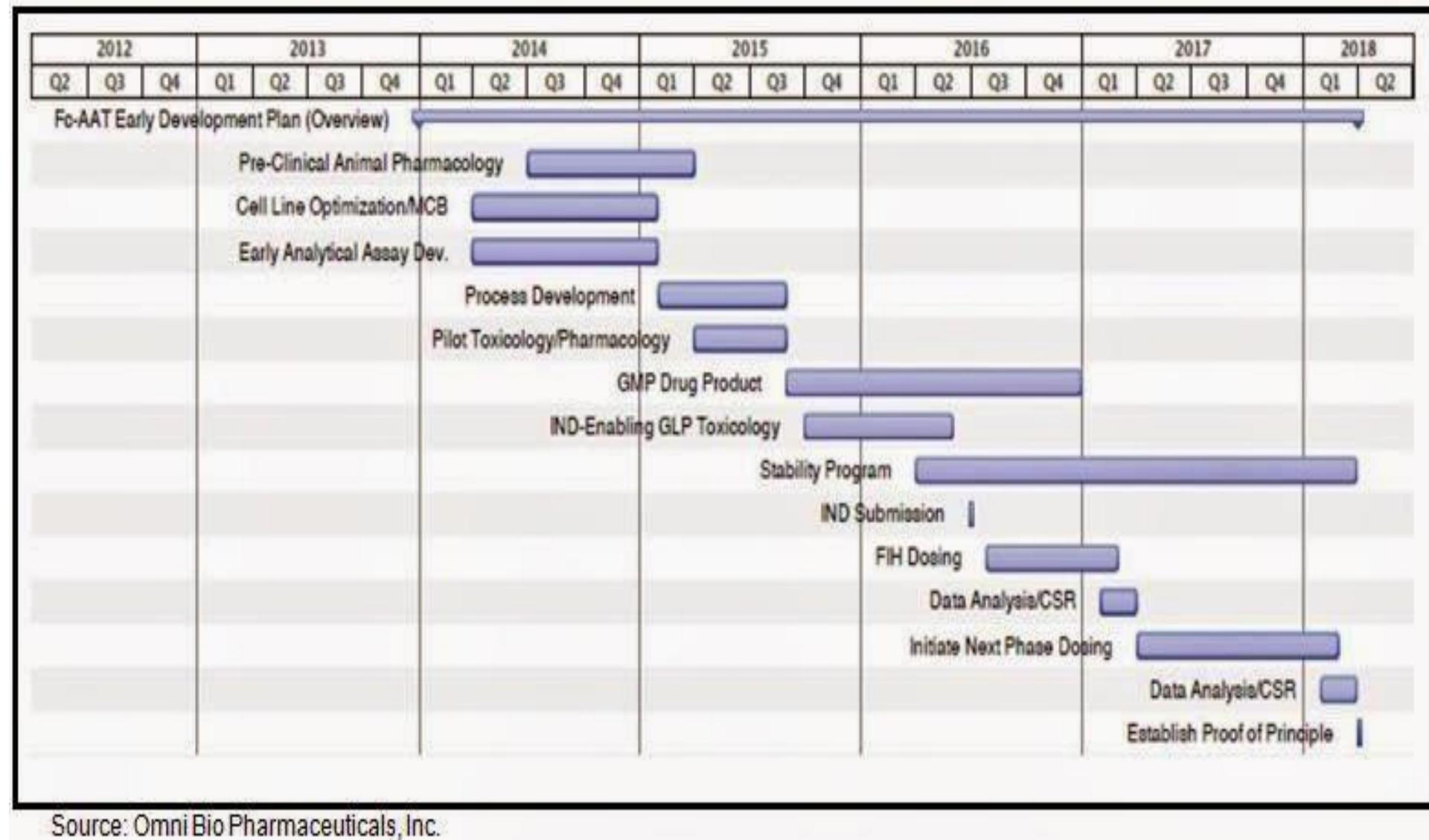
The long and windy road of BMEI product/service



Preclinical = pre-IND



Pre-IND = Preclinical + Manuf + QC



Source: Omni Bio Pharmaceuticals, Inc.

Pre-IND = 60% of your potential initial job

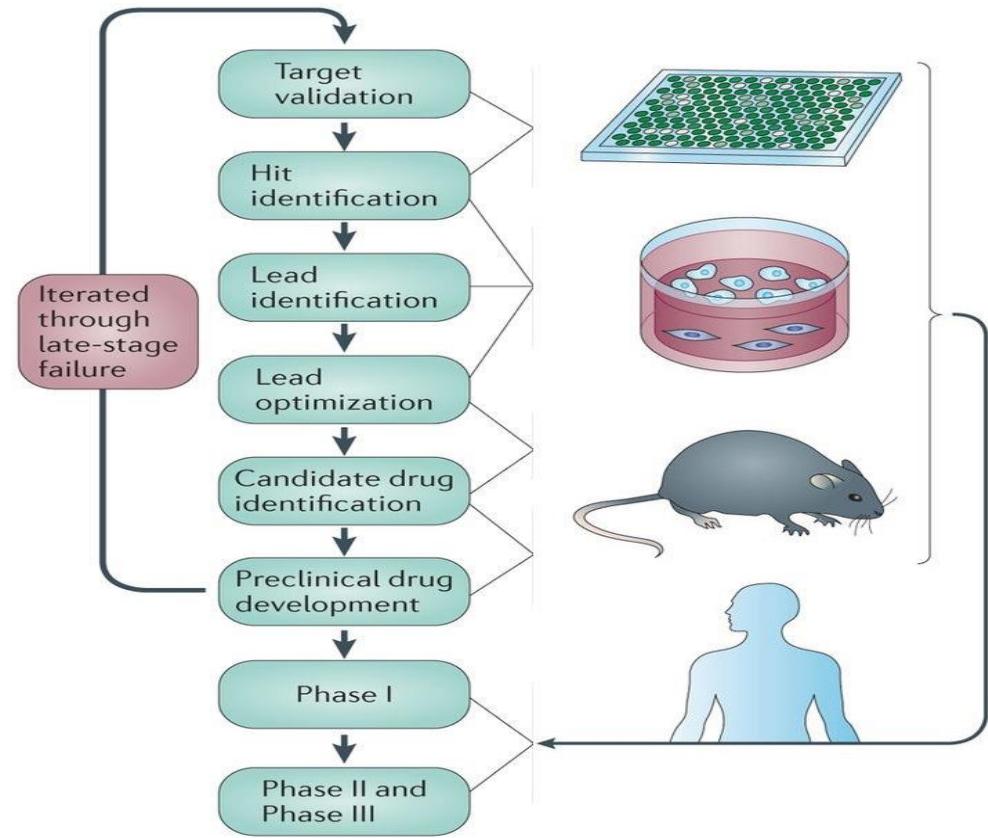
(after IP and QC)

- Mastering existing techniques under GXP
 - Magic and choreography
- Jumping into the new research needs
 - Scary but exciting and respected
 - Pharma
 - Dedicated projects
 - Biotech
 - Constant uncertainty:
technological,
organizational, and political
 - CROs
 - Serving customer needs



Preclinical common sense = Increase evidence before going into human patients.

Key topic is the pivotal experiment

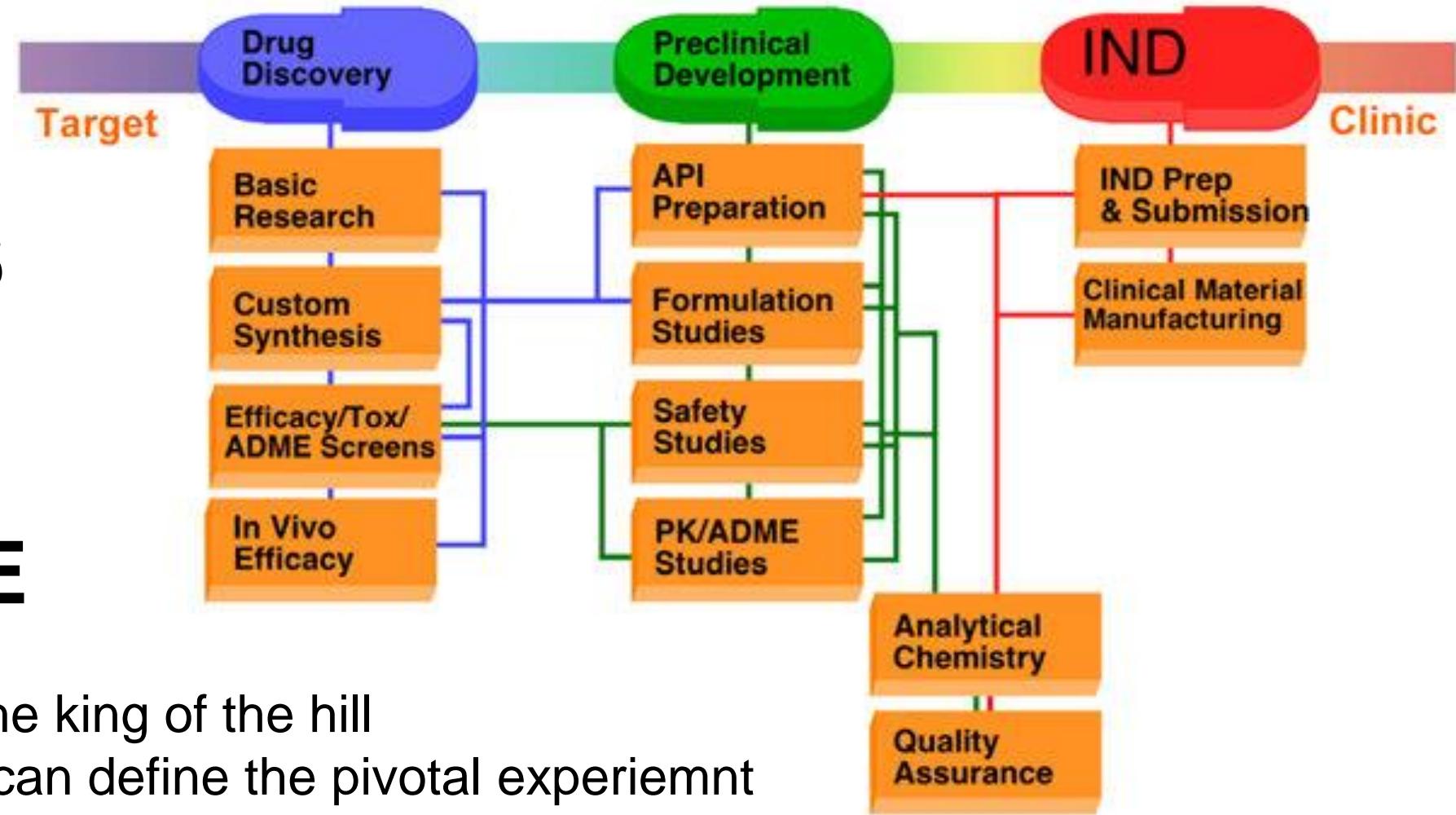


There are several steps involved with doing a Pre-Clinical Trial:

