

Innovation in veterinary medicines in Europe

including antibiotics

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Innovation in Veterinary Medicines

- Can we find some data / recommendations in the Global Benchmarking Study (2011)?
- Has the regulatory environment changed since?
- What about the new Regulation (“VMR”) and innovation?
- Antibiotics
 - Do we need innovation?
 - Can we get innovation?



From the Global Benchmarking Study, 2011

- serious disquiet with the current regulatory frameworks, ... Particular issues are seen as serious barriers to continued innovation and industry progress in the EU:
 - Lack of regulatory harmonisation within and between regions, resulting in corporate strategic decisions that do not favour the EU, such as going for USA approval for biologicals in preference to the EU
 - Unnecessary delays in administrative processes to achieve national licences following a DCP/MRP
 - Lack of uniformity in regulatory assessment, quality and mutual trust within the EU, so that DCP/MRP approvals can be derailed by just one assessor in one Member State during final-stage activities
 - Regulatory authorities whose assessment is bureaucratic, doctrinaire, or has a tick-box approach.
 - A wide degree of concern about over-stringency of manufacturing, pharmacy, quality and inspection requirements, seen as driven by human medicines standards without attention to the conditions of use, market-sizes and animal or disease targets of animal health products.
 - Concerns about ever-increasing demands for data on environmental impacts and on pharmacovigilance.
 - Frustration that politics is enforcing some regulatory approaches, notably the current attitudes to use of antimicrobials in animals and disbelief that the consequences of a ban, at a time when many parts of the world urgently need more, safer and cheaper food, have apparently been ignored.
- Most of the above have tremendous impacts, often cumulative, on the costs and resource-requirements of product-line acquisitions or corporate mergers and acquisitions. **There are also concerns that the current systems will actively hinder the emergence of innovative biological and biopharmaceutical methods of managing health and productivity, ...**
- In a broader context, it is perceived by the industry that politicians in the EU do not understand, or rate highly enough, the need for secure and safe food and the positive contributions that the animal health (AH) industry makes to this.

