Regulatory Requirements for Vaccine Development (Veterinary)

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Scope..

- The “Rules”
- The “Help”
- High level overview of Data requirements
- Regulatory support
- Topical points

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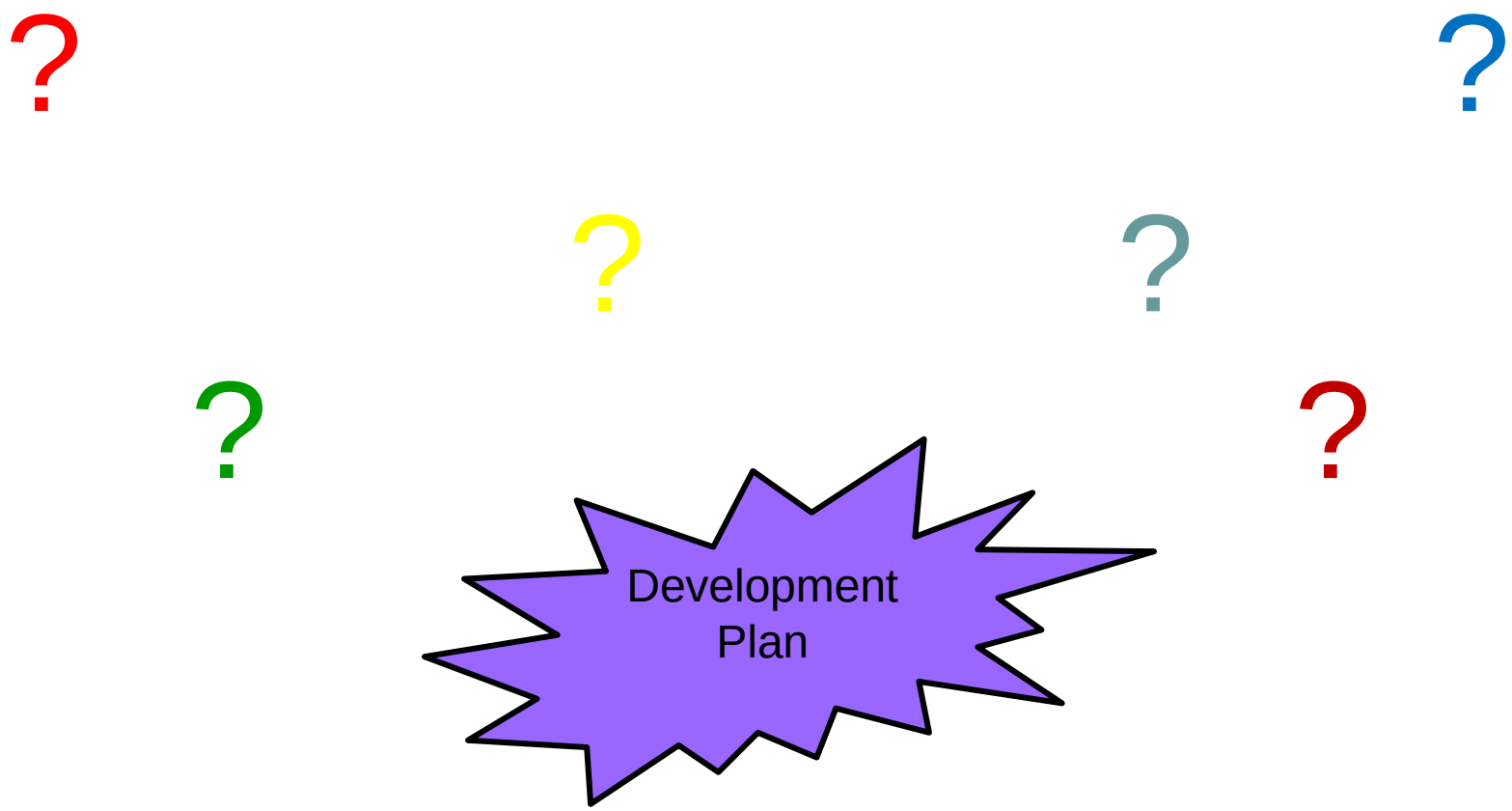
Regulatory Requirements for Vaccine Development (Vet)



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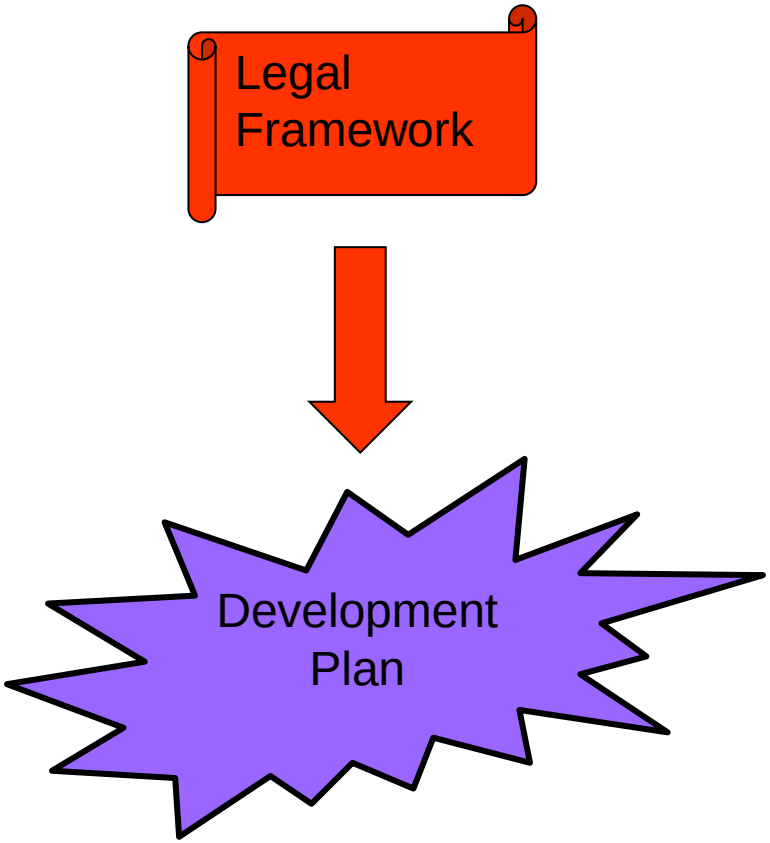