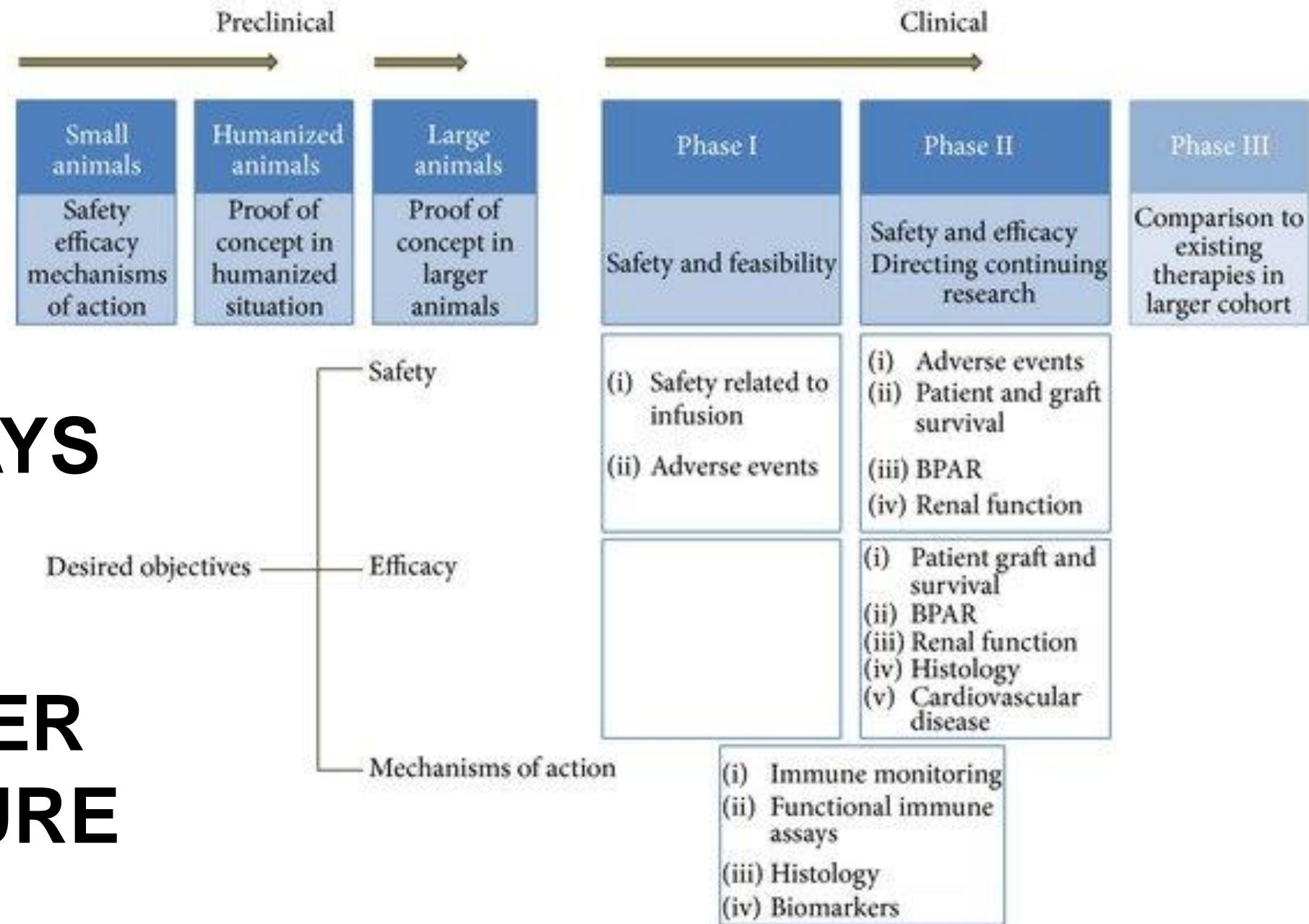
- 1 Identify a Drug Target
- 2 Develop a Bioassay
- 3 Screen the Drug in the Assay
- 4 Establish Effective and Toxic Doses
- 5 File for approval as an Investigational New Drug (IND)

ALWAYS SEE BIG PICTURE

- You are not the king of the hill
- But only you can define the pivotal experiment
- For many years safety was more important than efficacy and MOA
- Not anymore



ALWAYS SEE THE BIGGER PICTURE



THREE PILLARS YOU MUST PROMINENTLY DISPLAY IN YOUR PRECLINICAL DESIGN

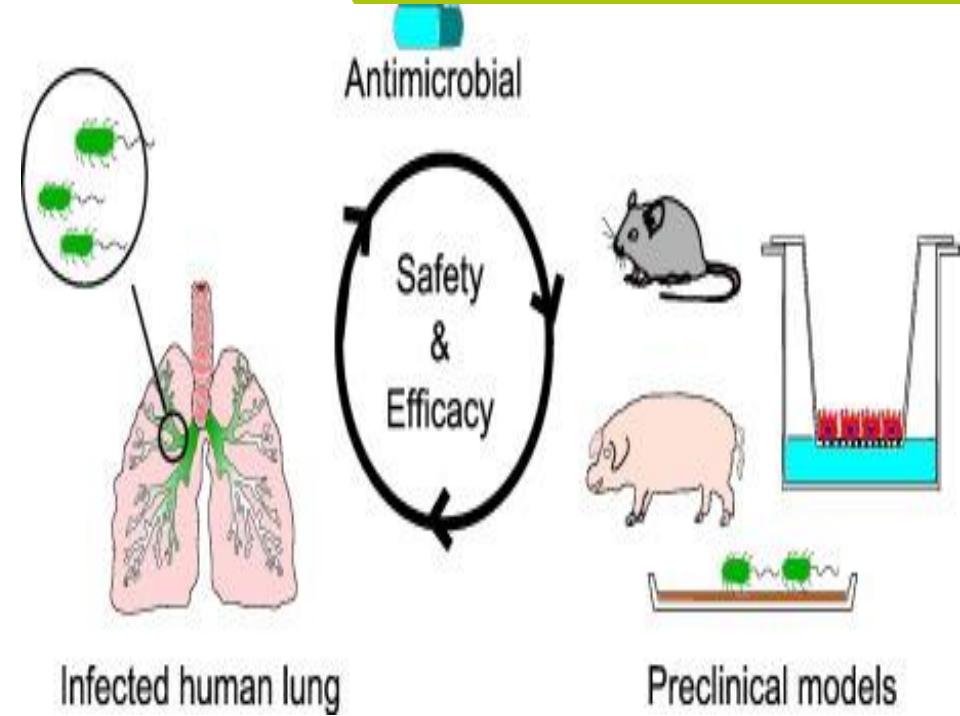
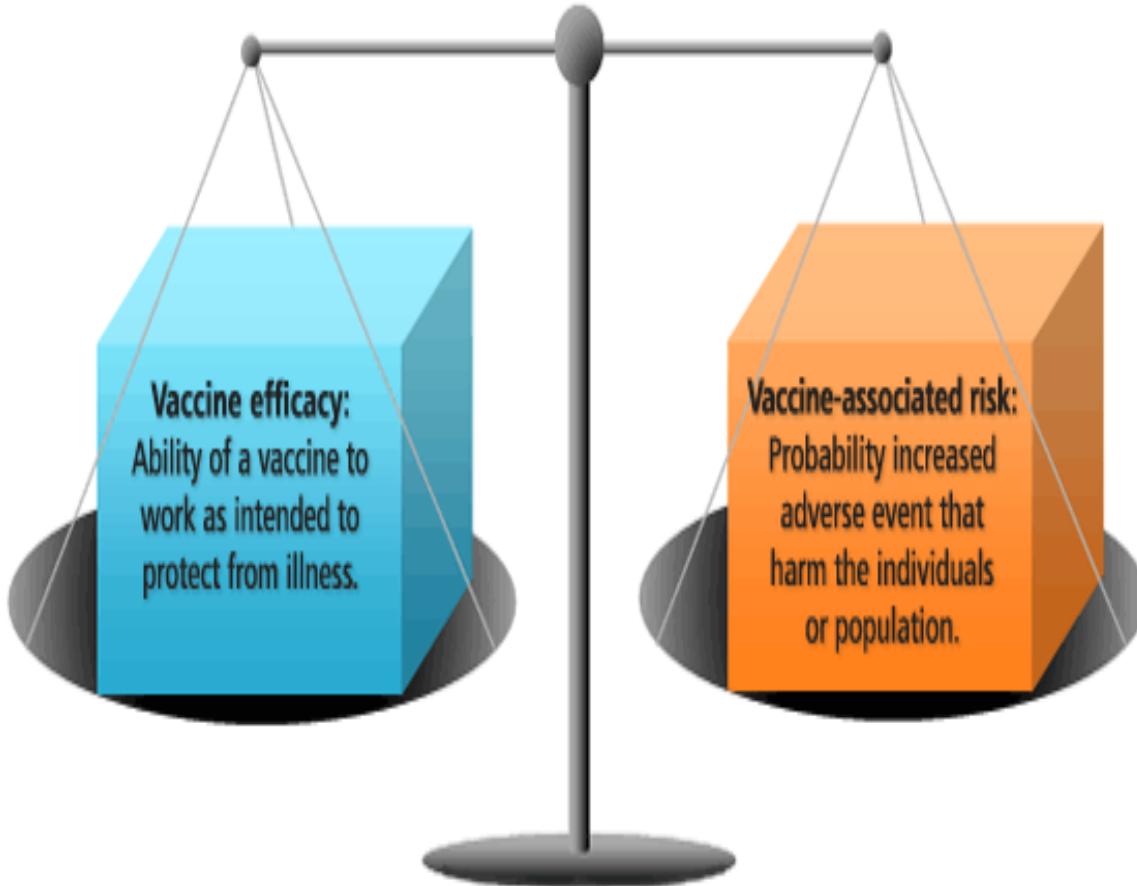


