GLOBAL BENCHMARKING SURVEY 2020

Benchmarking the competitiveness of the global animal health industry

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1. Executive summary

The HealthforAnimals Global Benchmarking Survey is run every 5 years and has now grown to include 11 countries in the 2020 survey. The purpose is to examine the interactions between industry and regulatory systems for veterinary medicinal products, particularly the impact of regulations on the animal health industry's ability to access markets, be innovative, continue to commercialise existing products and be competitive.

This report is the **first for India**. It summarises the data **from 15 India based international companies**, examines key trends, provides analysis, conclusions and recommendations. Data was collected through questionnaires in Q4 2019, which was aggregated and summarised to allow discussion in a subsequent workshop. The key points from the workshop discussions are an integral part of the report, which follows the questionnaire structure with 6 separate sections.

Key Conclusions

Section A - Economics of the animal health sector

The global animal healthcare industry continues to grow ($24 billion in 2015 and $41.5 billion in 2018), while the global veterinary pharmaceuticals market was estimated to be nearly $33.8 billion in 2018. The growth is driven by many factors. Acquisition is a common growth strategy to build competence and capacity in technologies, new science, new therapies and new geographies. The livestock and pet sector markets are themselves growing in size.

Section B - Impact of the Indian regulatory environment on ability to innovate

The regulatory environment of India for animal health products has changed positively with the formation of a dedicated Veterinary Cell at the Central Drug Standard Control Organization (CDSCO) in 2018. There is an effort from regulators, recognised by the industry, to align the policies and guidelines for the animal healthcare requirements. However, overall the regulatory policies are becoming more stringent, policy driven and in favour of public health.

Though India is a leader in livestock produce and one of the top suppliers of poultry products, the size of the animal health business is still small. This limits the allocation of financial resources and thereby hinders innovation and new product development. Also the availability of skilled man-power for R&D and sparse translational research from academia to industry are some of the limiting factors for innovation. Animal biotechnology is yet another sector that has not yet been explored well in India. Lack of access to biotechnological advances and its cost *vs* benefit ratio limits commercialisation of such concepts. Indian livestock sector and rearing is culturally and religiously driven. The growth of swine sector and beef rearing has not geared-up in India primarily because of the religious beliefs and customs.

The regulatory framework in India is evolving with greater focus on safety and quality of products. There are regulatory reforms undertaken in the last few years that are positive with respect to raising standards of Indian products but have increased the development cost, approval time, increased regulatory fees, as well the associated expenses. Consequently, bringing new products to market (both in the pharmaceutical and biological categories) has become more costly.

The other big challenge for registration of animal health products in India is that the regulatory procedure involves three regulatory authorities:

(1) The Central Drug Standard Control Organization, part of the Ministry of Health and Family Welfare; CDSCO is the prime authority that regulates pharmaceuticals and biological (both human and veterinary).
(2) The second authority is the Department of Animal Husbandry & Dairying (DAHD) under the Ministry of Fisheries, Animal Husbandry and Dairying, which does a technical evaluation.
(3) Third is the Genetic Engineering Appraisal Committee (GEAC) under the Ministry of Environment and Forests, which examines the biotech and genetically engineered products for their effect on the environment or non-target species.

The increase in regulatory process time is mostly due to this multistage and multi-department authorization, which makes the process and response a little complicated and delayed. For animal health products the process involves three stages:

1) First is technical evaluation and suitability of animal health products for Indian conditions by subject expert committee (DAHD), followed by
2) CMC data evaluation (CDSCO) and, finally,
3) testing of three consecutive batches (commercial size) at the National laboratory [Indian Veterinary Research Institute (IVRI) and Indian Pharmacopeia Commission (IPC)].

Defensive R&D expenditure has changed a little since 2015, primarily because of the changes in the regulation guidelines and norms for both existing and new products. The time to introduce a new product has also increased in past three years. At present to introduce a pharmaceutical product for animal healthcare, it takes approximately 2.3 years for both food and companion animals. Whereas it is slightly higher in the case of biologicals i.*e.* 3.2 years and 3.0 years for food and companion animals respectively.