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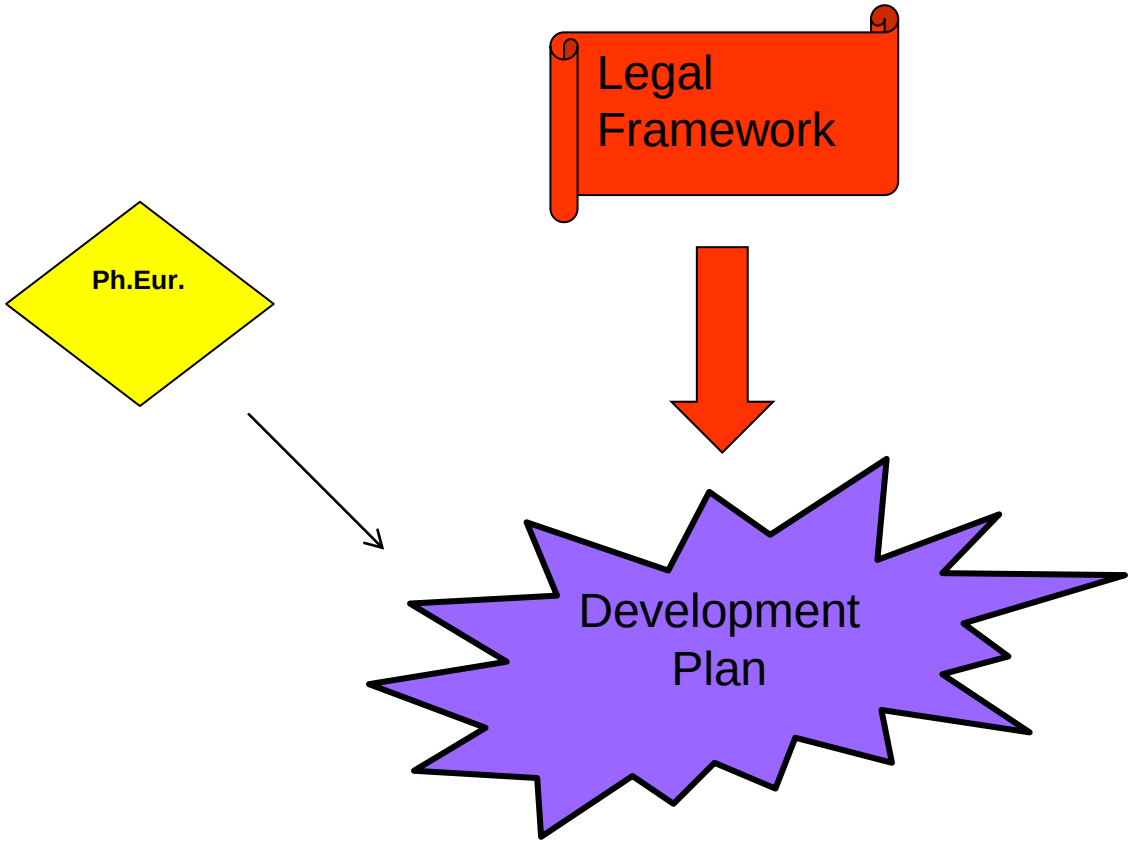

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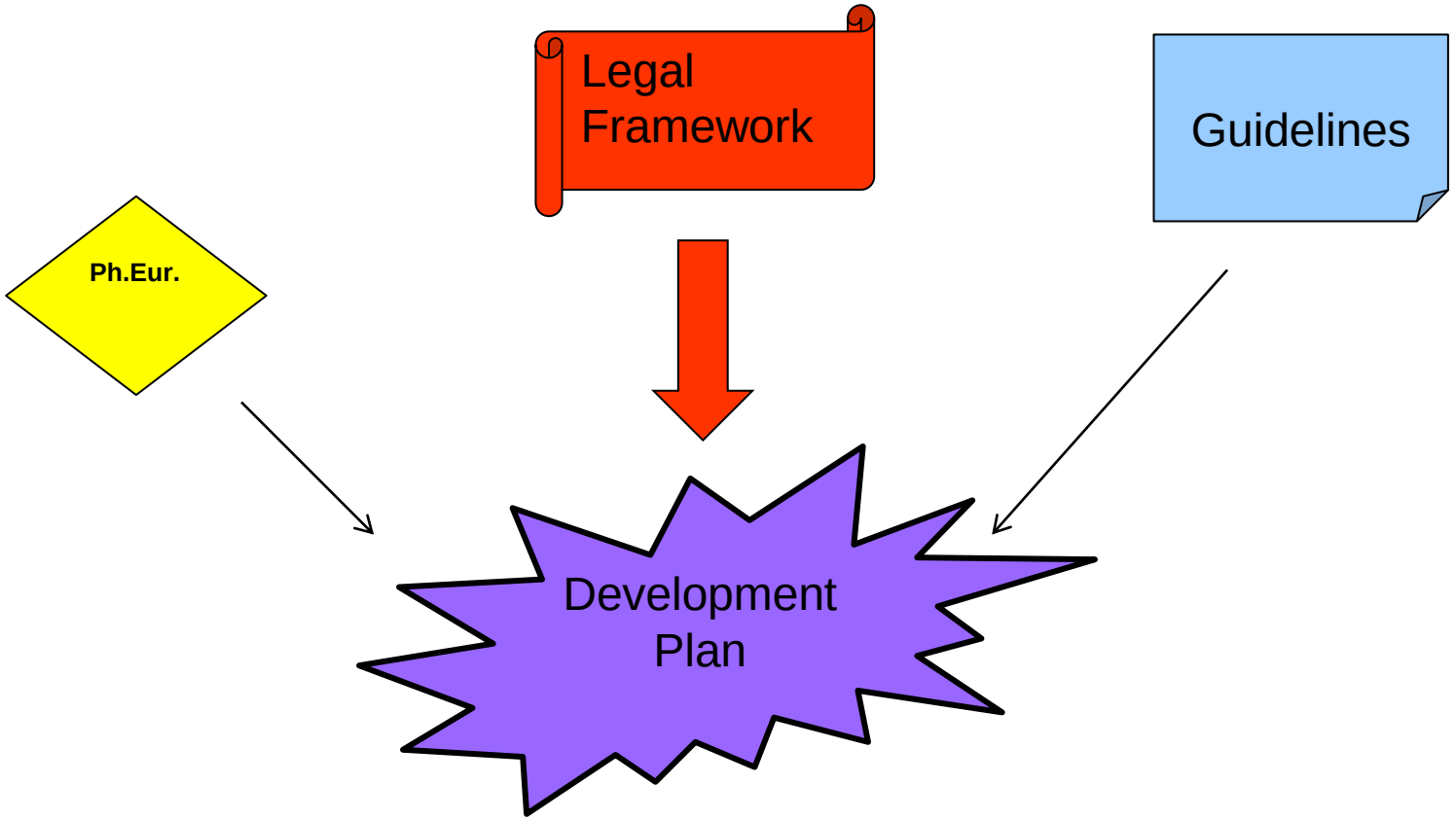