The process of drug development

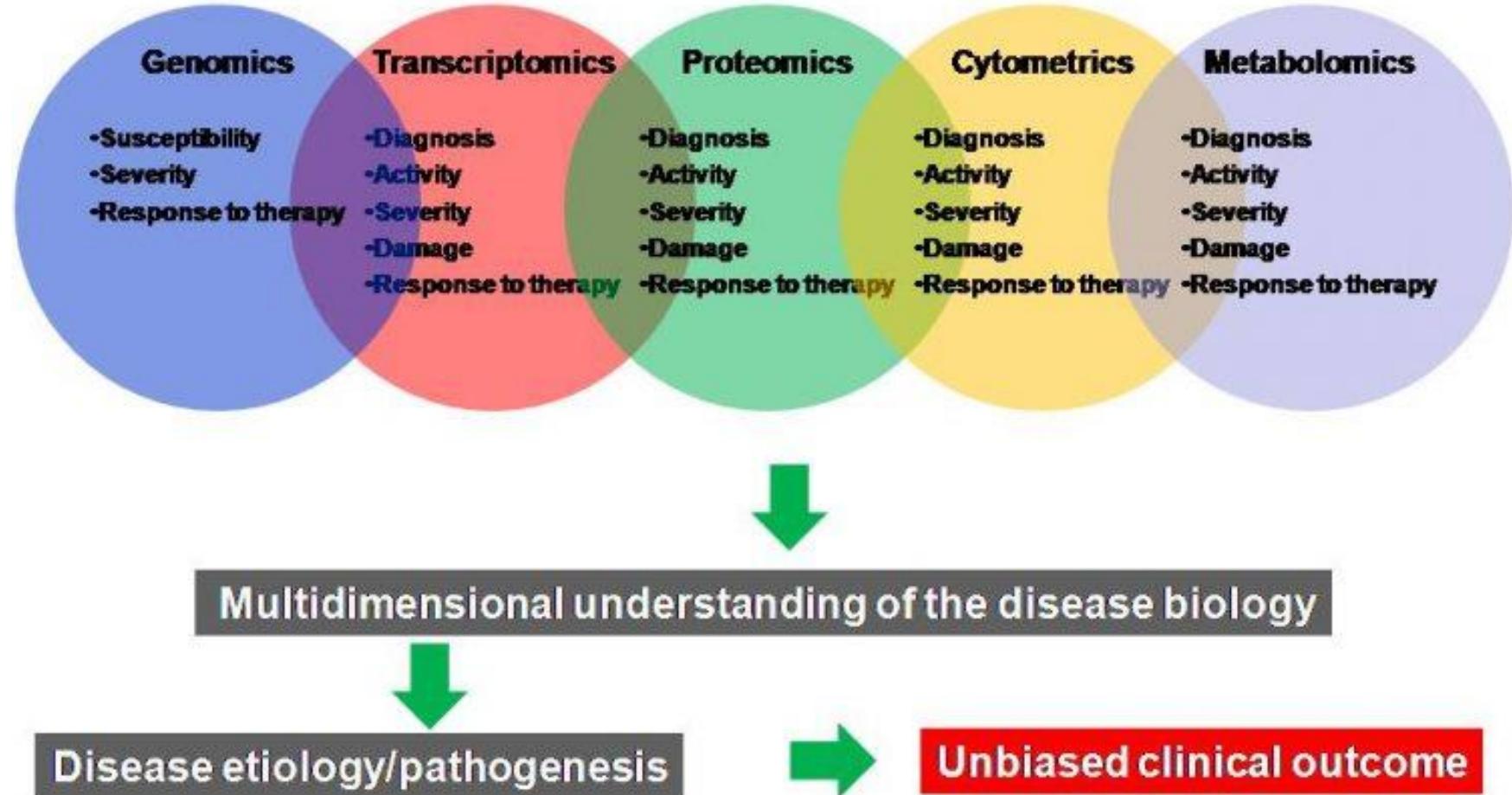
- Early Stage drug discovery and lead optimization (going fishing ?)
- Production of the active product and scale-up
- Does it work ? Biological models
- Is it safe ? Toxicity
- Can we bring it to the market ? Regulatory

SAFETY KILLS EFFICACY

Your job is scientific proof of the balance

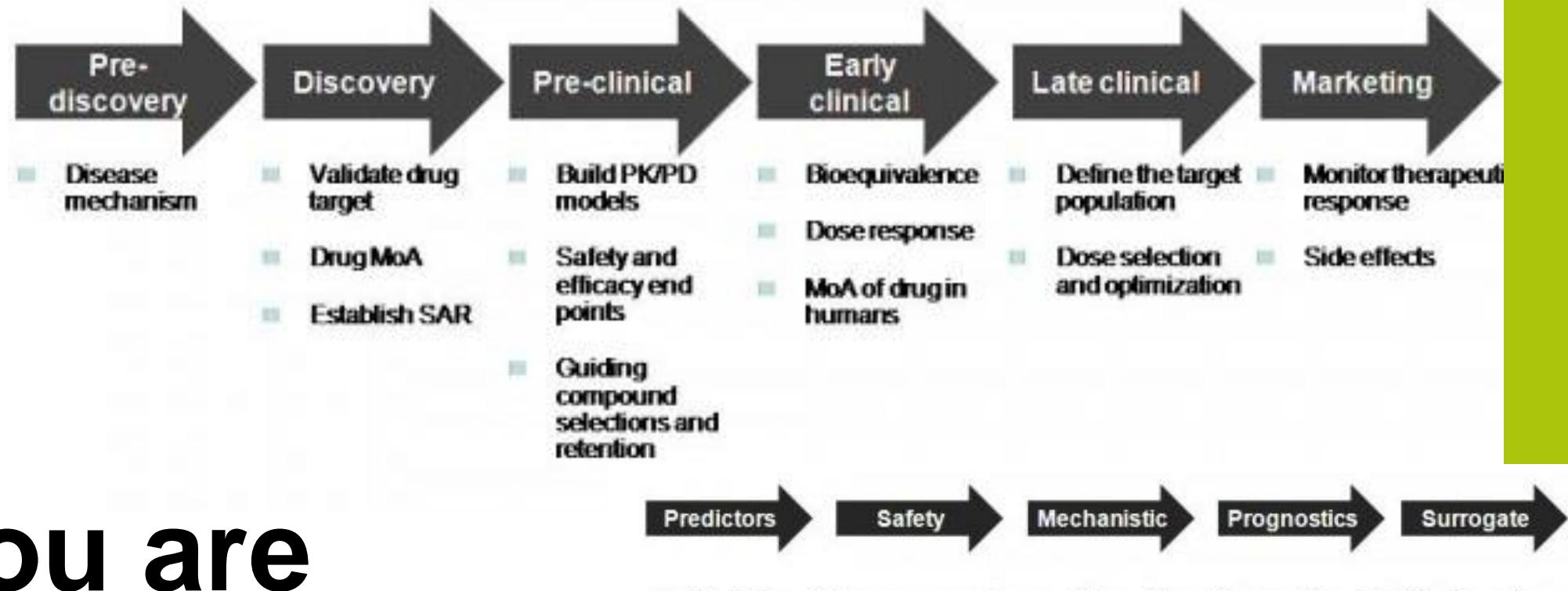


If you are in the Omics



If you are in the Diagnostics

Diagnostics universe



- Predictors of disease responsiveness. These biomarkers could predict at the time of patient's enrollment her/his responsiveness to specific therapeutic intervention/treatment.
- Safety biomarkers. These biomarkers could predict risk of major toxicity from a specific therapy.
- Mechanistic biomarkers. These biomarkers could explain or validate the mechanism(s) of action of a given treatment in humans.
- Prognostic markers. These biomarkers could predict overall outcome (survival/clinical benefit) independent of clinical responsiveness based on standard response criteria.
- Surrogate (clinical end point) biomarkers. These biomarkers could provide information about the likelihood of clinical benefit/survival at earlier stages compared to prolonged disease-free or overall survival analysis.

MEDICAL DEVICE UNIVERSE

7

Medical Devices Classification

| Class | Risk | Examples | Safety / Effectiveness Controls | Regulatory Pathway |
|-------|---------|---|--|---|
| I | Low | Tongue depressor, hospital beds | General Controls - With Exemption - Without Exemption | Self Registration Or 510(k) |
| II | Medium | Absorbable suture, blood pressure cuffs | General controls - With Exemption - Without Exemption Special controls - With Exemption - Without Exemption | <ul style="list-style-type: none">Most class II devices are approved under a 510(k) pre-market notification submission.Few devices of class II are approved under PMA10-15% devices require clinical trial |
| III | Highest | Implantable pacemaker, coronary stent | General controls Special controls Pre-market authorization | Pre-market approval (PMA) Almost all require clinical Data |



TOXICOLOGY UNDER GLP MUST BE STANDARD

| Typical IND-Enabling Preclinical Safety Studies | | | |
|---|----------------|------------------------------|-------------------|
| | <u>Species</u> | <u>Duration of Studies</u> | <u>Cost (\$)*</u> |
| (Bio)analytical | | Assay development | 1,000/day |
| | | Validation (per species) | 15,000-20,000 |
| | | Running samples | 70-100/sample |
| | | Dose formulation Analyses | \$5K/time study |
| Rat | | Single dose | 29,000-75,000 |
| | | 7 day DRF | 50,000-125,000 |
| | | 14 days | 165,000-200,000 |
| | | 28 days | 120,000-275,000 |
| Dog | | Maximum tolerated dose (MTD) | 30,000-65,000 |
| | | 7 day DRF | 75,000-145,000 |
| | | 14 days | 140,000-300,000 |
| | | 28 days | 200,000-450,000 |

* Pricing will vary depending on the actual study design, route of administration, numbers of groups, numbers of animals, bioanalytical determinations, special tests required, etc.



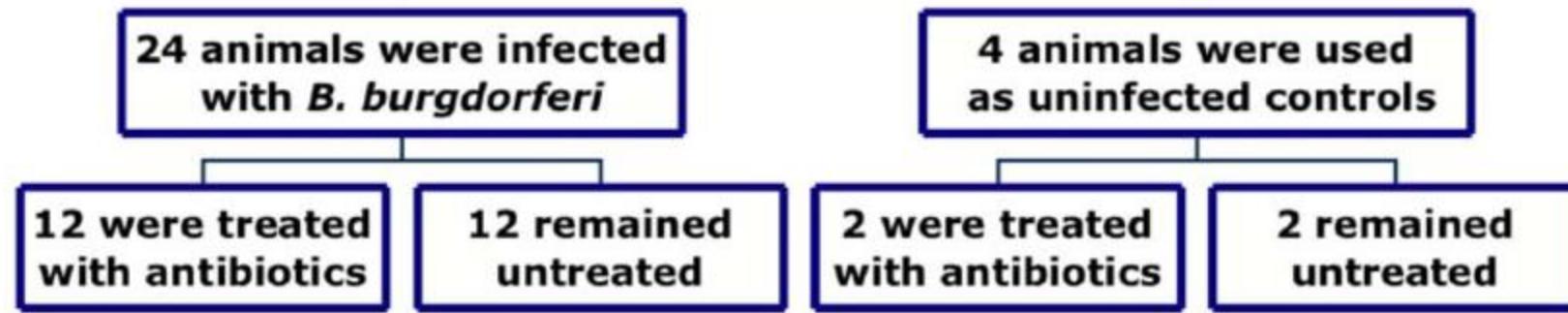
| Typical IND-Enabling Preclinical Safety Studies (cont'd) | | | |
|--|----------------|-------------------------------|-------------------|
| | <u>Species</u> | <u>Type of Studies</u> | <u>Cost (\$)*</u> |
| Monkey | | MTD | 75,000-125,000 |
| | | 7 day DRF | 100,000-240,000 |
| | | 14 days | 265,000-410,000 |
| | | 28 days | 280,000-550,000 |
| Genetox | | Bacterial mutagenicity | 6,000-8,000 |
| | | Chromosome aberration | 20,000-27,000 |
| | | Rodent micronucleus | 25,000-35,000 |
| Safety Pharm | | hERG inhibition (patch clamp) | ~16,000 |
| | | CNS rodent | 25,000-35,000 |
| | | Cardiovascular (telemetry) | 75,000-120,000 |
| | | Respiratory | 25,000-35,000 |

* Pricing will vary depending on the actual study design, route of administration, numbers of groups, numbers of animals, bioanalytical determinations, special tests required, etc.