The government is supportive of innovations and is providing exclusivity to support development of new ideas. The new technologies and products have exclusivity status provided by the Patent Law of India, which is quite robust and very effective in protecting the exclusivity for a reasonable time period. This encourages innovation and new product development.

Section C - Commercialisation of existing product

The regulatory framework is considered as the key factor impacting the commercialisation of existing products. The other important factor influencing commercialisation is the small size of the Indian animal health market. The competition among the similar products and generics further impacts competitiveness and commercialisation. Demand volatility and negative consumer attitudes are also, to some extent, relevant for the exploitation of existing products. GMP compliance has also increased the cost of manufacturing impacting the existing market.

Section D - Regulatory predictability and quality

The regulatory processes are generally predictable but the current issue impacting the industry are regulatory fees, which are same for human and veterinary products. It impacts the cost efficiency of businesses owing to their small size.

The registration of new products at Central Drug Standard Control Organisation (CDSCO) is very stringent and scientific. The biological products also face stringent regulatory requirements with limited data on prevalent strains and this hinders the regulatory authorization processes of these products. The final approval of new products undertakes efficacy, safety and quality parameters of investigations based on best available scientific and risk assessments.

The online registration window "SUGUM" brings in more transparency, ease and predictability into the system.

Maintenance of existing products for domestic manufacturers is appropriate and supportive to the industry. But, for imported products, the regulation is more restrictive with high registration fees.

Section E - Regulatory trends

The biggest change that has happened in the regulatory environment for animal health products is the creation of the Veterinary Cell at CDSCO. The industry and regulators are working in tandem to implement this new system, though its actual impact on industry is still awaited. Industry is closely working with this team to formulate regulatory guidelines specific to veterinary pharmaceuticals and biologicals and has high hopes to stream-line regulatory requirements considering veterinary needs.

The Indian government has been very active in the past few years in bringing digital reforms to various sectors. SUGUM, the digital window of CDSCO, facilitates the online submission and follow-up. Apart from ease, it brings transparency and predictability into the regulatory process.

H AND H_1 Schedule Classification and withdrawal period implementation are some of the important reforms that have also happened on the regulatory front.

The industry is still waiting for regulators to take a different approach towards veterinary products considering the small size of their businesses and lower return on investments. The regulatory fees are the same as the human products, which has cost implications. The registration and import certificate validity is 3 years and industry is requesting for it to be increased to 5 years to be in line with global standards.

One of the recent changes in regulatory practices that has made a huge impact on businesses is the pre-registration testing of imported product samples at IVRI / IPC, which has been made mandatory for new products and is negatively impacting product introduction timelines. Additionally, there has been a ten-fold increase of registration and renewal charges for both human and veterinary products. Industry is requesting abridged registration fees considering the small market size of animal health products.

Section F - Hopes and expectations for the next 5 years

Increasing transparency with respect to data disclosure and electronic submission tailored to animal health are considered some of the very helpful changes anticipated and expected in the future. Other helpful trends could be increasing the requirements for post-marketing surveillance and pharmacovigilance and increasing globalization of post-marketing surveillance outcomes.

Exclusive CDSCO guidelines for animal health products and movement towards a common technical document are also viewed as helpful and desirable changes for the near future.

New veterinary regulations will definitely bring focus on animal health products. Veterinary specific guidelines will help in minimizing the duration and cost of regulatory process. The next important step is to facilitate better co-ordination between the multiple authorities involved in the regulation of animal health products, i.e. CDSCO, DADF and IVRI.

Change still wanted

- The registration validity of imported products should be equal to the validity of domestically manufactured products, *i.e.* five years with renewal based on company declaration, registration fee payment and minimal documentation

- Duplication of check list documents for market authorization and registration applications should be avoided
- Exclusive guidelines and check list for submissions of veterinary drugs
- India should have harmonization of requirements with global authorities and minimize registration timelines (VICH Guidelines)
- The entire regulatory process should be predictable with continuous engagement of the Authority and the applicant to clarify scientific issues with open dialogue
- There needs to be a system for tracking the approval process in the single window system with defined timelines
- Better coordination between CDSCO and DAHD with time bound response system
- Reduction of registration fees
- Published timelines for veterinary pharmaceuticals and biologicals
- One to one meeting with the stake holders (CDSCO)
- Frequency of technical meetings at GEAC should be increased
- Exclusive Veterinary Experts panel for evaluation and No Objection Certificate (NOC) for veterinary products approvals.

