Basics of Animal Health Product Regulation

Differences and similarities to regulation of human drugs/vaccines

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Agenda

- Our experience
- Overview of the US regulatory pathways for veterinary products compared to human products
- Recommendations
- Q&A

US Regulatory Jurisdiction

- Human drugs, devices, and biological products, are reviewed by the FDA (CDER and CBER)

- Animal drugs are reviewed by:
  - FDA's Center for Veterinary Medicine (CVM)
  - USDA's Center for Veterinary Biologics (CVB)
  - EPA

Who's On First?

- FDA/CVM:
  - Animal drugs
  - Animal feed / feed additives

- USDA/CVB:
  - Veterinary biologics*

- EPA
  - Veterinary **topical** pesticides*

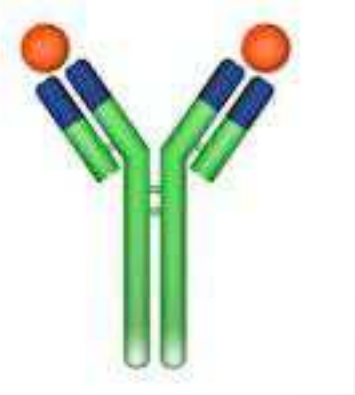
* that annoying footnote that changes everything

- BIOLOGICS
  - Typically USDA
  - Veterinary products: proteins that mediate the immune system
- PESTICIDES
  - **Oral** insecticides = FDA
  - **Topical** insecticides= EPA

Jurisdiction Is Sometimes Fluid

- Ask!

- Example
  - Monoclonal antibody for pain= FDA
  - Monoclonal antibody for canine lymphoma= USDA



Timelines and Requirements

- CVM approval (companion animal)
  - 5-7 years, $8-12M
  - GMP manufacturing at FDA-approved site
- USDA conditional license
  - 2-4 years, $3-5M
  - Manufacturing in USDA-approved site
- EPA approval
  - 5-7 years, $?
  - No GMP manufacturing

Grey Zone

- FDA does not conduct premarket reviews of veterinary devices
- Food claims
  - Any claim beyond nutritive value or gut health will be deemed a drug claim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Traditional Approval Process

- Phased review process
  - 3 major technical sections
    - Chemistry, Manufacturing and Controls
    - Target Animal Safety
    - Effectiveness
  - Other required sections
    - Environmental Impact – all species
    - Human Food Safety- production animals
- Opening an INAD triggers yearly sponsor fees
  - Fiscal year 2019 fees - $125,990