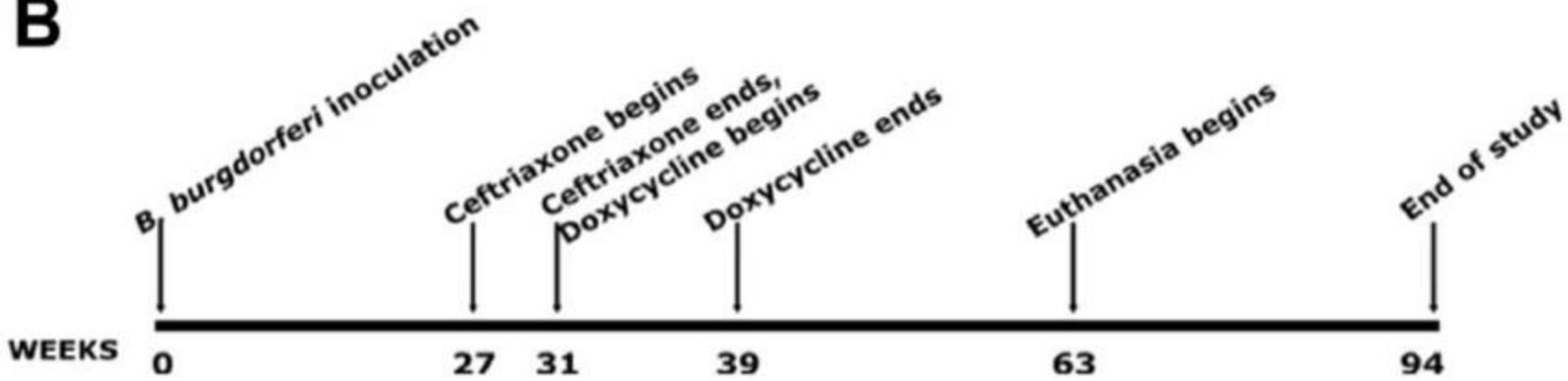


POC UNDER GLP MUST BE PRECISE

A



B



POC UNDER GLP MUST BE PRECISE

Generalized design of a repeated-dose rodent toxicity study

| Treatment Group | Dose (mg/kg/day) | Main (Terminal) | | Recovery | | Toxicokinetics* | |
|--------------------|---------------------|-----------------|--------|----------|--------|-----------------|--------|
| | | Male | Female | Male | Female | Male | Female |
| Vehicle | 0 | 10 | 10 | 5 | 5 | 0 | 0 |
| Low Dose | A | 10 | 10 | 0 | 0 | 9 | 9 |
| Mid Dose | B | 10 | 10 | 0 | 0 | 9 | 9 |
| High Dose | C | 10 | 10 | 5 | 5 | 9 | 9 |

- Number of animals depends on blood volumes required, number of timepoints, etc.
- GLP-compliance needed for a pivotal (clinical trial-supporting) study
- Toxicokinetic evaluations
- Standard *AND* drug- or disease-specific endpoints
- Histopathology

REGULATOR GUIDANCES

- FDA
- EMA
- WHO
- MZ RF

- Professional and peer-reviewed
 - Free and Priceless !
 - Amazingly diverse
 - Hard to read and digest
 - This is your work and art that you learn here

The screenshot shows the FDA's News & Events page. A specific news release is highlighted: "FDA outlines cybersecurity recommendations for medical device manufacturers". The release date is January 15, 2016. The text discusses the agency's draft guidance for postmarket management of cybersecurity vulnerabilities in medical devices. It includes social media sharing options (Facebook, Twitter, LinkedIn, Pinterest, Email, Print) and contact information for inquiries (Media: Angela Stark, 301-796-0397; Consumers: 888-INFO-FDA).

The screenshot shows the EMA's page for the ICH S9 Non-clinical evaluation for anticancer pharmaceuticals. It displays the current effective version (ICHMP/ICH/646107/08), published on 01/05/2010, effective from 11/02/2013, and includes keywords like Anticancer pharmaceuticals, advanced cancer, pharmacology, pharmacokinetics, toxicology, non-clinical. The description notes that the document aims to assist in the design of non-clinical studies for the development of anticancer pharmaceuticals.

The screenshot shows the EMA's page for Non-clinical studies required before first clinical use of gene therapy medicinal products. It displays the current version (ICHMP/GTWP/125459/06), published on 30/05/2008, and includes a cookie consent banner.

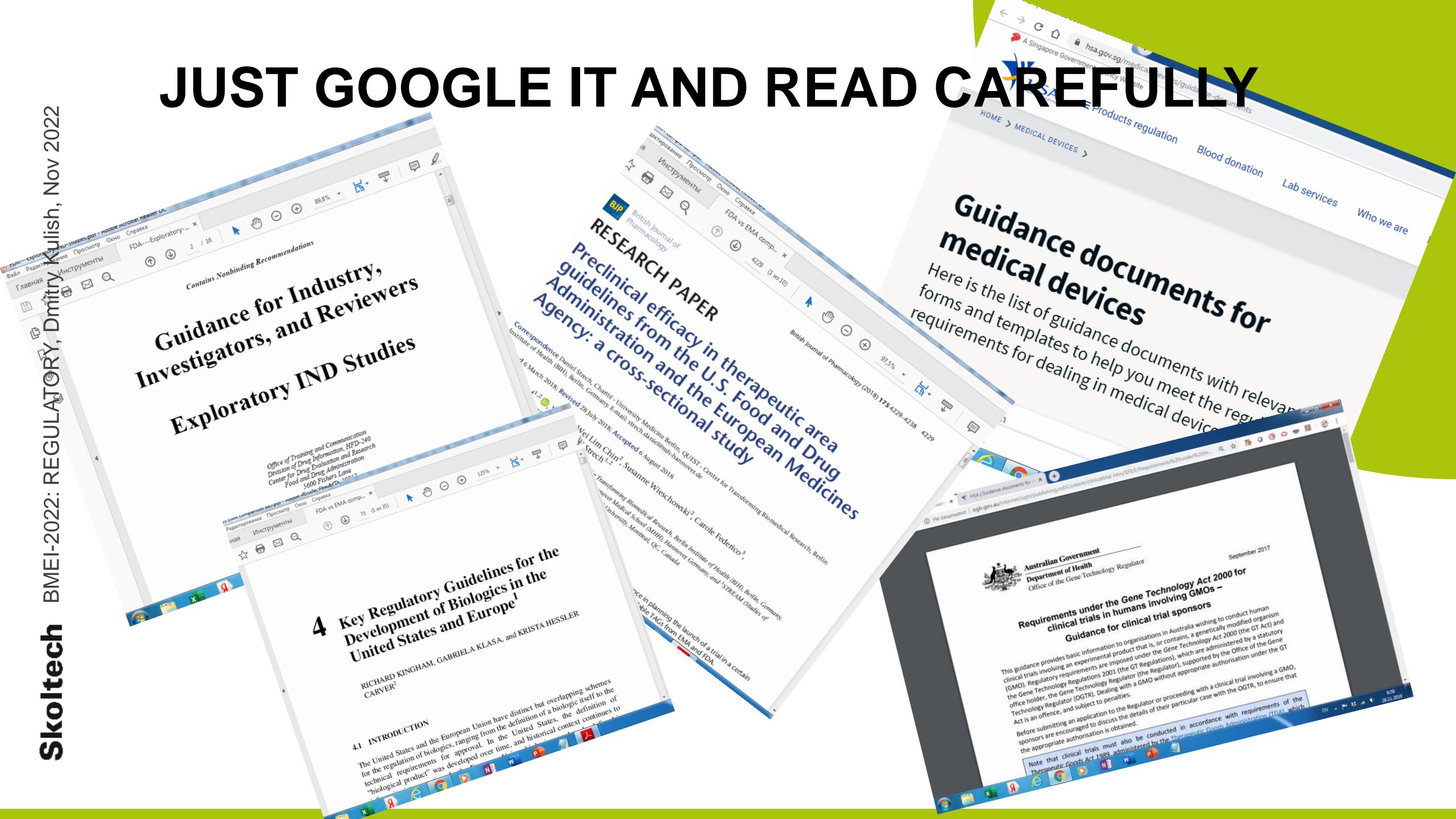
The screenshot shows the EMA's page for Non-clinical studies required before first clinical use of gene therapy medicinal products. It displays the current version (ICHMP/GTWP/125459/06), published on 30/05/2008, and includes a cookie consent banner.

trials with a view to implementing 3Rs

- ICH S6 (R1) Preclinical safety evaluation of biotechnology-derived pharmaceuticals
- ICH S9 Non-clinical evaluation for anticancer pharmaceuticals
- ICH M3 (R2) Non-clinical safety studies for the conduct of human clinical trials for pharmaceuticals
- Strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicinal products
- Non-clinical studies required before first clinical use of gene therapy medicinal products
- Evaluation of control samples for non-clinical safety studies: checking for contamination with the test substance
- Setting health based exposure limits for use in risk identification in the manufacture of different medicinal products in shared facilities