Summary and recommendations

Animal healthcare in India is under tremendous pressure and focus considering its significant contribution to the country's GDP. The economies of farmers are positively impacted with rearing of livestock, poultry and aqua culture. In India, the government is supporting animal husbandry and has created a separate Ministry (Ministry of Fisheries, Animal Husbandry and Dairying) to bring it more focus and attention. The Industry shoulders the responsibility to realise the vision of doubling farmer's income as promised by the Government of India. The holistic healthcare is a mandate to ensure uninterrupted animal production. The Industry players are optimistic to bring in more advanced and innovative products to ensure the optimum production and health of animals.

The Industry is optimistic about the dedicated Veterinary Cell created at CDSCO and anticipates realistic guidelines and reforms, which will benefit the veterinary healthcare industry. The challenge will be to facilitate the approval process, which involves multiple authorities, to reduce the total duration of registration process. Industry is calling for the validity of registration and import certificates has to be increased. Biologicals are facing tremendous challenges, especially those that are imported, as there is limited data to prove the efficacy against the Indian strains.

The cost of registration of a product is negatively impacting our small sized industry. The overall cost increase due to multiple new regulatory processes introduced and increase in the registration fees are implemented at CDSCO with respect to human medicinal products. Since there are no specific guidelines for animal health products with respect to these matters, the veterinary healthcare industry is feeling the heat of excessive cost.

The public health issues will play a pivotal role in regulatory decisions. Strict implementation of residue periods, AMR guidelines, restricted use of certain drugs and hormones are expected to change the way the Industry operates today. Businesses need to align themselves with the changing scenario.

Key recommendations

1. Exclusive regulatory guidelines for veterinary medicinal products, which include the cost, the process and final outcome
2. Enhanced collaboration between academia and industry to bring more innovation and relevance in new product development
3. Cooperation among the countries for knowledge exchange, regulatory harmonisation and trade

2. Introduction and background

The purpose of the HealthforAnimals Global Benchmarking Survey is to examine the interactions between industry and regulatory systems for veterinary medicinal products, particularly the impact of regulations on the animal health industry's ability to access markets, be innovative and be competitive. This includes the ability to bring new products to the market, as well as to retain and exploit existing products in the market and thus the impact on the availability of veterinary medicinal products.

The survey originally benchmarked the European and USA regulatory systems, but has since evolved to include the main VICH markets and has now grown to include 11 countries in the 2020 survey (see box).

The evolution of the Global Benchmarking Survey

1. 1996: Europe, USA
2. 2001: Europe, USA
3. 2006: Europe, USA, Japan, Australia, Canada,
4. 2011: Europe, USA, Japan, Australia, Canada,
5. 2015: Europe, USA, Japan, Australia, Canada, China, Brazil
6. 2020: Europe, USA, Japan, Australia, Canada, China, Brazil, India, South Africa, Russia, Mexico

The survey is run every 5 years with the cooperation and involvement of the HealthforAnimals national member associations. The purpose reaches beyond simple benchmarking, to include monitoring of trends and to identify the emerging issues in the regulatory environment that may have an impact on competitiveness, ability to do business and medicines availability. The survey is also a useful tool to gain insight into expectations of the industry over the next 2-3 years in response to current regulatory dynamics and to provide information that allows development of clear action plans for meeting any identified challenges.

The outcome of this survey provides a wealth of information to support informed policy decisions in the continual search for best regulatory practice and opportunities for improvement.

This report is **the first for India**. It summarises the data from **15 India-based companies**, examines key trends, provides analysis, conclusions and recommendations.

3. Outline methodology

The previous Benchmarking Survey **questionnaire** from 2015 was updated to reflect the requirements for the 2020 survey, including: retention of core questions important for global benchmarking and long-term trend analysis; removal of less useful questions; addition of new questions reflecting known new developments within regulatory systems; and addition of selected 'local' questions of importance to an individual country for local versions of the questionnaires.