Figure 3: The top regulatory concerns in Europe

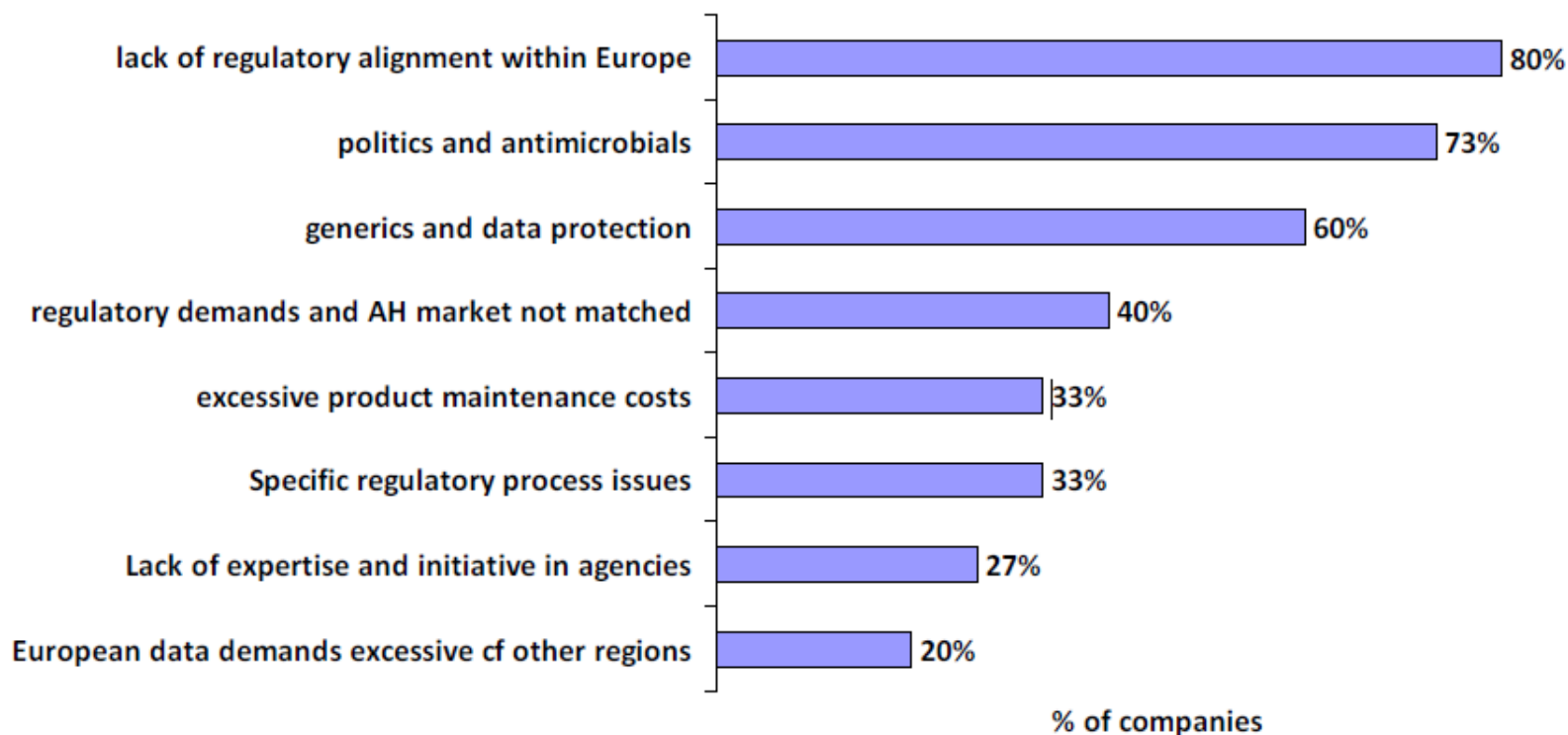