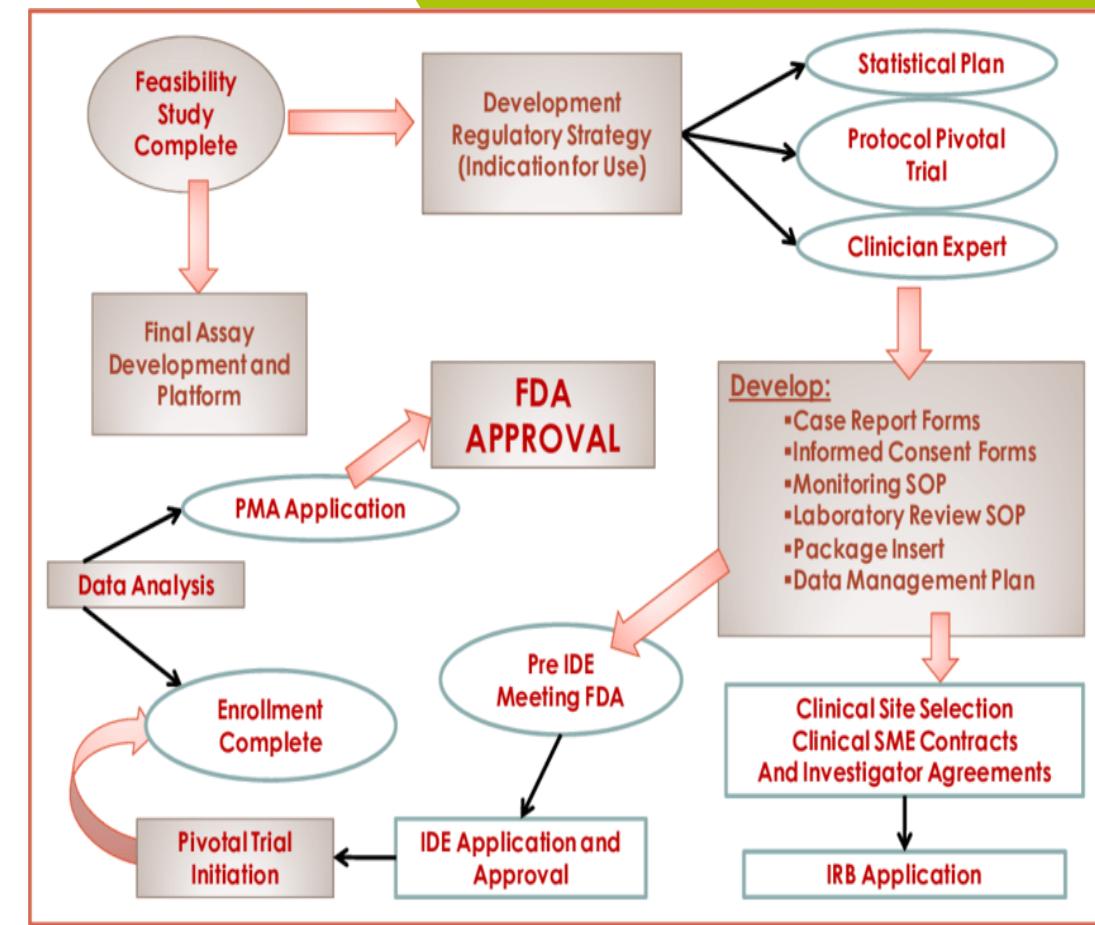
MZ (MOH) RF RULES ARE BASED ON THE EMA

JUST GOOGLE IT AND READ CAREFULLY



UNDERSTANDING REGULATIONS MAY BE MESSY HARD WORK

- **REGULATORY GUIDANCES MAY BE BULKY AND CONTRADICTORY**
 - Yes. It is your job to read them
 - And it will be your job to write them in future
- **THE BEST HINT FOR PROPER REGULATORY FRAMEWORK AND LINKS?**
 - The regulatory path of your comparator
- **HOW YOU FIND IT?**
 - May be tricky and confidential
 - Still, read the published clin trial reports, patents and just google



WHAT TO REPORT IN YOUR HW ABOUT GOVERNMENTAL GUIDANCES

➤ **GUIDANCES ON QC**

- Sets of methods

➤ **GUIDANCE ON PRECLINICAL**

- Pivotal experiments
- Pivotal toxicologies

➤ **GUIDANCE ON CLINICAL**

- Crucial stages

➤ **GUIDANCE ON MANUFACTURING**

- CMC (controls)

➤ **GUIDANCE ON DELIVERY**

- e.g. COVID test delivery

Regulations Along the Drug Life



Not Regulated

GLP

GCP

GMP

21 CFR 11 Electronic Records&Signatures

Lead to
Drug Target



IND

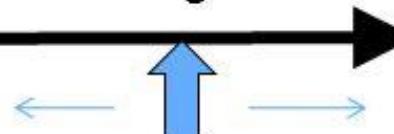
Submission &
Review



BLA/NDA

Submission &
Review

Post
Marketing
Surveillance



Safety, Quality, Efficacy

GLP = Good Laboratory Practices

GxP = GLP+GCP+GMP = Predicate Rules

GMP = Good Manufacturing Practices

IND = Investigational New Drug Application

GCP = Good Clinical Practices

BLA = Biologic License Application

NDA = New Drug Application

GXP is mutual responsibility

Good Laboratory Practice (GLP) is a **quality system** concerned with the organisational process and the conditions under which non-clinical health and environmental safety studies are **planned, performed, monitored, recorded, archived and reported.**

(OECD, 1997)



Fundamentals of OECD GLP Principles

Five Basic Points

- 1. RESOURCES:** Personnel, Facilities & Equipment
- 2. CHARACTERIZATION :**
 - Test Article - Identification, Quality
 - Test system - Identification, Health status...
- 3. RULES :** Protocols / Study Plans, Procedures
- 4. RESULTS:** Raw data, Final Report, Archives
- 5. QUALITY ASSURANCE:** Audit/Inspection - Training - Advice



The **5 P's** of Good Manufacturing Practices (GMP)



People

Comprehend roles
and responsibility



Products

Clear specifications
at every phase
of production



Processes

Properly documented,
simple, and consistent



Procedures

Guidelines for
undertaking critical
processes



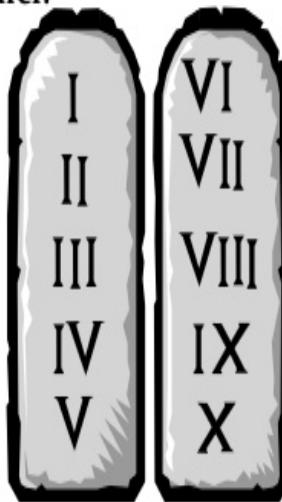
Premises

Cleanliness and
equipment calibration
at all times

GLP is written by waste, tears, and blood

GOOD LABORATORY PRACTICES PRINCIPLES.

- 1. Test Facility Organisation and Personnel.
- 2. Quality Assurance Programme(QAP).
- 3. Facilities.
- 4. Apparatus, Material and Reagents.
- 5. Test systems.
- 6. Test and Reference Substances.
- 7. Standard Operating Procedures(SOP).
- 8. Performance of The Study.
- 9. Reporting of Study Results.
- 10. Storage and Retention of Records and materials.



WHY WAS GLP CREATED?



- In the early 70's FDA became aware of cases of poor laboratory practice all over the United States.
- They discovered a lot fraudulent activities and a lot of poor lab practices.
- Examples of some of these poor lab practices found were
 - 1. Equipment not been calibrated to standard form , therefore giving wrong measurements.
 - 2. Incorrect/inaccurate accounts of the actual lab study.
 - 3. Inadequate test systems.

GLP is constructive and positive

Good Laboratory Practice (GLP) is a **quality system** concerned with the organisational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.

Why GLP?

- Development of quality test data
- Mutual acceptance of data
- Avoid duplication of data
- Avoid technical barriers to trade
- Protection of human health and the environment

(OECD, 1997)



Fundamentals of OECD GLP Principles

Five Basic Points

- 1. RESOURCES:** Personnel, Facilities & Equipment
- 2. CHARACTERIZATION :**
 - Test Article - Identification, Quality
 - Test system - Identification, Health status...
- 3. RULES :** Protocols / Study Plans, Procedures
- 4. RESULTS:** Raw data, Final Report, Archives
- 5. QUALITY ASSURANCE:** Audit/Inspection - Training - Advice

HONEST SCIENCE IS GLP

Rules & Characterization

- Protocols and Written Procedures:
 - main steps of research studies must be described in the study plan or protocol
 - for repeatability of the studies and reproducibility of results, routine procedures are described in SOPs
- Test item and the Test system
 - essential to know as much as possible about the test item and about the test system (often an animal or plant) to which it is administered.