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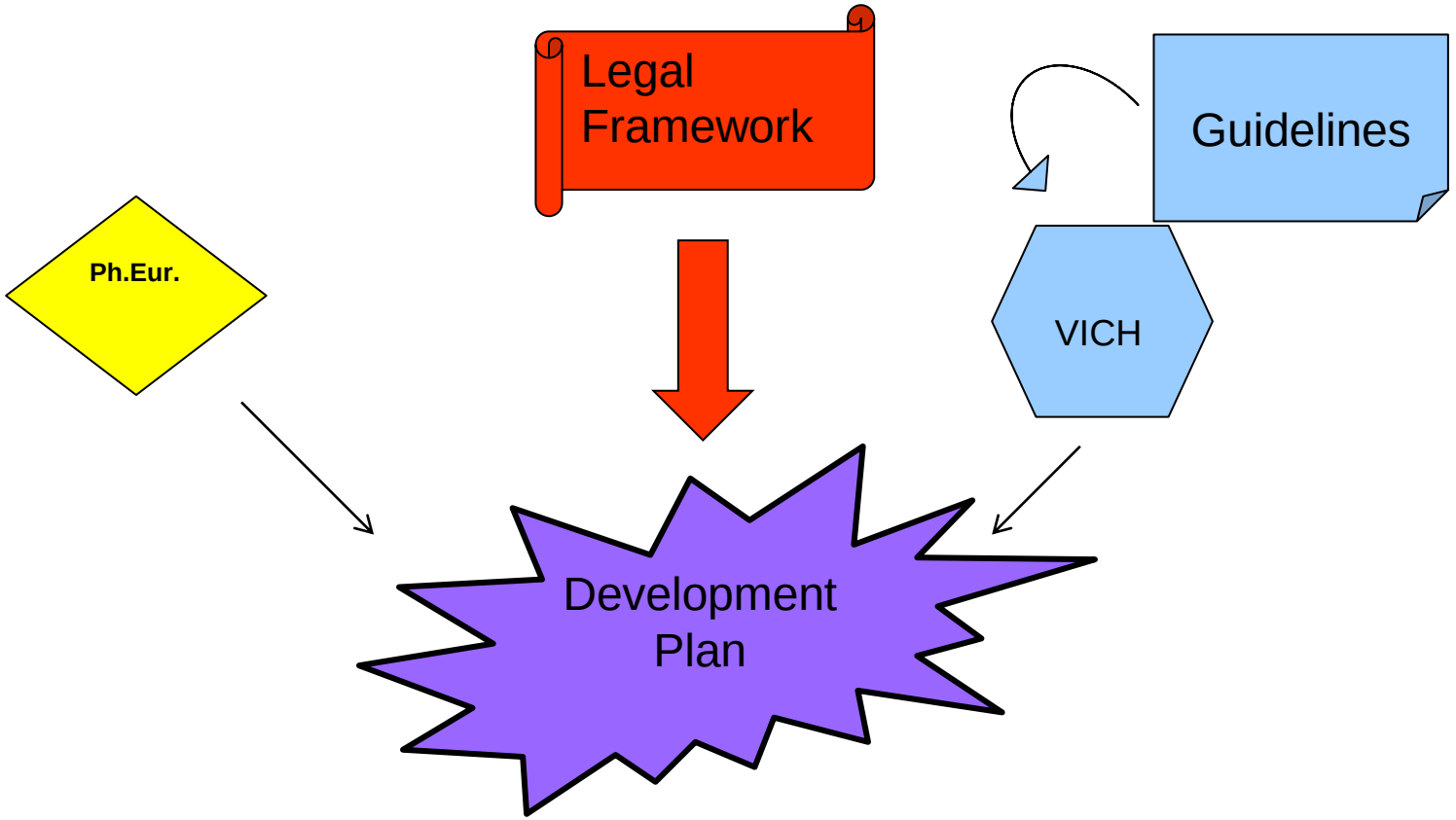