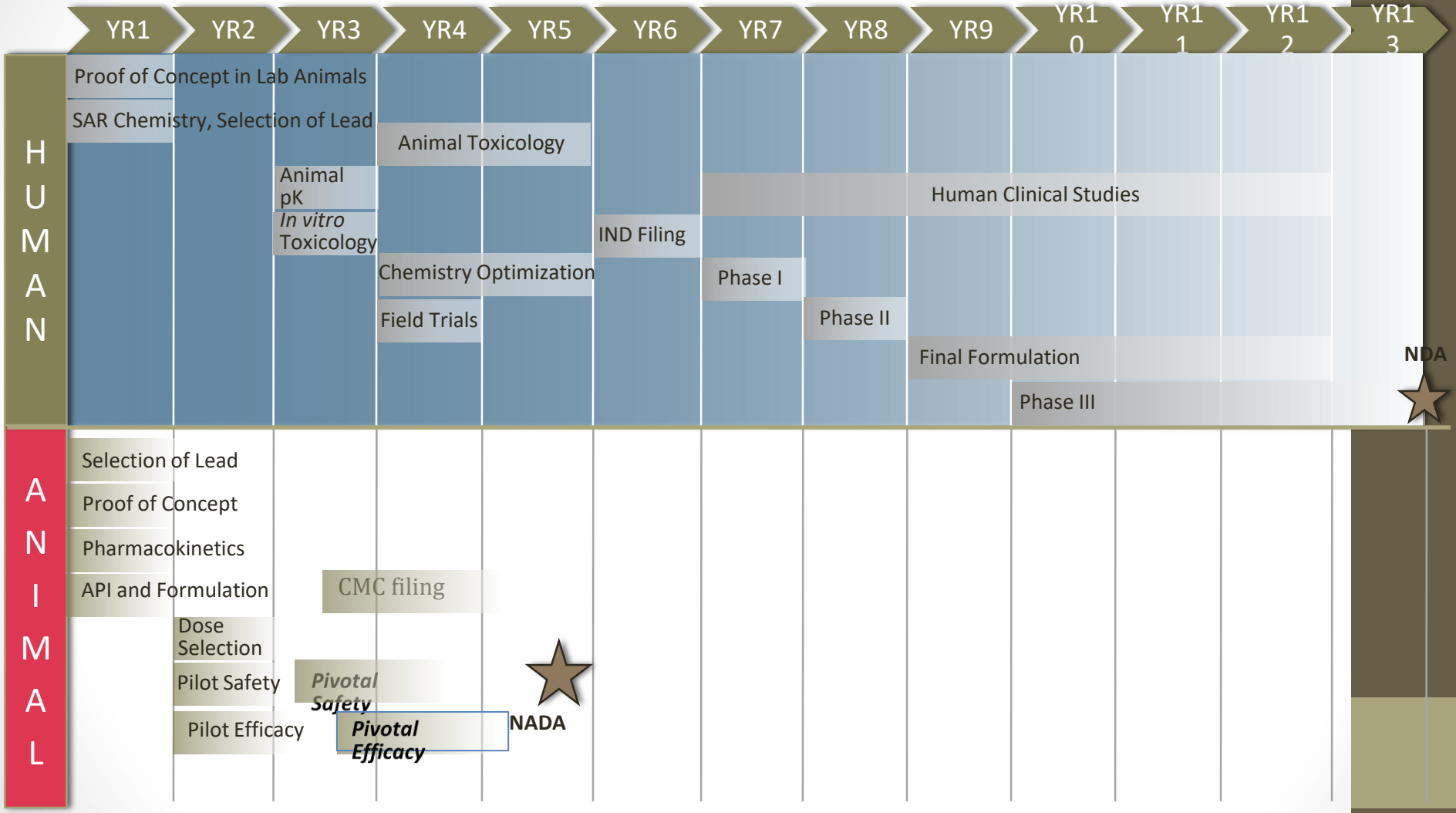
Alternative Approval Paths

- Minor Uses and Minor Species (MUMS)
  - NO TIME SAVINGS FOR NCE!
  - All major technical sections must be addressed
  - Should be reduced burden of proof (often not)

- CVB Conditional License
  - Unmet medical need and presumption of efficacy
  - Annual demonstration of progress to full licensure

Your Molecule for Dogs?

- **Toxicology studies in dogs**
  - Pharmacokinetics
  - Margin of safety
  - Understanding species differences:
    - Cats are not small dogs
    - Dogs are not small humans
- **Chemistry, Manufacturing and Controls**
- **Proof of concept**
  - Dogs
  - Rodents
  - Humans?


YR1
YR2
YR3
YR4
YR5
YR6
YR7
YR8
YR9
YR10
YR11
YR12
YR13
HUMAN
Proof of Concept in Lab Animals
SAR Chemistry, Selection of Lead
Animal Toxicology
Animal pK
In vitro Toxicology
Human Clinical Studies
IND Filing
Chemistry Optimization
Phase I
Field Trials
Phase II
Final Formulation
NDA
Phase III
ANIMAL
Selection of Lead
Proof of Concept
Pharmacokinetics
API and Formulation
CMC filing
Dose Selection
Pilot Safety
Pivotal Safety
NADA
Pilot Efficacy
Pivotal Efficacy

CVM compared to CDER

	Animal Drug	Human Drug
FINAL API, formulation	Early in development	Late in development
Initiate submissions at FDA	INAD – paper exercise	IND – significant pre-clinical work required
Safety	Tested early in target species – early signal. Pivotal study in lab using target species.	Phase I – may not see signal until late in development
Effectiveness	Early pilot study(ies). Pivotal field study in client-owned animals.	Phase II
Pivotal clinical studies	One study, n=250-300; cost ~$1.5M	Phase III Large, expensive studies
CMC	Identical processes for GMP, stability, etc.	

INTERACTING WITH CVM: TRICKS OF THE TRADE

CVM is a Different Animal

- ADUFA (Animal Drug User Fee Act)
  - Fees
    - INAD
    - NADA
    - Manufacturing sites
  - Submission review timelines (6 months)

  - Opportunity for agency interaction – meetings are encouraged

The 9 Most Terrifying Words

"I'm from the government and I'm here to help."

"The degree to which CVM is helpful to a sponsor's application generally is inversely proportional to how close a company is to approval."

L. Rhodes

The FDA told me…..

- When Sponsors “call CVM” they will often get information and say that “the FDA told me X, Y and Z”
  - No agreement unless documented in minutes

Opinions and Precedents

- READ the FOI summaries of similar products
- EU approval does not mean CVM approval (and vice versa)
- Conduct effectiveness and safety studies using a concurred protocol
- Guidance documents may not reflect current CVM policy

HELP!

- Use an regulatory consultant who has successfully worked with CVM – it's not enough to have experience on the human side

Conclusion

- It’s complicated!
- CVM is not the FDA you think you know from CDER and CBER
- Quicker speed to market via all agencies
- Requires appropriately experienced help to navigate

Q&A