Figure 23: Obstacles to innovation in Europe 2011

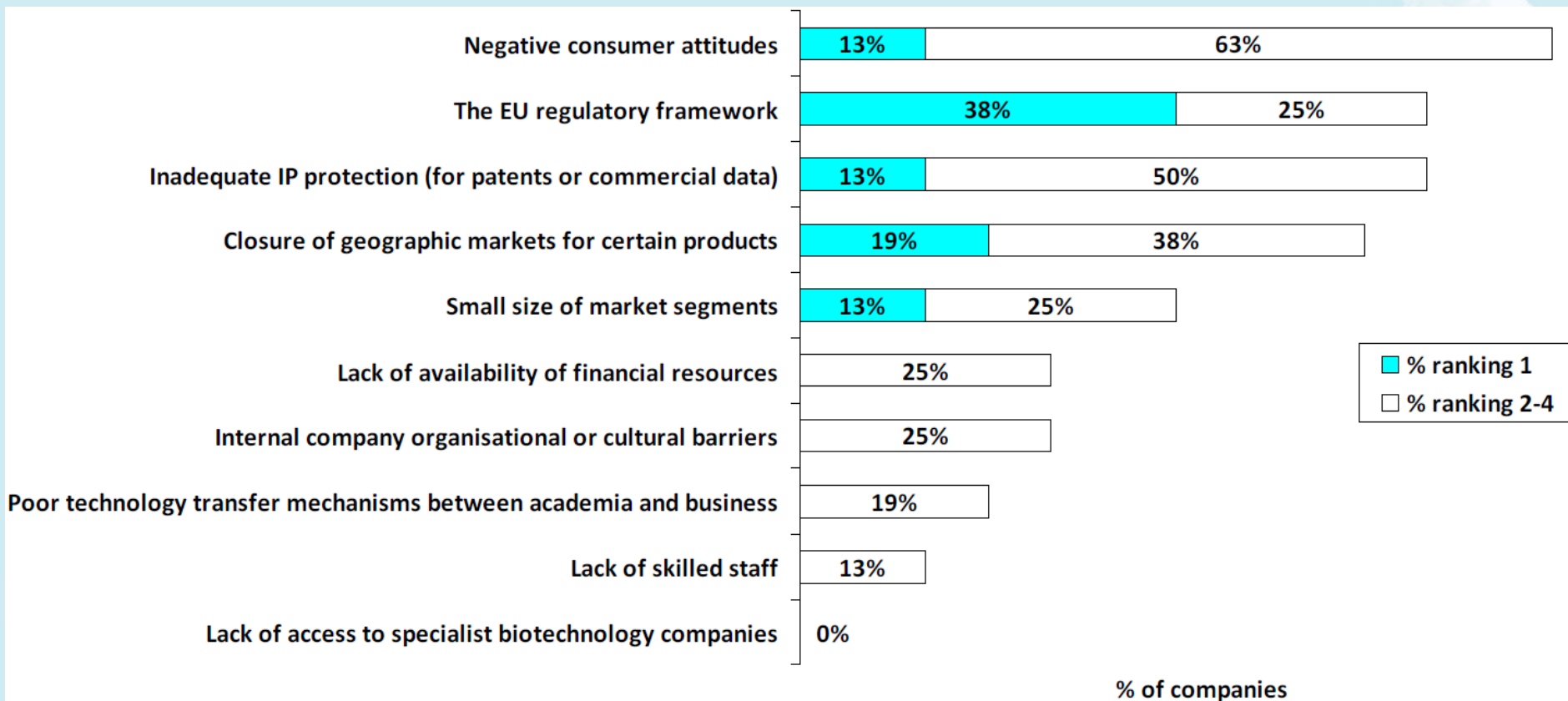


Figure 27: Mandatory Defensive R&D in Europe 2011

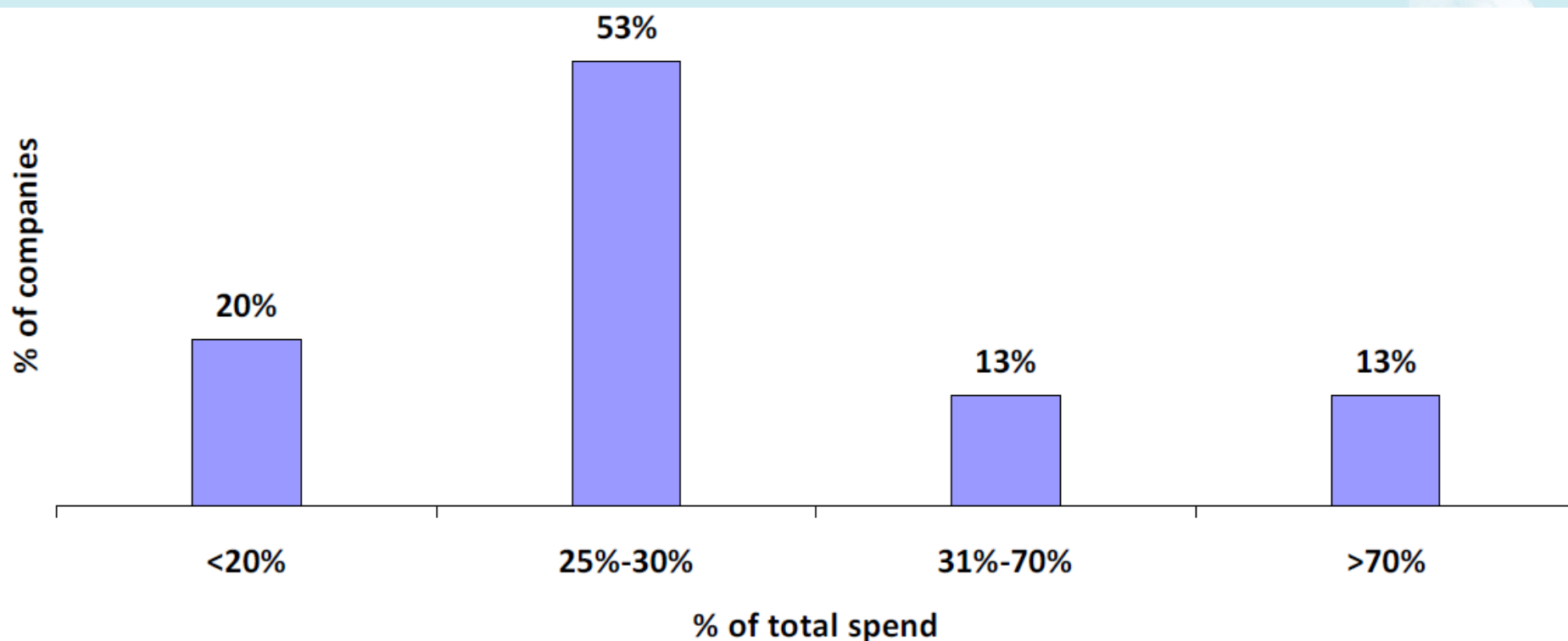
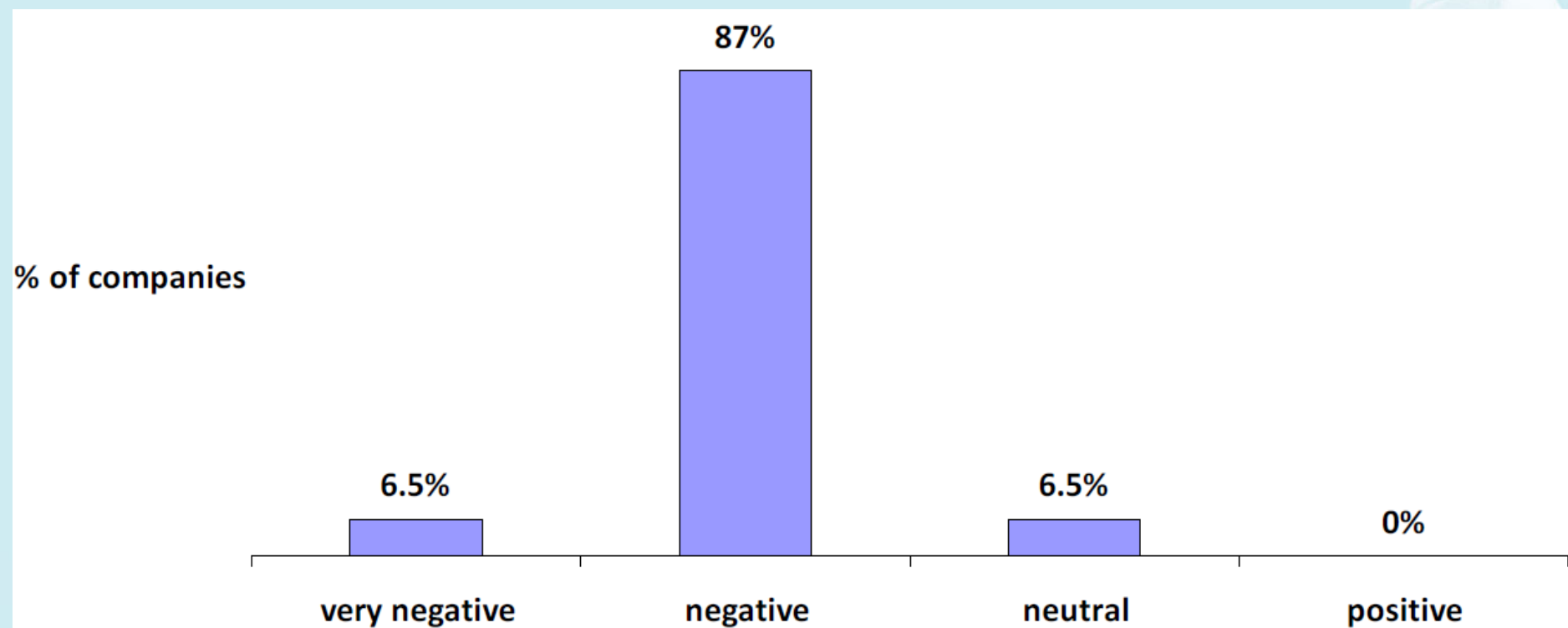