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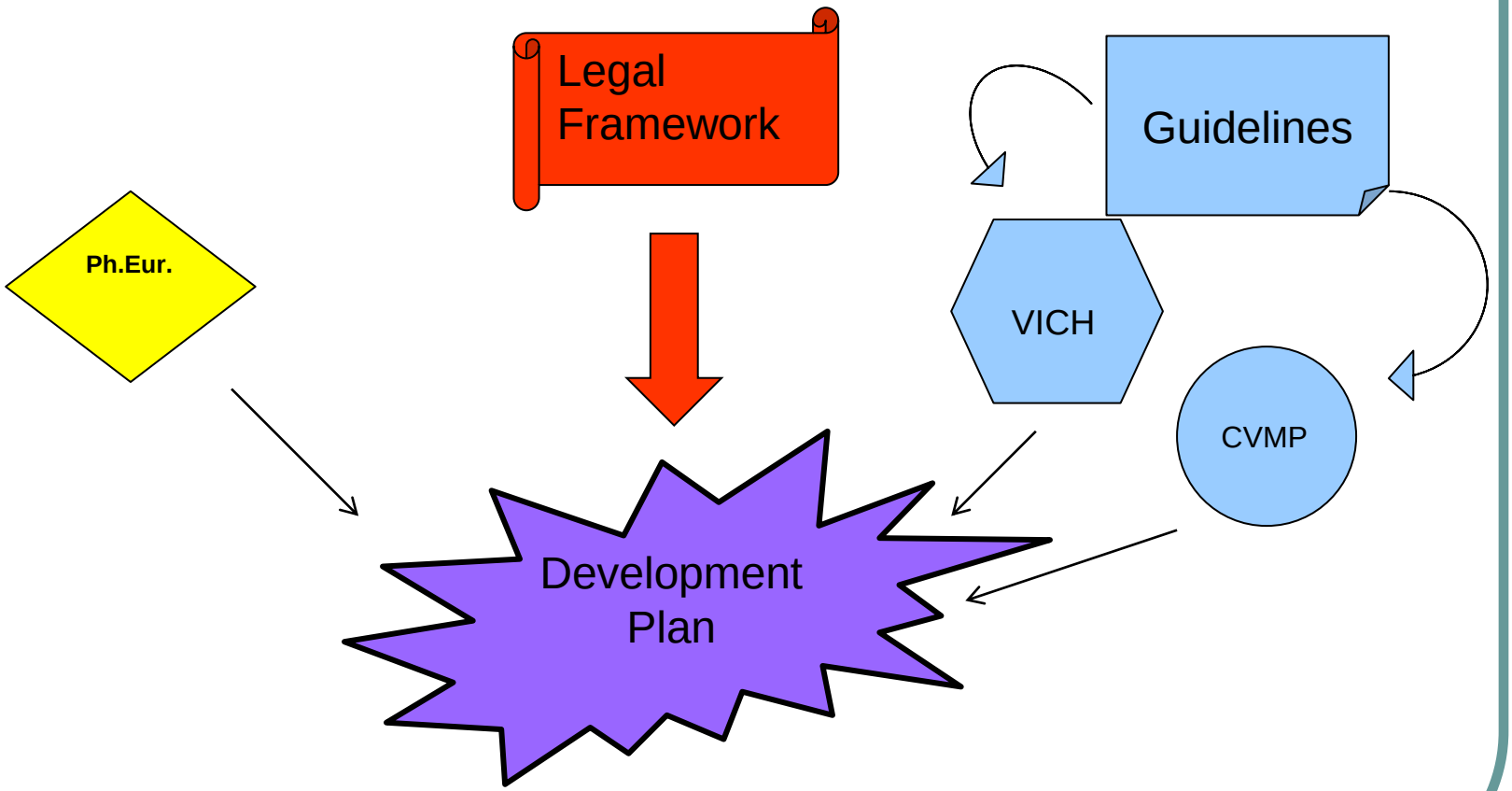
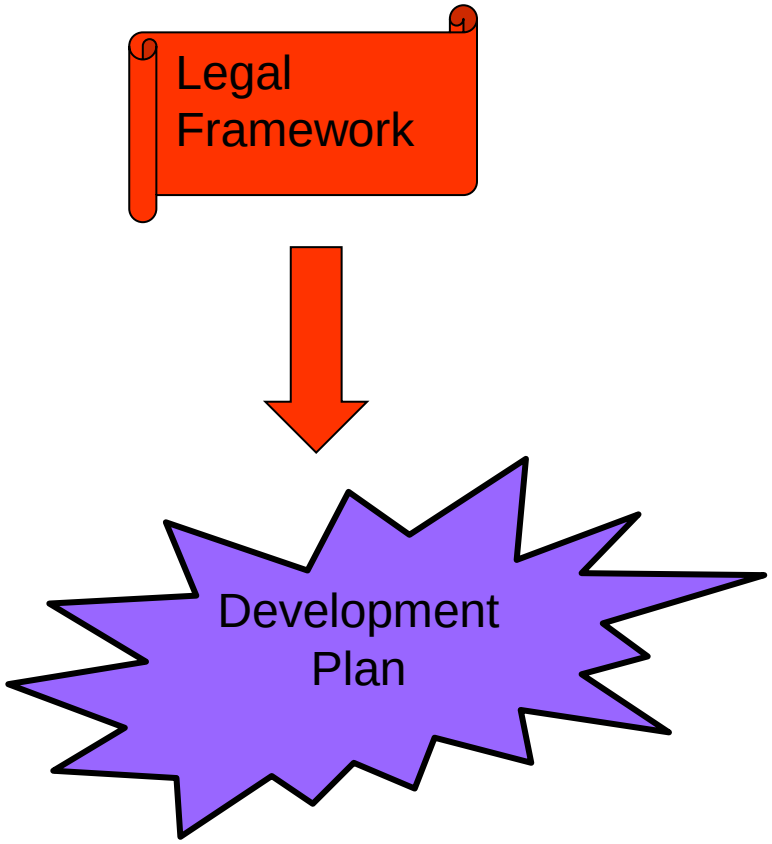