The national associations were responsible for requesting their members to complete the questionnaires, to collect and collate the results using a standard template and to organise a local 1-day **workshop** with those companies participating in the survey. At the workshop an aggregated summary of the data for each question was presented and discussed in order to explore and record different views and the local context important for an understanding of the reasons behind a particular outcome.

The assimilated questionnaire data and the workshop 'narrative' explaining the findings formed the basis of each **country report**. The **report structure** follows the list of questions, which are used as sub-headings. The question is reproduced at the beginning of each question section in a box below each sub-heading.

Details for India

In India, the Indian Federation of Animal Health Companies (INFAH) collected completed questionnaires from **15 member companies** from December 2019 to January 2020, and all these companies participated in the Indian workshop on 14 February 2020. During the survey, all points were discussed, debated and the outcome was recorded with the consensus of every participant member during the workshop. A few responses were revised during the discussion by respondents and these have been updated and summarized.

For more information on the Indian Federation of Animal Health Companies, please visit:

https://www.infah.org/

Final output: The country reports and a global overview report will be published on the HealthforAnimals website: https://HealthForAnimals.org/GBS2020

4. The findings for India

Section A – ECONOMICS OF THE ANIMAL HEALTH SECTOR

Global context

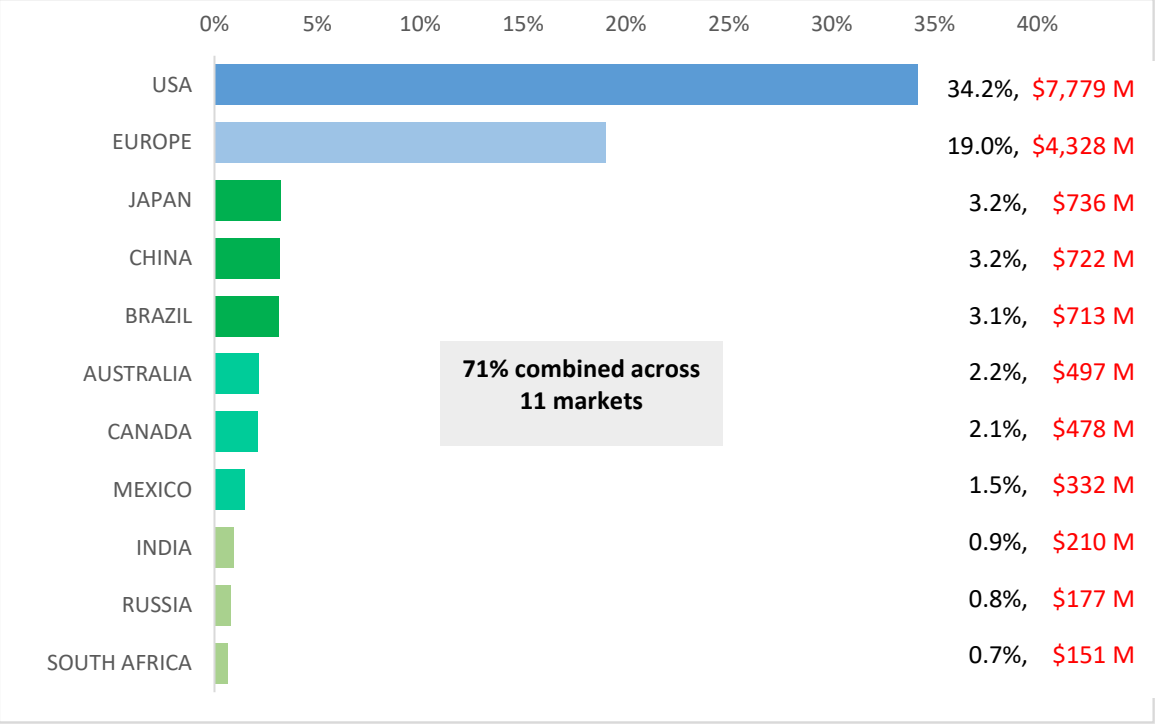
The financial data covers the 2018 full financial year. All data is presented in US dollars ($).

