


A decorative pattern of white-outlined squares of various sizes is scattered across the blue background. Some squares are arranged in vertical columns, while others are isolated. The squares vary in size, with some being quite small and others being larger.

Transitioning to a Career in Research and Development

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I hope if dogs ever take over the world, and they chose a king, they don't just go by size, because I bet there are some Chihuahuas with some good ideas.

--Jack Handy, "Deep Thoughts"

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Objectives

- Overview:
 - Veterinary research and development
 - Drug development process
- From private practice to pharmaceutical research and development

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Veterinary Research and Development



Aspects of Pharmaceutical R & D

- Nonclinical ~ safety, pharmacokinetics, toxicology
- Clinical ~ efficacy
- CMC (Chemistry, Manufacturing, and Controls) / Product Chemistry
- Regulatory Affairs
- Quality Assurance

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Research

- The process of identifying drug, pesticide (e.g., flea and tick product), or biologics candidates
 - Discovery, screening, and pre-clinical testing
 - Dose determination (PK, laboratory efficacy studies)
 - Preliminary safety and effectiveness data
- Objective = product with predictable outcomes

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Development

- Safety and effectiveness must be demonstrated in controlled studies and in the field
 - Safety in the target species
 - Label claims supported by development data

1937 – Elixir of Sulfanilamide

- Sulfanilamide: used to treat streptococcal infections (commonly administered to children)
- A liquid form of the drug was produced using diethylene glycol (antifreeze) as the solvent
- Existing laws did not require studies to ensure drug safety → 107 people died including many children
- Federal Food, Drug, and Cosmetic Act of 1938 – new drugs must be proven safe before marketed

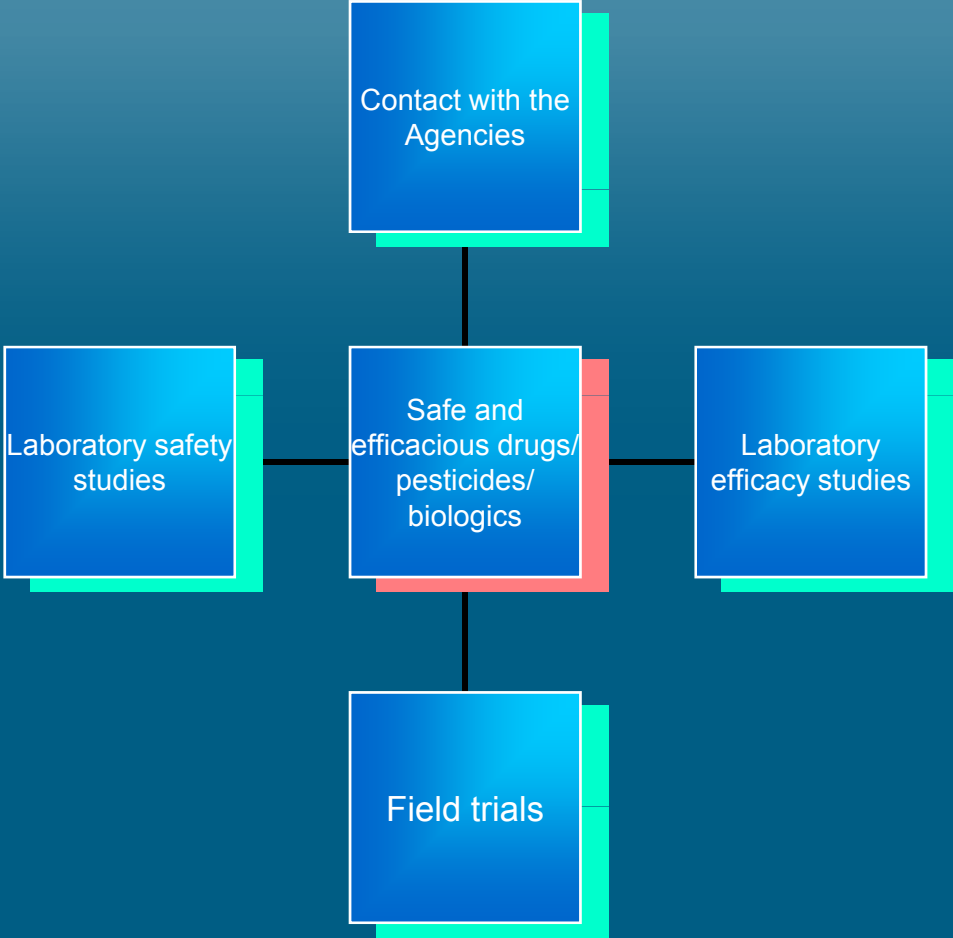


1961- Thalidomide Crisis



- Marketed in Europe; used to treat insomnia, morning sickness in pregnant women
- Crosses the placental wall resulting in catastrophic effects:
 - Peripheral neuritis – nerve disorder
 - Birth defects – deafness, blindness, disfigurement, cleft palate, internal defects, phocomelia
- Kefauver-Harris Drug Amendments – greater requirements for demonstration of safety and efficacy prior to release in the market

Components of Product Development



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**Research and development is
a partnership with the
regulatory agencies**



Regulatory Agencies

- In the US, there are three veterinary regulatory agencies:
 - FDA-CVM (pharmaceuticals)
 - EPA (ectoparasiticides / insecticides / pesticides)
 - USDA (vaccines / immunotherapies)
- In Europe, there is an umbrella organization: EMEA
- Efforts are ongoing in the ‘harmonization’ of regulations between the EU, USA, and Japanese regulatory authorities = ‘VICH’ guidelines