Legal Framework



- Directive 2001/82/EC as amended by Dir. 2004/28/EC & **Dir. 2009/9/EC**

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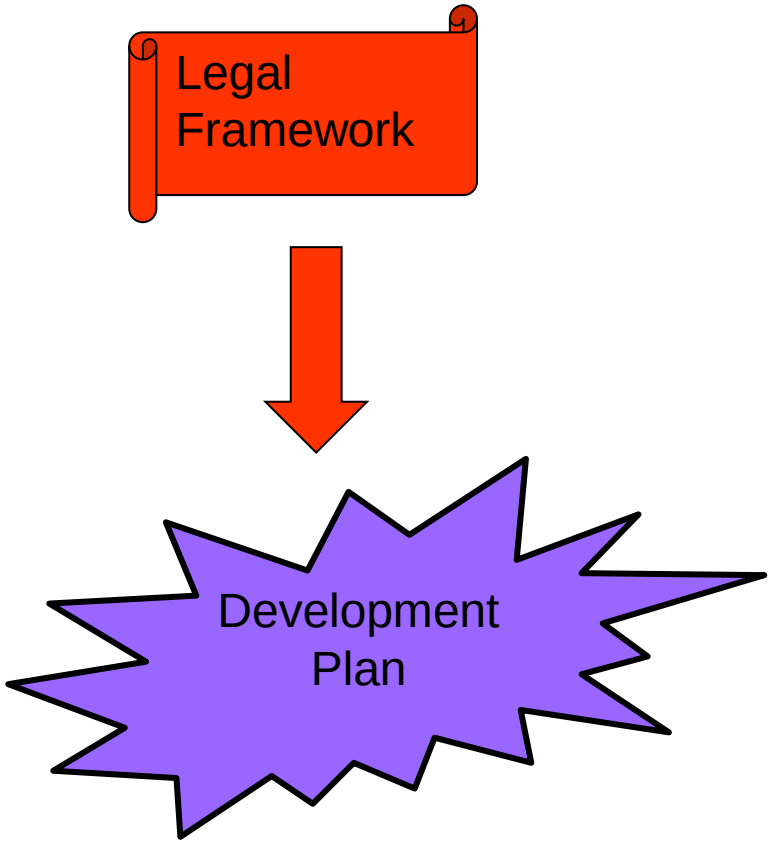
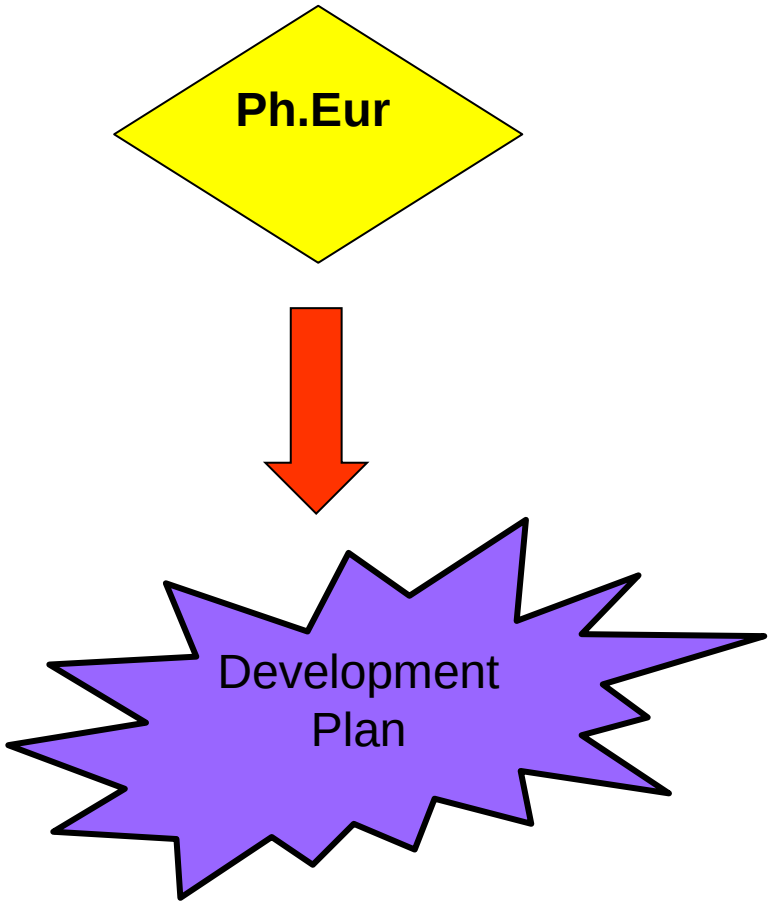
Community Code relating to Veterinary Medicinal Products

Legal Framework



- Directives
  - 2001/18/EC
    Deliberate release of GMOs
- Regulations:
  - EC/470/2009
    EU/37/2010
    (MRLs)

European Pharmacopoeia



- General monographs:
  - 0062 Vet Vaccines
  - 50206 Safety of Vet Vaccines
  - 50207 Efficacy of Vet Vaccines
- Lots of monographs relating to quality
- Specific vaccine monographs

Disease Specific Monographs - examples

- 1952 – BVDV (inactivated)
- 0361 – Clostridium chauvoei
- 0064 - Swine erysipelas (inactivated)
- 2326 – Coccidiosis vaccine (live)
- 1581 – Vibriosis vaccine (inactivated)
- 0964 – Canine Parvovirus (live)
- 0451 – Rabies vaccine (inactivated)
- 0249 – Equine influenza (inactivated)