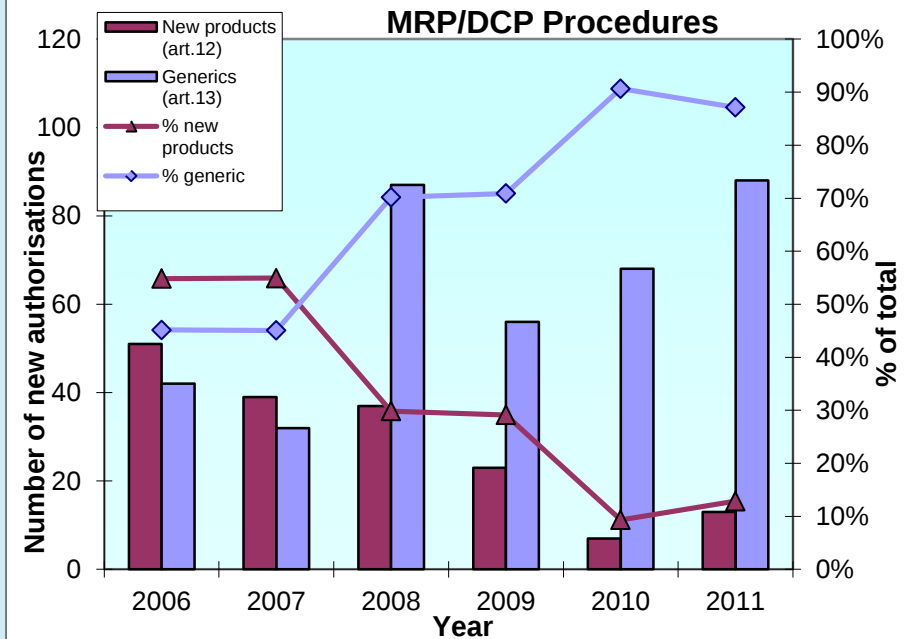
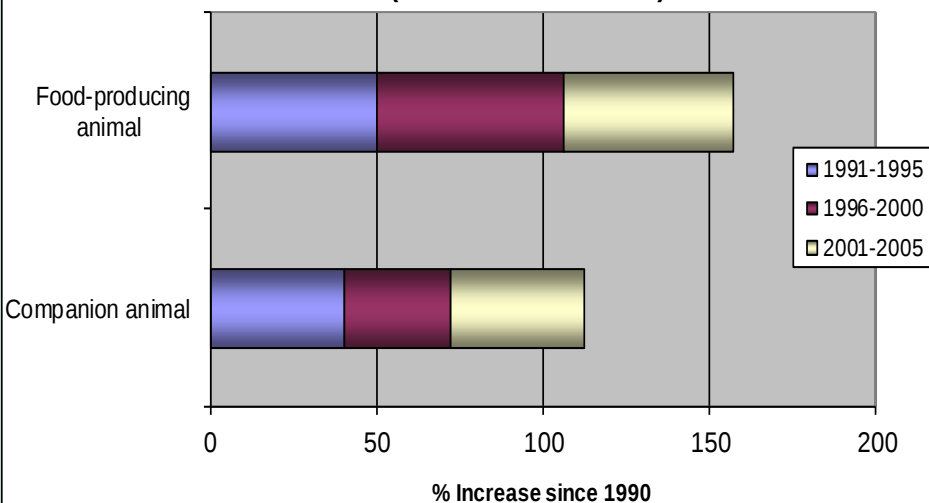