CRO IS THE SERIOUS JOB AND CHALLENGE

Staff Characteristics

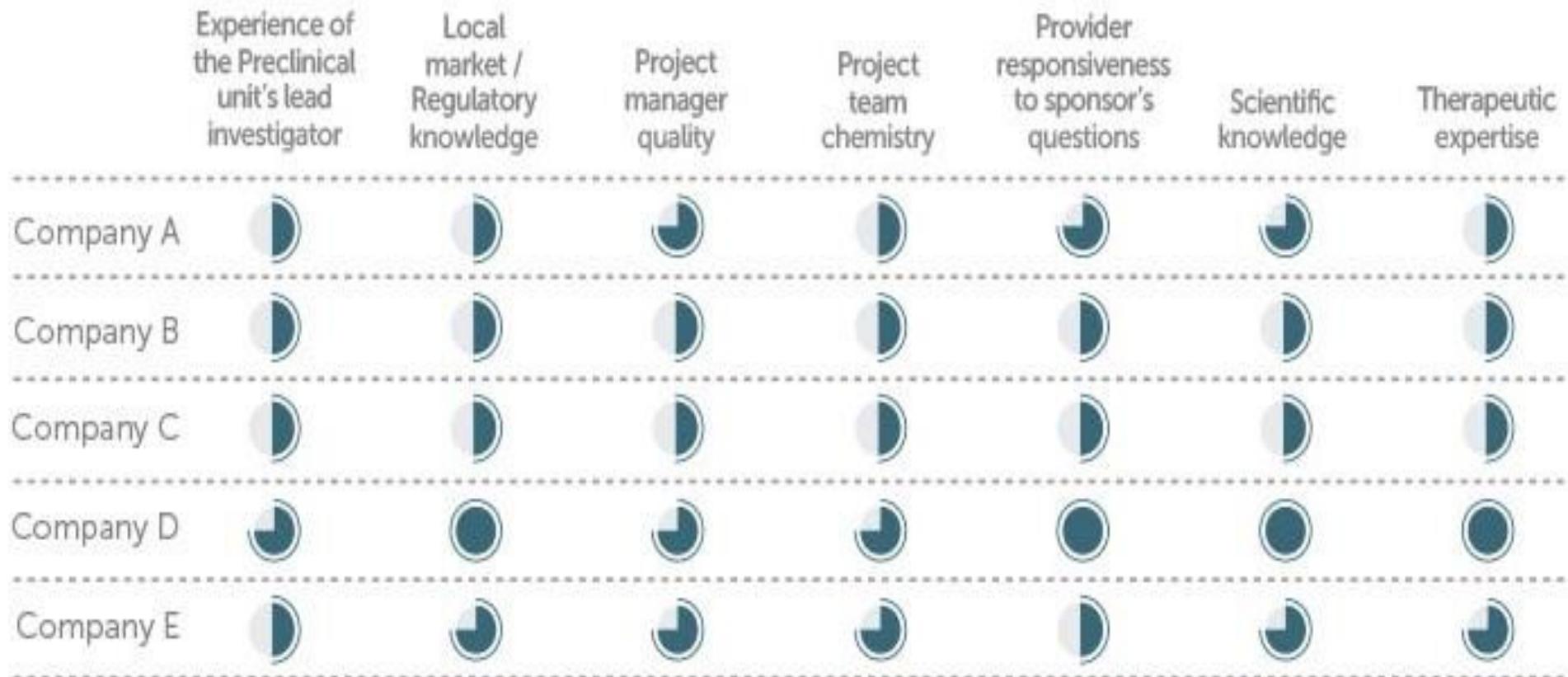


Table 5: Strategic alliances between CROs and pharma companies

| Pharma company | Location | CRO | Location | Comments |
|----------------------------------|-------------|-----------|----------|-----------------------------------|
| Merck and Co | US | Parexel | US | Biosimilars development |
| Samsung | Korea | Quintiles | US | Biosimilars development |
| Lilly | US | Advion | US | Analytics |
| Nycomed | Switzerland | Quintiles | US | Transfer of staff |
| Elan | Ireland | PPD, Inc | US | All development functions |
| Lilly | US | Covance | US | Drug development services |
| Sanofi-aventis | France | Covance | US | All drug development |
| Lilly | US | Parexel | US | Asia Pacific functional services |
| Bristol Myers | US | Parexel | US | Clinical development |
| Bristol Myers | US | ICON | Ireland | Clinical development |
| Bristol Myers | US | Wu-XI | China | Bioanalytical |
| Lilly | US | i3 | US | Medical writing and biostatistics |
| Pharmasset | US | BaSI | US | Preclinical |
| Product Development Partnerships | US | Quintiles | US | Clinical development |
| Janssen (J&J) | Belgium | Precos | US | Oncology development |
| Takeda | Japan | Avacta | US | |
| Pfizer | US | Parexel | US | Clinical development |
| Pfizer | US | ICON | Ireland | Clinical development |
| GSK | UK | Parexel | US | Clinical development |
| GSK | UK | PPD, Inc | US | Clinical development |
| Takeda | Japan | Covance | US | Clinical development |
| Takeda | Japan | Quintiles | US | Clinical development |

TOP 10 CROs 2016

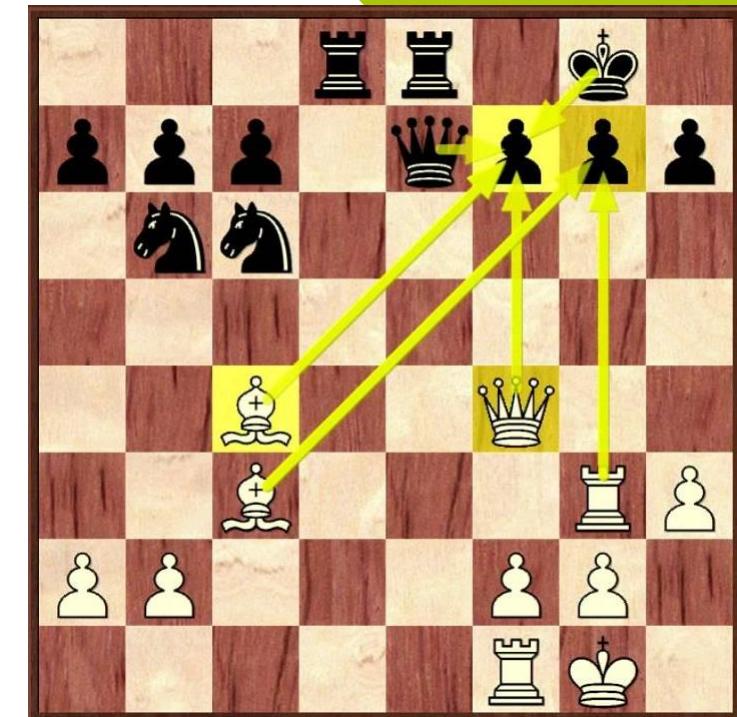
| | | | Revenues, 2016 (USD million) | Income Ratio, 2016 | Expense Ratio, 2016 | Service portfolio (units) |
|---|----|---|---------------------------------|-----------------------|------------------------|------------------------------|
| QuintilesIMS™ | 01 | QUINTILES IMS HOLDINGS, INC. | 6,878.0 | 2% | 91% | 92 |
| LabCorp <small>Laboratory Corporation of America</small> | 02 | LABORATORY CORPORATION OF AMERICA HOLDINGS (Covance) | 9,437.2 | 8% | 87% | 31 |
| PAREXEL® | 03 | PAREXEL International Corporation | 2,426.3 | 6% | 91% | 79 |
| PPD® | 04 | Pharmaceutical Product Development, LLC | 1,837.8 * | 5% * | 95% * | 44 |
| inc Research® | 05 | INC RESEARCH HOLDINGS, INC. | 1,610.6 | 7% | 87% | 38 |
| PRAHEALTHSCIENCES | 06 | PRA Health Sciences, Inc. | 1,811.7 | 4% | 91% | 27 |
| ICON | 07 | ICON PUBLIC LIMITED COMPANY | 1,666.5 | 16% | 81% | 4 |
| WuXi AppTec <small>药明康德</small> | 08 | WUXI PHARMATECH (CAYMAN) INC. | 919.9 * | 10% * | 78% * | 5 |
| charles river | 09 | CHARLES RIVER LABORATORIES INTERNATIONAL, INC. | 1,681.4 | 9% | 86% | 4 |
| inVentiv Health | 10 | Advent International (INVENTIV HEALTH, INC.) | 2,321.3 ** | -7% ** | 97% ** | 4 |

Sources: Annual reports and SEC filings.

*Estimated **2015.

- **YOU ONLY START !**
- **Find proper FDA/EMA/WHO guidance**
 - Cite and summarize
- **Explain product and QC**
 - How you protect yourself from chaos?
- **Explain Efficacy preclin**
 - Often identical to POC
- **Explain Safety Preclin**
 - Usually mandated
- **Watch manufacturing**
 - economics and QC
- **Watch clinical study**

Your project post-POC



PRODUCT AND QC PRECLIN PARANOIA

- PRODUCT ENTERING THE GLP PRECLIN IS YOUR FINAL PRODUCT
 - If you change the product later, the regulator will reasonably send you for another GLP study
 - Shocking discovery for many scientists
- QC IS YOUR ONLY PROTECTION FROM MANAGEMENT FAILURE
 - Storage mistakes
 - Logistics mistakes
 - Third party mistakes
 - How you protect your time and reputation and money?
 - Only by the standardized QC passport
- STABILITY IS PAIN BUT IT CAN NOT BE BYPASSED
 - Are you sure your preparation may reach SPB?



Your job in clinical trials

Clinical trials related services and activities



- Preparation of all clinical studies documents (Investigator brochures, Clinical study protocols, Case report forms, Informed consent forms, Patient information sheets, Clinical study reports, and others)
- Content drafting for corporate internal and external scientific and medical communications
- Writing and publishing of scientific articles for industry publications
- Professional translations

Looks scary

| Protocol Design Trends | | |
|--|-----------|-----------|
| A TYPICAL PHASE III PROTOCOL | 2001-2015 | 2011-2015 |
| Total number of endpoints | 7 | 13 |
| Total number of eligibility criteria | 31 | 50 |
| Total number of procedures | 110 | 187 |
| Total number of procedures per visit | 10 | 13 |
| Proportion of procedures not targeting a primary or key secondary endpoint | 18% | 31% |
| Total number of countries | 5 | 10 |

Source: Tufts CSDD

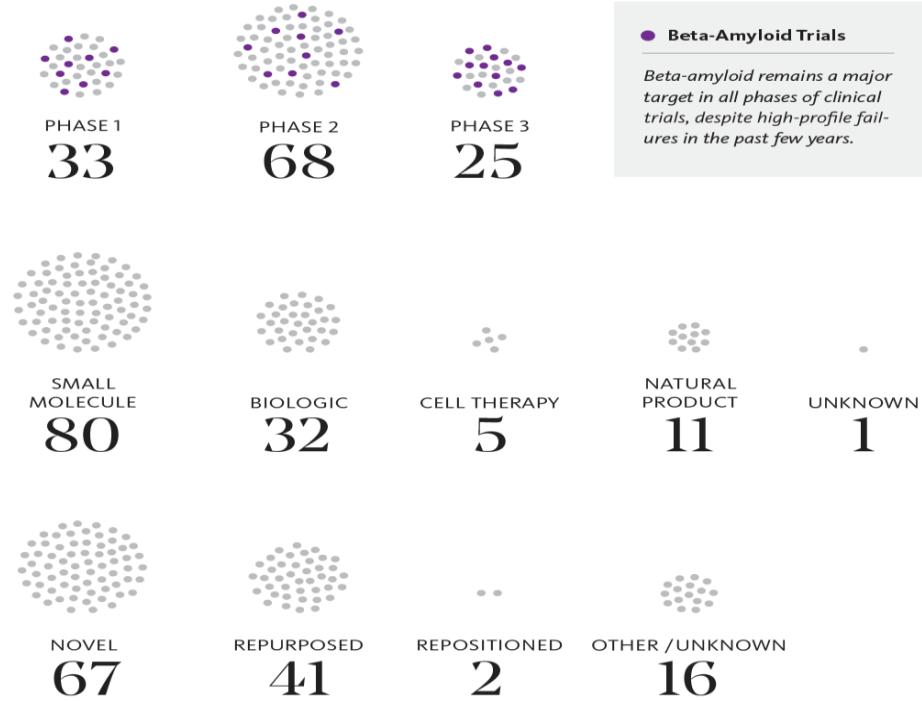
The 10-year change in protocol design practices.

Trial Phase

Type of Therapy*

*Some combination therapies fall into multiple categories and are represented here twice.