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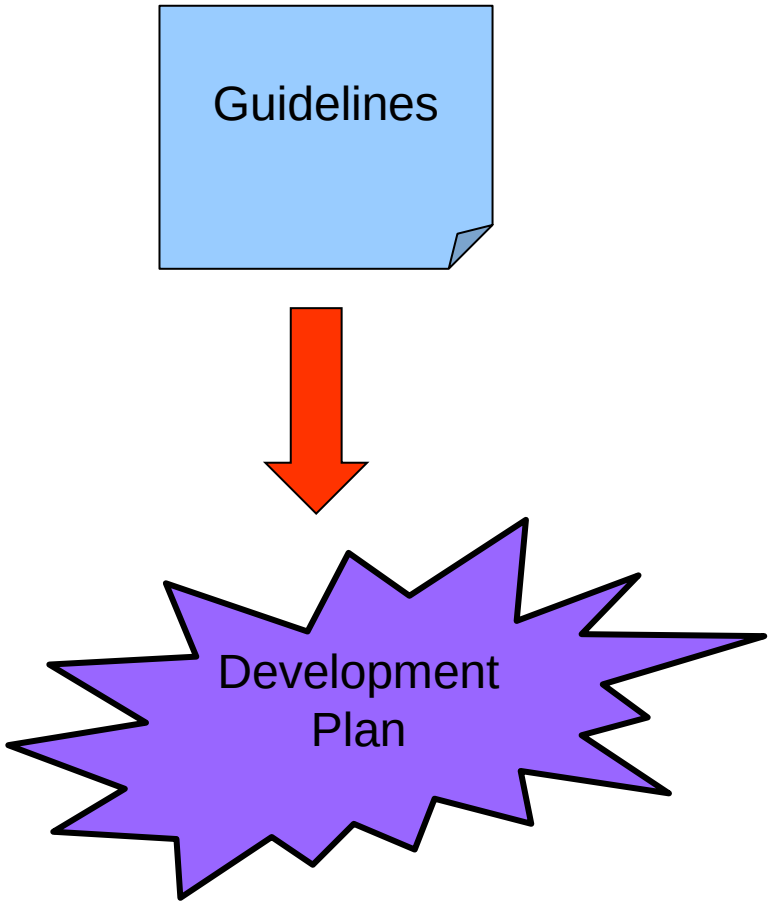
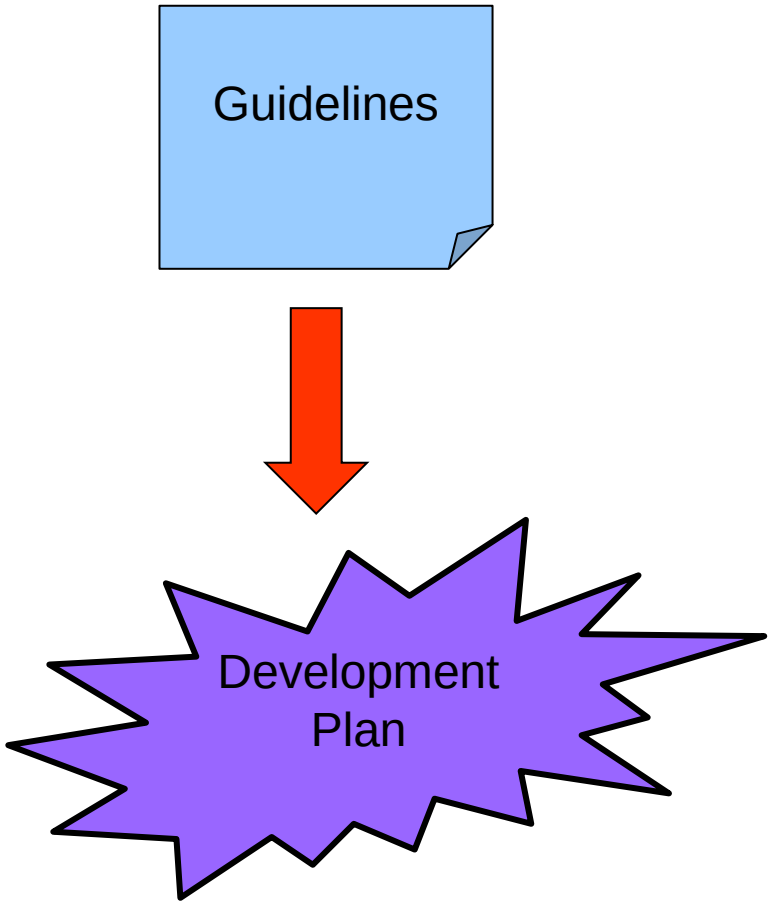
Guidelines - VICH



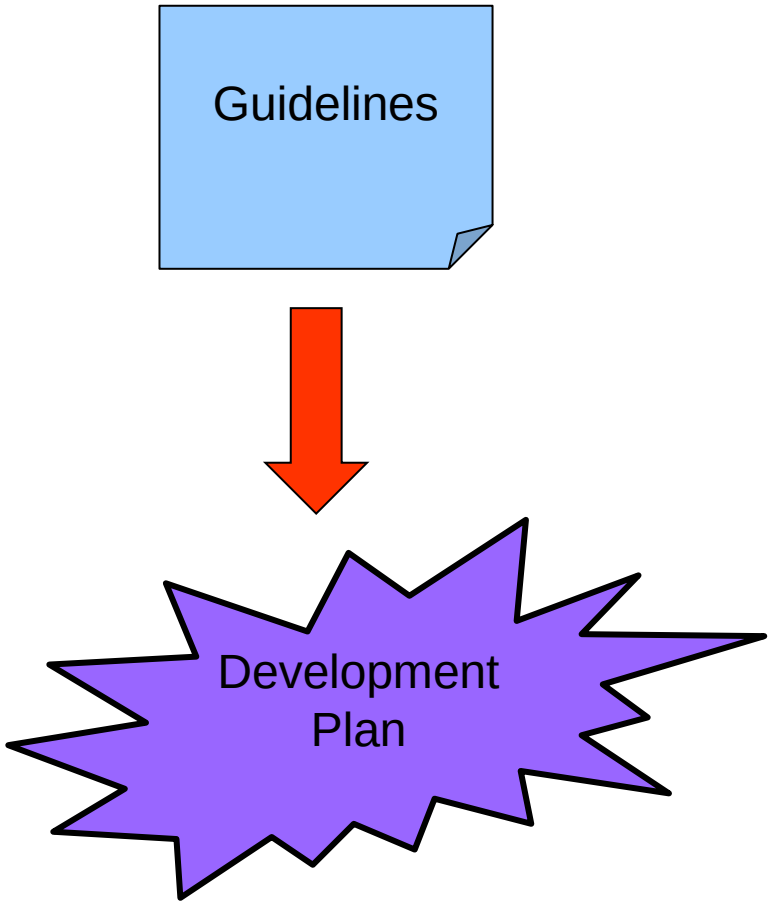
- VICH
  - GL41 – Target Animal Reversion to Virulence
  - GL44 – Target Animal Safety
  - GL9 – Good Clinical Practice

Guidelines - CVMP



- CVMP
  - EMA/CVMP/IWP/594618/2010 Combined vaccines & associations
  - EMA/CVMP/IWP/314550/2010 Fish vaccines
  - EMA/CVMP/IWP/206555/2010 Production & Control of IVMPs
  - EMA/CVMP/IWP/220193/2008 Bluetongue

Guidelines - CVMP



- CVMP
  - EMA/CVMP/IWP/105506 /2007 Multistrain dossiers – AI/BTV/FMD
  - EMA/CVMP/IWP/439467 /2007 MDA Studies
  - EMA/CVMP/682/99 Duration of Protection
  - EMA/CVMP/852/99 Field Trials

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What data should be generated during product development?