The GBS2020 Part 1 report on financial data is published separately. Key findings from that report are cross-referenced where-ever relevant in this report for India, such as in the sections on product development trends and defensive R&D.

In 2018, the global animal health market was estimated to be worth $45.8 billion[1]. The 10 HealthforAnimals company members held over 50% of that market with a combined revenue of $22.7 billion, and an average of $2,274 million, of which 7% was invested in research and development.

The 11 benchmarked markets accounted for 71% of HealthforAnimals companies' global revenues (Figure 1), with India representing just under 1% of that revenue.

Figure 1: Revenue distribution of HealthforAnimals member companies across 11 markets in 2018



Overall, top international companies directed their R&D spending mostly towards pharmaceutical (62%) and biological (24%) products. Investment in pesticide-based medicines remained a small segment of product portfolios (4%). Contribution of companion animals is 51% and major food species 49% to the total animal healthcare market.

[1] Market Research Reports - https://www.marketremsearchreports.com/blog/2019/09/05/world%E2%80%99s-top-10-animal-health-companies

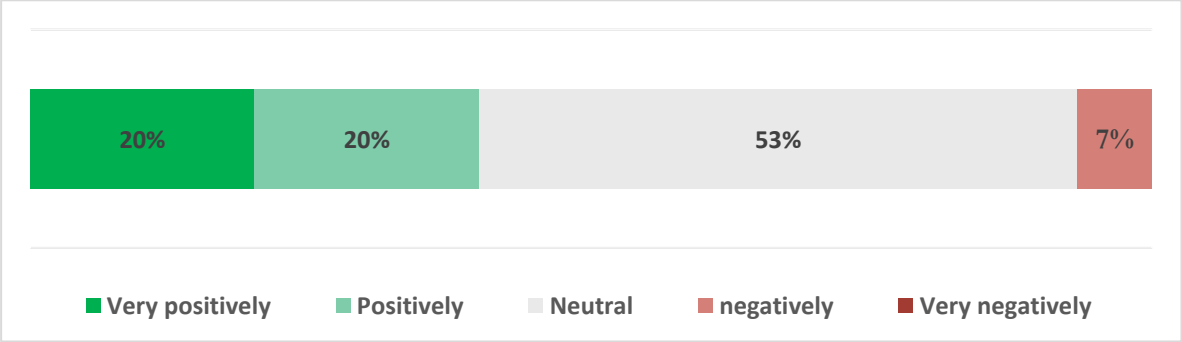
Section B – IMPACT OF REGULATIONS ON INNOVATION

1. Impact of the Indian regulatory environment on ability to innovate

How does the regulatory environment in India impact your ability to innovate?

Opinions have ranged from neutral to positive (53% neutral vs 40% positive). Positive responses generally come from companies operating in the nutrition and natural/herbal products sector.

Figure 2: Impact of the Indian regulatory environment on ability to innovate



Participants claimed that the small size of the Indian animal health sector is a major hindering factor to innovation. In the recent past, companies have observed ten-fold increases in application fees leading to a decline in the return-on-investment.

All participating companies recognized that the creation of the Veterinary cell in CDSCO (MOHFW) has facilitated their understanding of the compliance requirements for veterinary medicines and improved the overall transparency of the regulatory system.

MOHFW regulators are more approachable and redressal is easier. They are supportive for newer ideas and developments if these are backed with scientific data and rationale. The group also expressed that regulators are open to accept the norms as per globally approved guidelines.

Participants expressed inconsistency in discussions and reviews on the part of the regulators, as different evaluators have different opinions. Outcomes are dependent on their understanding of the concept and varies from person to person.

2. Factors relevant to innovation in the animal health industry

Below is a list of factors relevant to innovation in the animal health industry. Which of these, if any, are significant for innovation in your business in India? Rank from 1 (highest significance) to 11.

The overall ranking of the list of factors is shown in Tables 1 and 2 below. While participants had differences in ranking, a vast majority felt that the biggest limiting factor for the Indian animal health industry is its **small market size,** which limits allocation of financial resources.