Figure 22: Impact of reg environment in Europe on innovation 2011

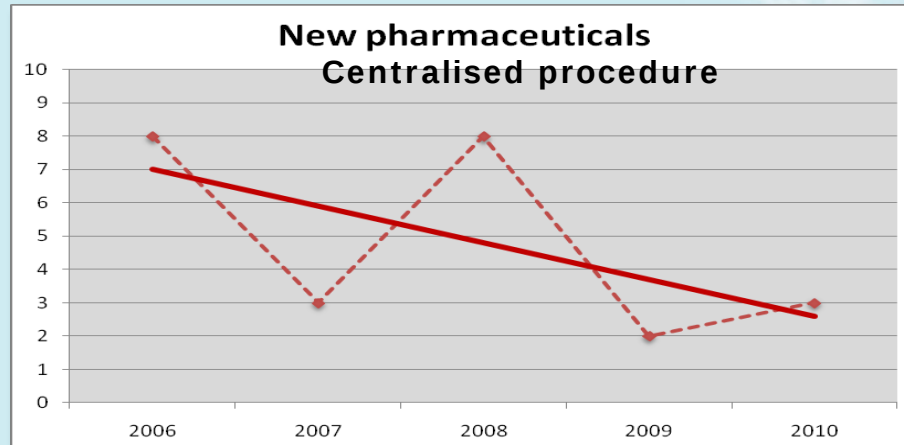


Dis-incentives to innovation

IFAH Benchmarking Survey 2006: Increase in real development costs
(Indexed 1990 = 100%)



- higher R&D costs
- reduced data protection
- decline in innovation



Recommendations from the Global Benchmarking Study 2011

- **Industry and Innovation:**
 - **Authorities must respond to the negative impacts of Directive 2004/28/EC on innovation.**
 - **Apply a realistic solution to the problems caused by inadequate data protection to innovator companies, particularly for product species/indications extensions.**
 - **Build on EMA meetings with industry, looking at new technologies; offer specific seminars in future technology areas that might pose problems.**
- Efficiency and best practice in regulatory authorities:
 - Authorities must respond to the disproportionately high costs in Europe of defensive R&D and maintaining existing products on the market...
 - Keep encouraging all positive aspects towards increased efficiency, such as work-sharing and variations grouping; practicable electronic submissions; time-line and clock management; straightforward acceptance of JECFA agreements on residues of non-contentious molecules.
 - Investigate a system of conditional approvals for certain products through the Centralised Procedure
 - The continued application of 'serious risk' objections by single member states whose objections are then over-ruled on referral to CVMP is highly inefficient and must be controlled...
 - minimise negative impacts of Chemistry-Manufacture-Control (CMC), pharmacovigilance and manufacturing-inspection philosophies and actions being conditioned by inappropriate human pharmaceutical expectations; without jeopardising the industry's aim to produce safe effective animal health products.

Recommendations from the Global Benchmarking Study 2011

- Single market:
 - Work on practical aspects of managing conversion of approval of products registered in single or restricted range of countries to a wider range or all of EU.
 - roll-out of approval to be regarded as a simple admin step without months of delay by national agencies.
 - Continue to shape and scope of a more efficient regulatory framework for veterinary medicinal products.
- Management of older products:
 - Industry is concerned that agencies sometimes demand additional and in practice excessive detail and changes to manufacturing and quality when product licences are renewed.
- Future challenges:
 - Work on practical aspects of collecting, interpreting and managing pharmacovigilance data – Pharmacovigilance and Post-marketing Surveillance systems are perceived as a large ‘black cloud’ by the industry; a forward-looking series of joint seminars might be of assistance (cf. the joint workshops on packaging and labelling).
 - Review the scope for a specific or radical approach for MUMS products, following an assessment of the reasons why industry has not taken up the EMA’s initiatives. The HMA-V working group activities on medicines availability need to be robustly assessed and the current regulatory approach changed in order to accelerate MUMS developments (noting that attention to data protection for species/indication extensions may also be needed).
- Industry, Regulation and Society:
 - Involvement of the Industry in providing safe food for human health and healthy animals for human well-being must continue to be stressed to politicians as well as European citizens.
 - The industry very strongly supports science-based regulatory actions, with regard to antimicrobials, for example, and is concerned that this is undermined by the increasing public involvement in aspects of the regulatory process, mainly because of companies’ experiences of the combination of pressure groups and politics.