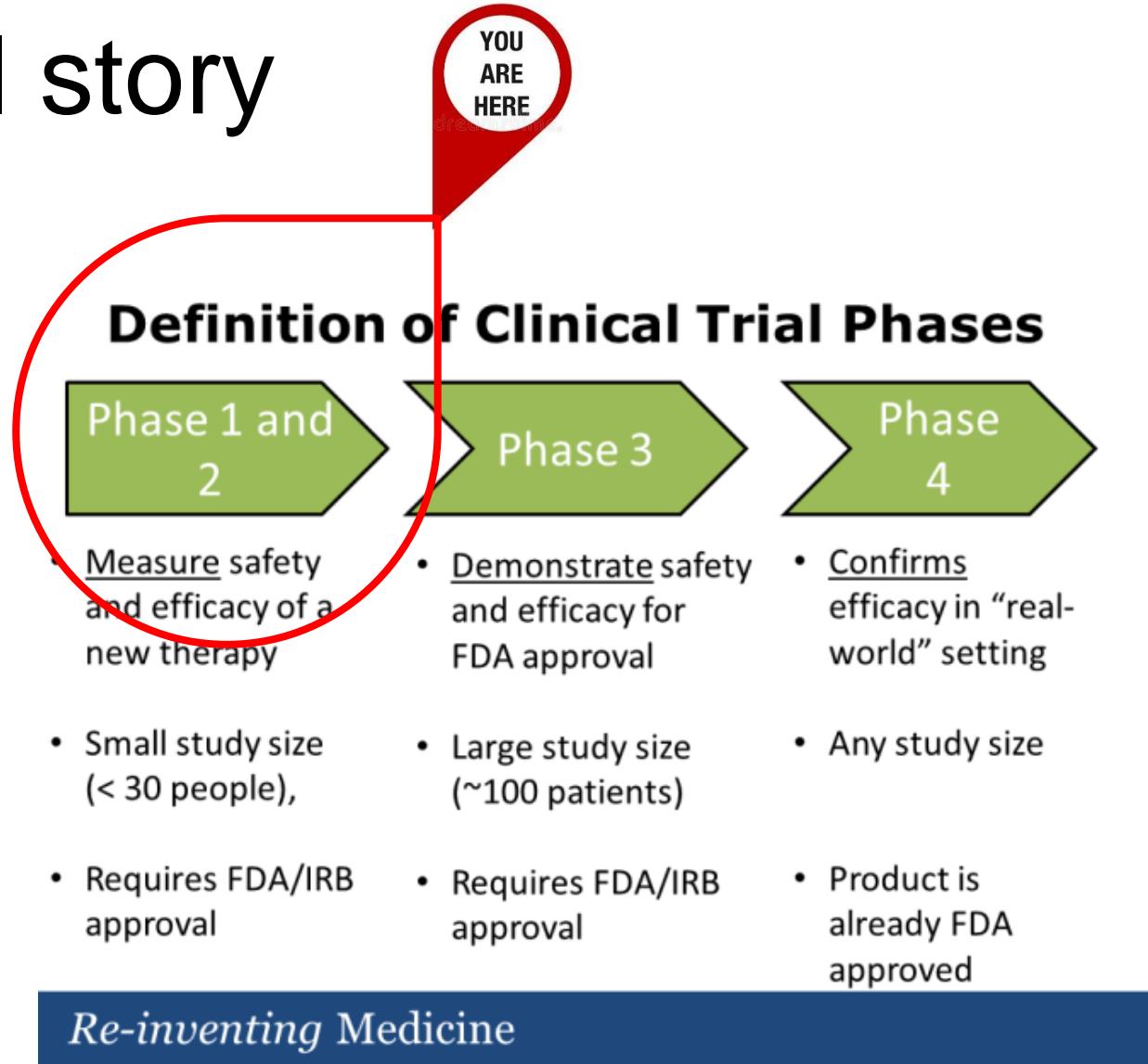
Path to Clinic



Beta-Amyloid Trials

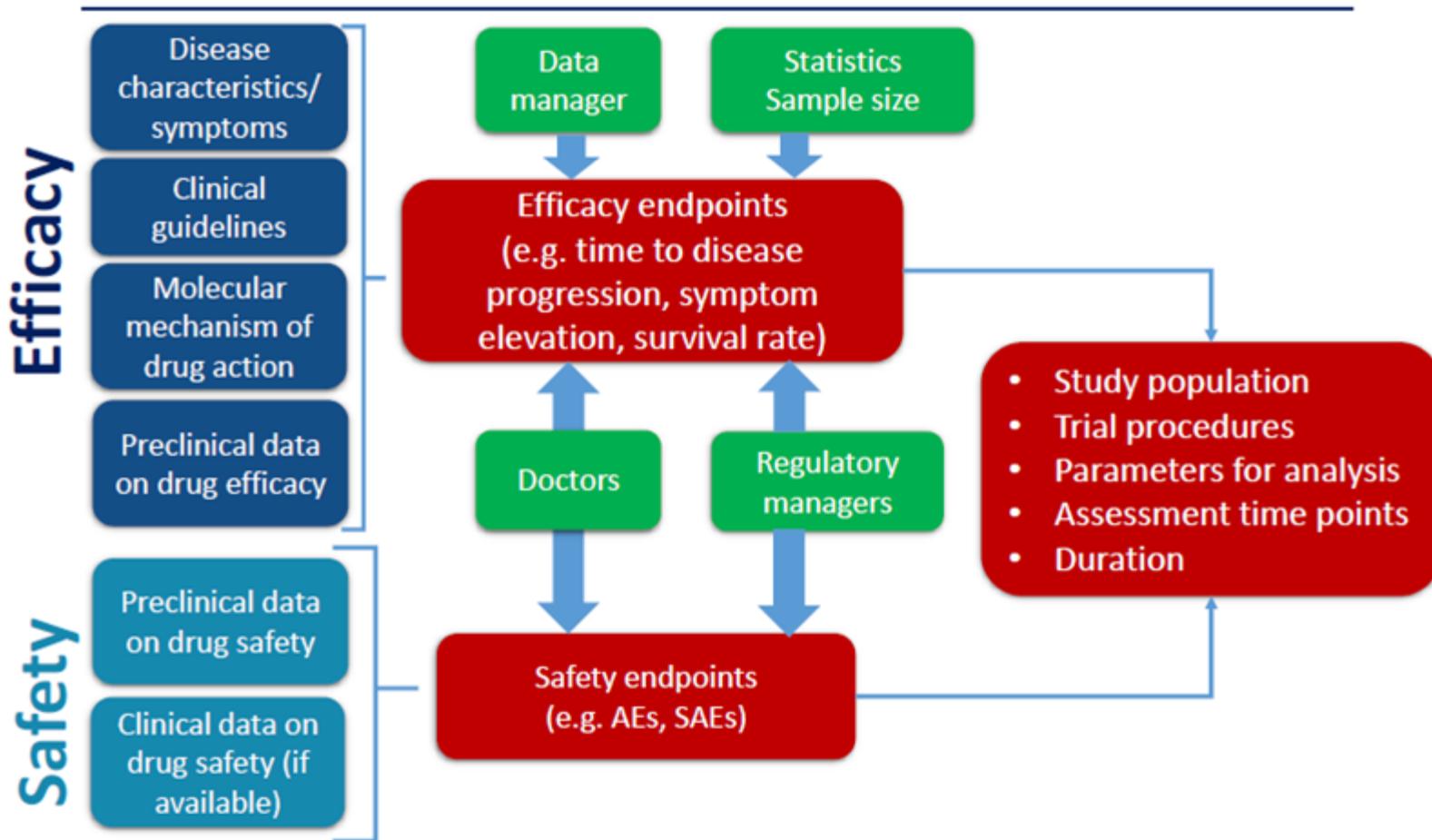
Beta-amyloid remains a major target in all phases of clinical trials, despite high-profile failures in the past few years.

General story



ENDPOINTS

Clinical trials: Protocol design

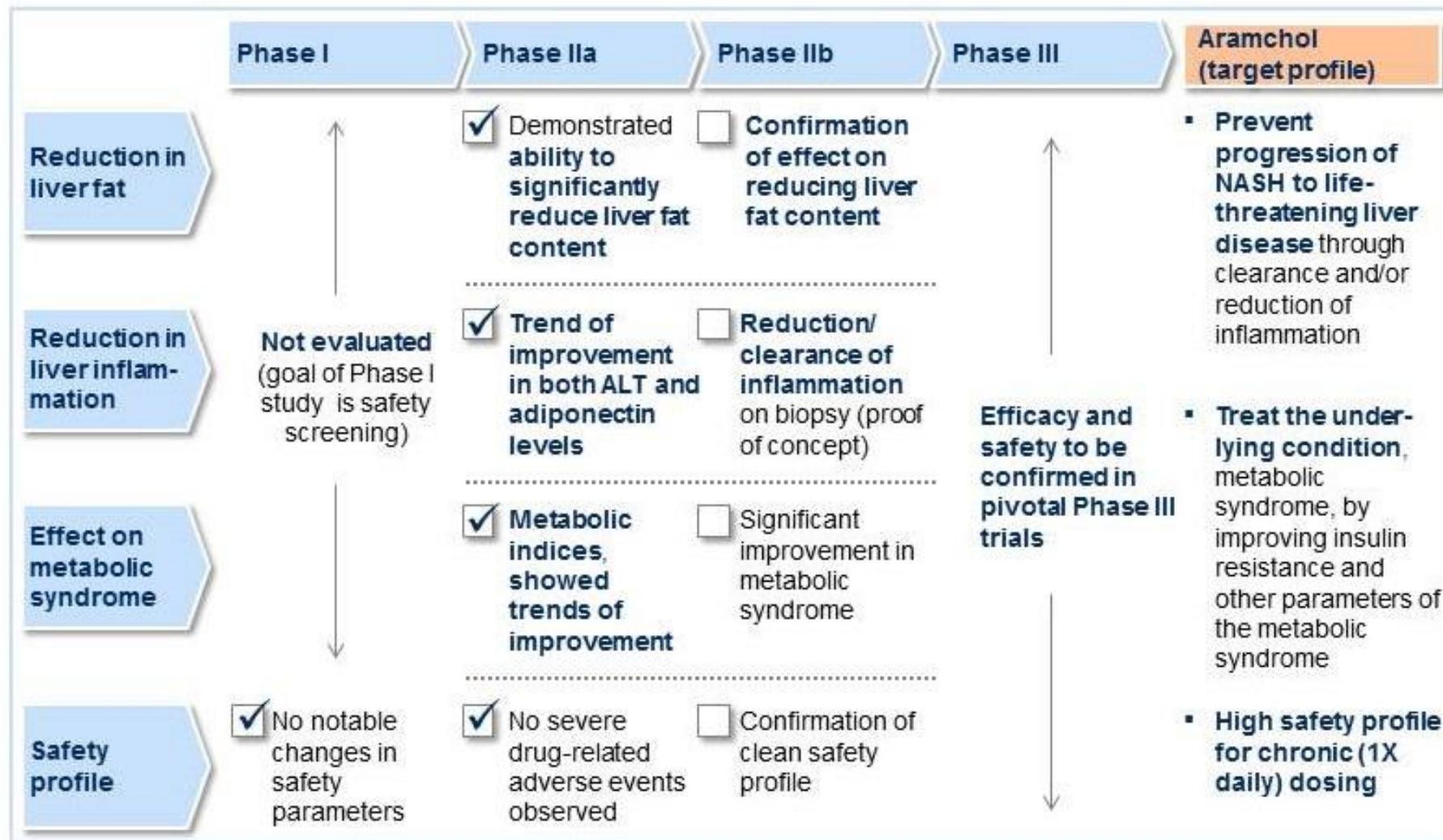


Details matter



| Stage of Development | Phase 1 | Phase 2 | Phase 3 | Phase 4 |
|----------------------|---|--|--|---------------------------------|
| End Point | Safety | Efficacy | Efficacy | Efficacy |
| Specific End Point | Safety Profile | Cardiac Output | Reduction in Mortality Rate | Reduction in Mortality Rate |
| Types of Studies | Different Indications; Single or Multiple Dose | Placebo Controlled; Dose Escalation | Placebo Controlled; Long Term Follow Up | Comparative; New Indications |