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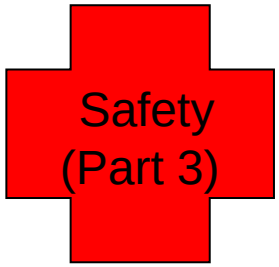

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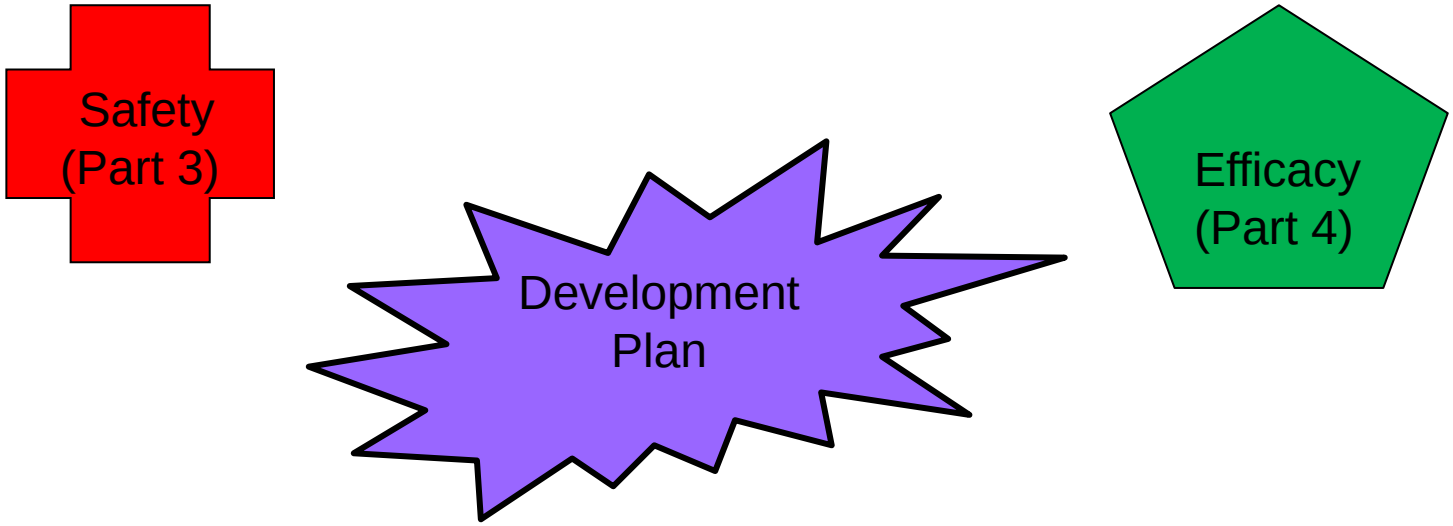

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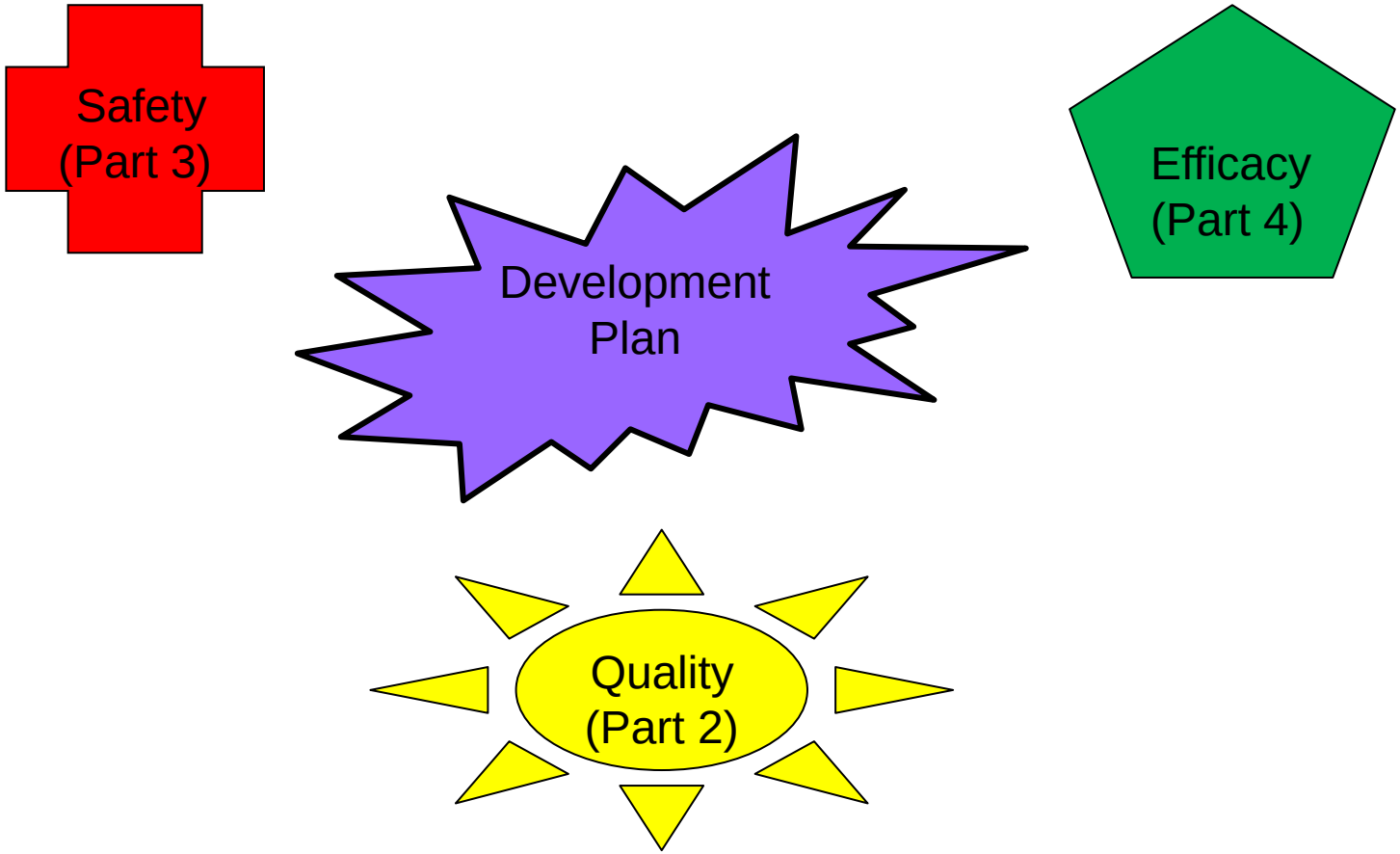

Part 3 - Safety

The Legislation states:

3.A.