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Are the Agency and CVMP moving and are they fostering innovation?

- **Yes, they do focus on getting new technology through**
 - Scientific Advice Working Party @CVMP
 - Innovation Task Force
 - ADVENT
 - **AD**hoc group on **V**eterinary **N**ovel **T**herapies
 - Portfolio reviews
 - Trans-Atlantic agreements and simultaneous advice
- **No, they can't fully do so**
 - Boundaries of the current and future legislation
 - Bureaucracy & admin burden,
 - Excessive control & Overregulation



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Innovation and the new Veterinary Medicines Regulation

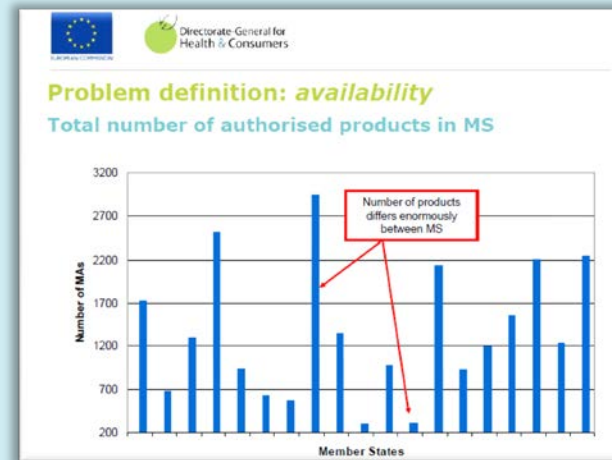
“true” innovation: “new products or claims”

- Product categories and definitions in draft VMR unclear
- No provision for “established” novel therapies
- Special focus on antimicrobials
- Big driver = protection technical documentation
 - New products (minority)
 - Developing existing products (VAST MAJORITY)



Innovation and the new Veterinary Medicines Regulation

- **Innovation for “some markets”**
 - Harmonisation existing MA?
 - Labelling and packaging



- Let's look at these **IFAH Europe's priorities versus the current draft** of the new VMR

1. Protection of technical documentation

- Objective: stimulate and protect innovation - for all significant investments and innovation (not just minor species)

	Current	COM(2014) 558	What is needed
New data packages for existing products			5 years (stand-alone)
1 st product (1 st species) - can be extended	10 years	10 years	10 years
- extended by adding another species	+1 for food-species	+1 for a major species* +4 for a minor species**	+3 for a major species* +5 for a minor species** Also when in original dossier
Deadline	Obtain new licences within +5 years	Submit applications 3 years before end of the initial protection period	Change the deadline to "submit within 3 years of the end of the protection period"
Max. prolonged period	13 years (i.e. 10+1+1+1)	18 years	20 years
Minor species	13 fish and bees only	14 for minor species 18 for bees	15 for minor species 20 for bees
NEW antibiotic	-	14 years	20 years

* Cattle, sheep, pigs, chicken, **dogs and cats**; ** **other species than major species and bees**

2. Innovation also for existing products?

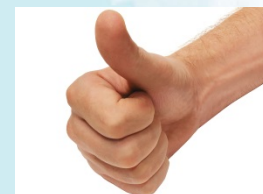
- Incentives to develop existing products in draft VMR?
 - So after the maximum PTD...
 - Art 35.4 VMR draft:
 - “Where an applicant for a marketing authorisation *for a veterinary medicinal product* or for a variation to the terms of the marketing authorisation submits an application *in accordance with Regulation (EC) No 470/2009* for the *establishment of a maximum residue limit*, together with clinical trials during the application procedure, other applicants shall not use those trials for a period of 5 years from the granting of the marketing authorisation for which they were carried out, *unless the other applicant has obtained written agreement in the form of a letter of access with regard to those trials.*”
 - Unclear and not sufficient
 - Limits to also providing new MRL dossier?