ALWAYS Stay scientific



DESIGNING CLINICAL TRIAL

- INDICATION
 - Which disease you treat
- DESIGN
 - What is the product under investigation?
 - What is comparator (control)?
 - Is it ethical? Check WHO standards.
 - What is treatment protocol?
- WHAT ARE ENDPOINTS?
 - What you measure?
- WHAT IS INCLUSION CRITERIA?
 - Which patients you study?
- WHAT IS THE NUMBER OF PATIENT?
 - Statistics
 - Rumor is that 27 is minimum minimorum

MEDICAL DEVICES

VALIDATION, NOT QC

Trained technicians do it for you every morning
Give them executable protocol

PMA is full expensive clinical trial

You want to avoid it!
Try to get EUA

Your dream is 510k

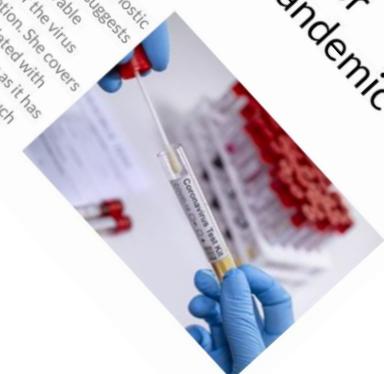
Find existing comparable
Run experiment proof of your identity – it becomes
your preclinical !!!
Receive approval for clinical trial

Regulatory Focus™ > News Articles > 2020 > 8 > FDA requirement updates for EUAs for diagnostics to support COVID-19 pandemic

FDA requirement updates for EUAs for diagnostics to support COVID-19 pandemic

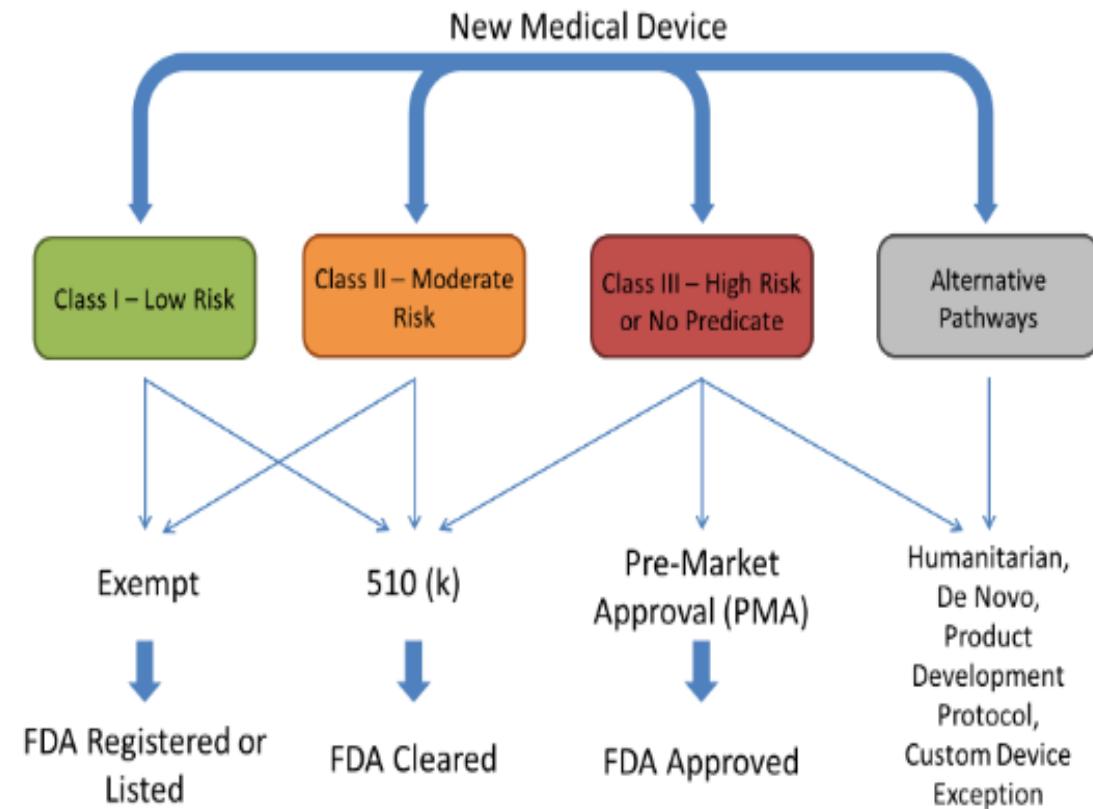
Posted 17 August 2020 | By Ashley Clark, MSc, RAC | [PDF](#)

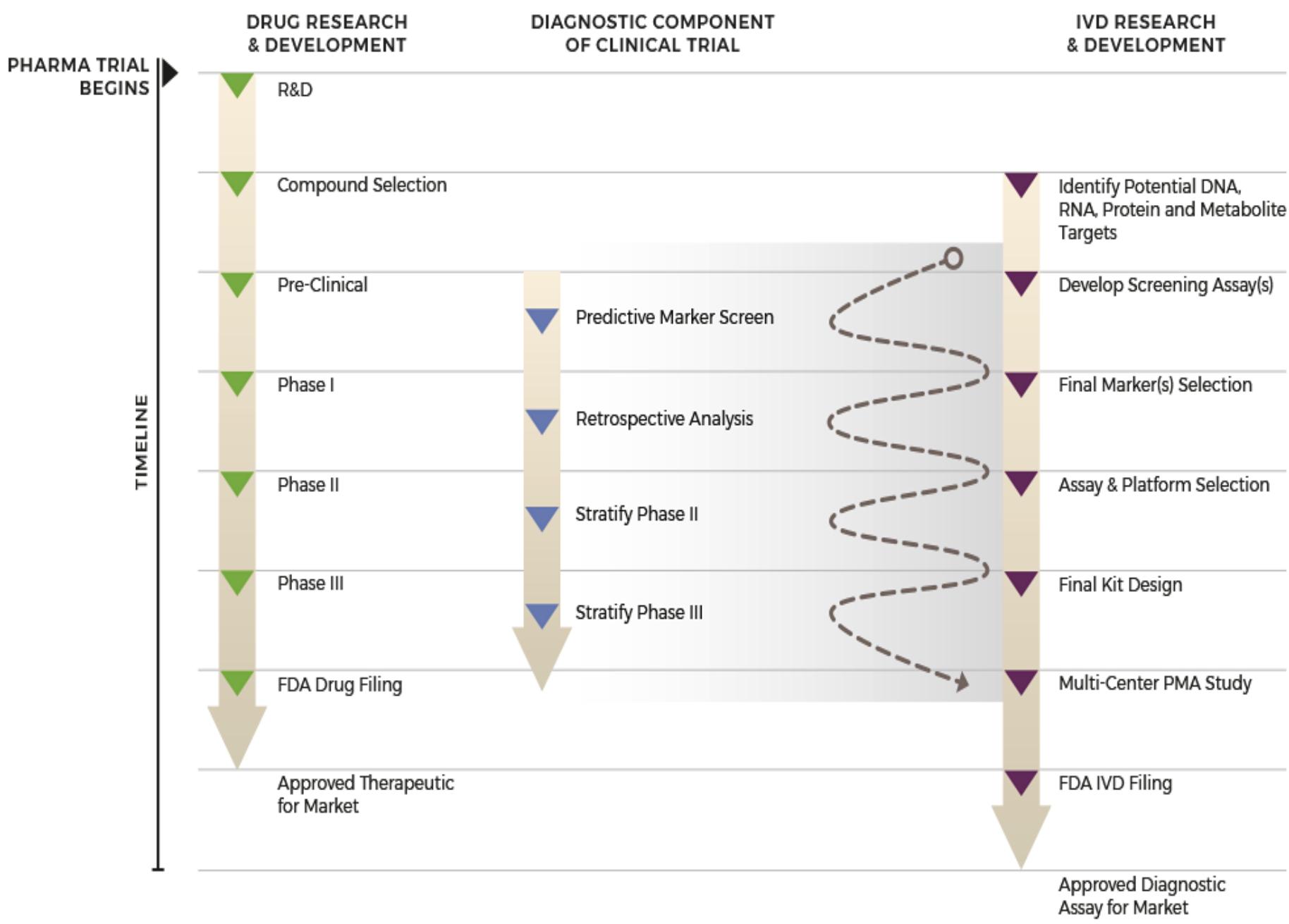
This article discusses the evolution and implementation of the emergency use authorization (EUA) by the US Food and Drug Administration (FDA) for diagnostic devices during the COVID-19 pandemic in the United States. The author suggests that this limited oversight will affect future requirements for demonstrable superiority claims after the EUAs are terminated and diagnostics associated with such devices undergo increased scrutiny by the agency for marketing authorization. She covers the implications for the diagnosis and treatment of COVID-19 associated with such devices. The article also covers molecular diagnostics and antigen and serologic tests.



MEDICAL DEVICE MUST TRY 510(k)

- Prove to the regulator that you do the same job as the existing approved comparator
- Obtain 510(k) clearance for immediate start of sales while doing observational clinical trial
- **Enjoy immense time and money savings !**





510(k) vs generic pharma

- Generic pharma laws are written to approve only the products 100% identical to those that went through proper clinical trials and extensive market approbation
 - Hence even minor innovation (like replacing ampule with a syringe) requires the new clinical trial
 - If you bypass clinical trials, the market looks down upon you
- 510(k) laws are written to open the commercial markets to those devices that are proven to be functionally equivalent to some approved device
 - You remember that 99% of innovation has current alternative
 - Otherwise you risk doing something irrelevant
 - Hence your job in medical devices is to find an equivalent and go for 510(k) and market embraces you

HOMEWORK

- **REGULATOR GUIDANCES**
 - Cite and analyze the 3 closest guidances
 - FDA, EMA, WHO: Preclin, Clin, Manuf, QC
- **PIVOTAL PRECLINICAL EFFICACY TEST**
 - Design and citations
 - **Check publications on your best comparator/competition**
- **PRECLINICAL SAFETY TESTS**
 - Design and citations
 - *may be omitted for diagnostics*
- **CLINICAL DESIGN**
 - Table of 3 phases. For each phase:
 - Indication + Design + Endpoints + # of patients
 - guidances and sci citations

PRESENTATION #3

- **SLIDE 1: Indication**
- **SLIDE 2: Product/service + MOA + BENEFIT**
- **SLIDE 3: POC experiment design and results**
- **SLIDE 4: THREE PATENT CLAIMS**
- **SLIDE 5: REGULATORY GUIDANCES**
 - Cite and analyze the 3 most relevant guidances
 - FDA, EMA, WHO: Preclin, Clin, Manuf, QC
 - Table similar to NOVELTY (3 patents)
- **SLIDE 6: PRECLINICAL EFFICACY & SAFETY**
 - Pivotal efficacy experiment + standard safety experiments
 - citations
- **SLIDE 7: CLINICAL DESIGN**
 - Table of 3 phases. For each phase:
 - Indication + Design + Endpoints + # of patients
 - guidances and sci citations

thx.



Skoltech