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Agency Interaction

- Guidance documents
- Development plan meetings
 - Informal communications (e.g., teleconference)
- Protocol reviews
- Technical submissions
- Product approval / registration / licensure

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Timeframe

- Dependant on the type of veterinary product (e.g., drug, pesticide, vaccine)
- 2 years to 10+ years
- Factors:
 - Food animal product? For use in breeding animals?
 - Is the product to treat or prevent a condition which itself is slow to manifest?
 - Unexpected study results



Regulatory Fees

- Paid by the sponsor company to offset the governmental expense of reviewing applications for new drugs.
- These fees also justify requiring the Agencies to adhere to a time-line for review.
- EPA (Pesticide Registration Improvement Act [PRIA])
 - New Active, Food Use: \$542,115
 - New Active, Non-Food Indoor Use: \$209,475
 - New Active, Non-Food Outdoor Use: \$376,635
 - New Use of an Existing Active, Non-Food: \$11,025
- CVM (ADUFA [Animal Drug User Fee Act])
 - NADA (New Animal Drug Application) Submission: \$246,300
 - Supplemental Application: \$123,150
 - Annual product, sponsor, and manufacturing site fees



**How does all of this
translate into a career?**

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Primary Job Description

- Designing, performing, interpreting, and reporting laboratory experiments or field trials
- Team interaction
- Agency interaction

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Evaluate Available Information

- Sponsor representative will evaluate available data and research known characteristics of the product class if available
- What do we know about the safety and efficacy of the product
 - In the target species
 - In other species

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'Pilot' Studies

- Initial evaluation of product efficacy and safety
- Studies performed in the laboratory

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Development Plan Meeting

- Product claims
- Dose justification
- Study designs - efficacy and safety
- Product formula / manufacturing
- Analytical testing


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Protocol Design

- Study protocol prepared by study director with the assistance of the sponsor representative
- Driven by agency guidelines



Target Animal Safety

- Target animal species = species for which the drug will be labeled
 - The product is administered at elevated doses and for extended durations:
 - Determine the toxic syndrome
 - Characterize potential adverse reactions in the idiosyncratic population
 - Study design is based on the agency with which approval is being sought:
 - CVM - 0, 1, 3, and 5x label dose for 3x label duration
 - EPA - 0x and 5x label dose ('limit test')
- 

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Clinical Development

- Laboratory efficacy studies and clinical field trials
- Establishment of a product's effectiveness is based on carefully defined endpoints and statistical design
- Safety component: adverse effects

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Study Design

- Variables measured:
 - Body weight, food consumption, clinical observations, and clinical pathology
 - Additionally, there may be variables specific to the product's potential toxicities and past study experience (e.g., ECG, cardiac ultrasound)
 - FDA-CVM requires necropsy with gross and histopathologic evaluation

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Study Placement

- Laboratory studies are performed by contract research organizations (CROs), conducted by study director
- Clinical field trials performed in client-owned animals; private practice veterinarian acts as the ‘investigator’ (~ study director)
- Study placement based on multiple factors
 - Prior experience
 - Proximity to sponsor facility
 - Special resources needed

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Protocol Review and Concurrence

- Protocols submitted to CVM / EPA for concurrence
 - CVM ~ 60 days
 - EPA ~ 90 days

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Study Monitoring

- Sponsor representative may make multiple trips to the CRO site to observe and evaluate study progress
- “the best-laid plans”

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Report Writing

- Study report prepared by study director
- Assistance may be provided by the sponsor representative based on project history and sponsor expertise

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Submission

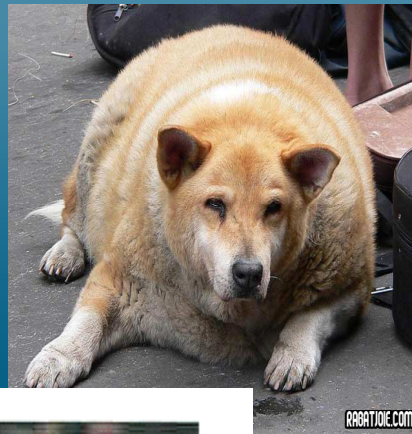
- Study report(s) presented to the appropriate agency in a technical submission
 - FDA-CVM requires all study raw data
- Review times:
 - CVM ~ 6 months
 - EPA ~ 20 months

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Product Launch

- Product introduced at a national veterinary conference if possible
- Adverse events are monitored and evaluated post-launch by Veterinary Technical Services

Transitioning from Clinical Practice to R&D



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Everything is funny as long as it is
happening to someone else.

--Will Rogers

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Primary Differences

- Change in client; R&D = project teams, company shareholders, government agencies, practicing veterinarian
- Decreased direct contact with animals; limited to monitoring studies
- Focused intellectual effort dependent upon current project(s)

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Getting 'Up to Speed'

- Principles of GLP and GCP
- Protocol and report writing (or writing technical documents in general)
- Agency requirements and principles of interaction
- Study monitoring and interaction with CROs
- PK, toxicology, user safety, manufacturing...

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Disadvantages

- Very little immediate gratification – the path to product approval is a long road
- Few opportunities to be ‘the hero’
- Corporate employer = decreased job security?
- Travel

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Advantages

- Travel
- Steady, predictable schedule
- Increased opportunities for professional development
- Increased earning potential
 - 2007 mean professional income
 - Private practice = \$115,447
 - Industry = \$165,668

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The bottom line:

- Both fields offer challenging and rewarding careers
- What challenges / advantages would it offer you, personally?

Questions?