"*The safety tests shall show the potential risks from the IVMP, which may occur under the proposed conditions of use in animals; these shall be evaluated in relation to the potential benefits of the product*"

Part 3 - Safety

3.B. Laboratory Studies

- GLP standard (in most cases)
- Under controlled conditions
- Intensive monitoring
- Home Office License

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Part 3 - Safety

3.B. Laboratory Studies

- 3.B.1 – Single dose Safety
- 3.B.2 – Overdose Safety
- 3.B.3 – Repeat dose Safety
- 3.B.4 – Examination of Reproductive function
- 3.B.5 – Examination of Immunological function

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Part 3 - Safety

- 3.B.6 – Special requirements for live vaccines (cover for each antigen)
  - 3.B.6.1 – Spread
  - 3.B.6.2 – Dissemination
  - 3.B.6.3 – Reversion to virulence
  - 3.B.6.4 – Biological properties
  - 3.B.6.5 – Recombination / genomic reassortment
- 3.B.7 – User Safety
- 3.B.8 – Residues
- 3.B.9 - Interactions

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Part 3 - Safety

3.C. Field Studies

3.D. Environmental Risk Assessment

3.E. Additional Information - GMOs

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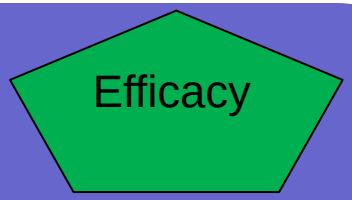
Part 4 - Efficacy



The Legislation states:

4.A.

"*The purpose of the trials in this Part is to demonstrate or to confirm the efficacy of the IVMP. All claims made…..with regard to the properties, effects and use of the product, shall be fully supported by results of specific trials*"

Part 4 - Efficacy

4.B. Laboratory Studies

- 4.B.1 – Dose determination
- 4.B.2 – Onset of Immunity
- 4.B.3 – Duration of Immunity
- 4.B.4 – Effect of MDA
- 4.B.5 – Booster effect
- 4.B.6 – Interactions
- 4.B.7 – Diagnostic tests (DIVA vaccines)

4.C. Field Studies

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Part 2 - Quality

DON'T FORGET TO CONSIDER QUALITY!

What goes in the Part 2 Dossier?

- Everything related to Manufacture and Control of the Vaccine!

……

Part 2 - Quality

- 2A – Qualitative & Quantitative Composition
- 2B – Manufacturing Process
- 2C – Control of Starting Materials
- 2D – In-Process Control Testing
- 2E – Finished Product Control Testing
- 2F – Batch to Batch Consistency
- 2G – Stability
- 2H – Additional info (Eg. For GMOs)

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Part 2 - Quality

- Quality issues concern a large proportion of the questions received during assessment
  - Not enough thought given to the Part 2 during research and development
  - Can be difficult to fill the holes further down the line
  - Therefore essential that you include “Quality” in your Development Plan

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Part 2 - Quality

- Points to consider at an early stage:
  - What will be in the final formulation?
  - Have you prepared and fully tested your Master Seed(s)
  - Do you have a defined manufacturing process?
  - Is your intended manufacturing process robust, scaleable and affordable?

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Part 2 - Quality

- Points to consider at an early stage:
  - Are your active substance(s) and finished product stable?
  - Do you have a validated potency test?
- Why is all this important???

…..because the Vaccine used to generate Quality, Safety & Efficacy data must be fully representative of the product to be licensed

Regulatory Support:

- Easy then??.....occasionally
- BUT…..The legislation and guidelines don't tell you all you need to know
- Experience counts for a lot
- Make use of the help that is out there…..
  - Consider seeking Expert Regulatory Advice (cost effective)
  - Don't be afraid to speak to the Regulators

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Regulatory Support:

- Register as a SME if applicable (fee reductions, fee deferrals)
- Request MUMS status for your product if appropriate (data reduction, possible financial incentives)
- Consider:
  - Scientific advice (EMA/parallel)
  - Innovation Task Force (ITF)

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Conclusions:

It is very important to have a clear Roadmap before you depart!

- Take into consideration the relevant Legislation, Ph. Eur. Monographs & Guidelines
- Always keep in mind the commercial aspects of vaccine development
- Seek advice when in doubt

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Topical points –

Veterinary Medicine Legislation Review

History – key changes

- **1965**: Marketing authorisation (MA) required for veterinary medicines
- **1981**: Two Directives establishing EU legal framework for veterinary medicines
- **1990**: Regulation 2377/1990 introducing MRLs
- **2004**: Major revision of the legal framework
- **2009**: new Annex I, new variations regulation, new MRL legislation
- **2010**: Implementing MRL Regulation

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VMP Legislation Review

- VMP Legislation (Dir. 2001/82/EC as amended) is under review
  - Review was due after 10 years – but initiated early due to deficiencies in the current Legislation.
  - Main stakeholders involved in the review:
    - IFAH-Europe (industry)
    - HMA-Veterinary (National regulatory agencies)
    - European Commission (EU law)

IFAH-Europe (International Federation for Animal Health) is a federation representing the VMP industry & animal health associations – such as NOAH (National Office for Animal Health) in the UK

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Timeline?

- Ref. No. 2012/MARE/002
- Proposal Adopted: 10 September 2014
- Co-decision procedure (18 months) ~ Q1/2016
- Should be published in the OJ ~ end Q1/2016
- Transition period (24 months); comes into operation around Q4 2017 / Q1 2018

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What's likely to change?

- The 'Directive' will become a 'Regulation'
- Procedural changes:
  - Streamlined
- Extended data protection
- Simplified packaging & labelling
- Harmonised clinical trial procedure (timelines)
- National helpdesks for SMEs
- No major changes to data requirements foreseen!

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Want to read more?

http://ec.europa.eu/health/veterinary-use/rev_frame_index_en.htm

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Thank you for your attention

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