2. Innovation also for existing products? (2)

- So new article proposed on “Protection of technical data generated for existing products”
- Where a marketing authorisation holder submits new test and study reports to the authorities or to the agency, those reports shall benefit from a 5 year period of protection, provided that those test and study reports were
 - a.necessary to extend an authorisation such as a new species, pharmaceutical form, administration route, dosage form or indication, or
 - b.necessary for a reassessment requested by the authorities or the agency post authorisation.
- Other applicants shall not use those new tests and reports out unless the 5 years of protection period has elapsed, or the other applicant has obtained written agreement in the form of a letter of access with regard to those tests and study reports.

3. Innovation is also better availability

- **Improve internal market for existing products**
 - Chapter on SPC harmonisation in new Regulation
- **Major issues with the COM proposal**
 - Only proposal to harmonize SmPC, not MA's
 - Need to bring in CMC!
 - Does not result in European MA – no motivation/benefit for industry
 - Lower risk products – simple administrative procedure 😊
 - But majority of products excluded by the conditions
 - Products needing re-assessment of specific items
 - Use referral procedure!
 - If change in original product for safety: immediate referral for generic seems logical
 - Harmonisation by product class
 - No motivation/benefit for industry; anti-competitive
 - Changes the basis of registration of VMPs



4. Innovation is also... better labelling and packaging rules

- **Labelling chapter layout greatly improved**
 - 1 article per packaging element
 - Quantity of mandatory text on immediate label reduced
 - Pictograms and standard abbreviations are allowed
- **But requirements are overly prescriptive:**
 - **only** the defined text can appear on immediate label
 - **only** the defined text can appear on the outer packaging
 - *It is not 'future proof' to allow future innovation in packaging (e.g. QR codes, smart phone technology)*
 - “For animal treatment only” remains mandatory (outer pack)
 - Information on “take back schemes” (outer pack)



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Do we still need (new) antibiotics?

- Alternatives:
 - ➡ Vaccines: protect against specific pathogens
 - ➡ Probiotics: growth of desirable bacteria
 - ➡ Prebiotics: improve growth of beneficial bacteria
 - ➡ Enzymes: improve growth of beneficial bacteria
 - ➡ Organic acids: inhibition of bacterial growth
 - ➡ Herb extracts: bacteriostatic or immune-stimulating
 - ➡ Symbiotics: probiotics + prebiotics
 - ➡ Bacteriophages: specific bacterial targets
 - ➡ Immunomodulators, genetics: enhance resistance to infection
 - ➡
- Potential to reduce the need for antibiotics
- So far: no replacement for AB treatments



Need for (new) vet antibiotics...

- Availability of veterinary antibiotics = important
 - For animal health and welfare,
 - For farmers' livelihoods
 - For sustainable agriculture
 - For food safety
 - For public health.



There are severe challenges :

- To the continued availability of veterinary antibiotics
 - From the potential for development of antibiotic resistance.
 - From the reserved-use lists for human medicine (CIA)
 - From the lack of protection of technical documentation if a company is required to make major investments in the re-development of an existing product (e.g. to modify dosing regimes).
- To the continued development of new vet antibiotics (costing millions of €'s over 5-10 years);
 - **Increased product development costs**
additional data requirements introduced
 - **No market predictability**
an antibiotic can be reserved for human use only at any time;
 - **Additional restrictions on the use** of veterinary antibiotics
reduces the market size.
 - **Increased maintenance costs**
 - new post-authorization studies to monitor resistance development.



What does industry need?

- **Science-based regulation:**
The Regulation should reflect the recommendations reached by the European Medicine Agency's Antimicrobials Expert Group when considering restrictions on use and reserved lists.
- **Stimulate research and innovation** in the development of new veterinary antibiotics **by providing an extended period to protection of the technical documentation.**
- **Protect new data on existing antibiotics**
so that companies can continue to support existing antibiotic products
and make some of the "older antibiotics" not often use in human medicine available in more convenient forms for use in animals.
- **Fair competition**
same post authorisation requirements (e.g. resistance monitoring) for all Marketing Authorisation Holders of products with the same active ingredient
- **A predictable regulatory environment**



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