The next prime reason highlighted was **the pressure of competition and competitiveness** from similar products available within the country.

The next identified factor was **the demand volatility of certain segments**. The group agreed that price, demand and competition decide the volatility of certain segments. In a few segments, demand is primarily driven by outbreaks as the market is more reactive than preventive in its approach.

Lack of skilled manpower in R&D was also identified as an important reason for limited innovations in the sector.

The group also felt that **translational research from academia to industry** has been one of the limiting factors for innovation. Most research tends to be of academic purpose, and not directed to practically address the issues faced by the livestock sector.

The Indian companies also felt that **negative consumer attitudes and cultural barriers** within the organisation and in society also has an impact on product selection. The growth of the swine sector and, conversely, a lackluster growth in beef rearing are both due to these cultural and social norms.

The small market size and increasing regulatory fee structure was also identified as a constraint for innovations in the Indian animal health market as funds have been directed to mandatory defensive R&D.

Lack of access to biotechnological advances and its cost vs benefit ratio limits commercialisation of such concepts.

Inadequate intellectual property protection and closure of other geographical markets were not regarded as limiting factors for innovation.

Table 1: Companies ranking of factors relevant to innovation

Factors relevant to innovation	Importance Average ranking score
Small size of market segments	1.8
Negative consumer attitudes	4.9
Lack of access to specialist biotechnology companies	4,3
Inadequate intellectual property protection (for patents or commercial data)	5.2
Lack of availability of financial resources	5,2
Poor technology transfer mechanisms between academia and business	5.2
The Indian regulatory framework	5.8
Lack of skilled staff	6.9
Internal company organisational or cultural barriers	7.0
Closure of the US and/or other geographic markets for certain products	7.0
Other (Specify_____)	See Table 2

Table 2: Other factors reported relevant to innovation

Other factors reported	Ranking
Haziness in the regulatory framework across the globe	1
Lengthy approval process	3
Registration fee is high	6

3. Regulations that have improved competitiveness

Have Government regulations HELPED to improve competitiveness of your business in any of the following ways?

The participants felt that government regulations have primarily to do with implementation and abiding of the law.

The group felt that the government sector provides a positive, congenial and stable business environment for industry growth. The newer rules and regulations have ensured a better and improved product quality and also reassured the public about the safety of animal health products. Animal health products and their safety for human consumption is an important area of discussion and the government is pro-actively supporting the industry with all its initiatives.

A glance through the time for market commercialisation suggests that the current policies and regulations have negatively impacted and increased the time to commercialisation. The regulatory process has slowed down the process of developments and has adversely impacted innovation.

The discussions also highlight that the timelines outlined for registration and commercialisation are primarily for human products dealing with one regulatory body (CDSCO, MOHFW). For animal health products, multiple regulatory agencies (CDSCO, MOHFW; DAHD, MOFAHD) are involved, with the consequence that timelines for regulatory approvals are not adhered to most of the time. The participants confirmed that in the last two years, the timelines for registering and commercialisation has increased by 6-8 months compared to the earlier average of 2.6 years. This increase in registration time has negatively impacted business.

The participants also felt that the government regulations have not promoted innovation or helped or provided any confidence for investment in innovation.

The industry has observed a few positive changes in the regulatory framework of the country for the animal health sector but the positive impact of this is yet to be felt. Initiatives such as exclusive guidelines for veterinary biologicals have been a welcome step after creation of the Veterinary Cell at CDSCO.

Table 3: Impacts on Business Competitiveness due to regulations

Business Competitiveness Impact	Importance Average ranking score
Improved product quality	3
Provided a stable business environment	3
Other (Specify: Formation of veterinary cell in CDSCO)	3
Prevented dangerous products entering the market	4
Provided confidence to invest (added to certainty and predictability)	5
Reassured the public about the safety of animal health products	5
Improved access to other geographic markets	6
Protected investments in innovation	7
Helped redirect resources to innovation	7
Triggered innovation in new production processes	8
Speeded up time-to-market	8
Created new market segments	9

4. Impacts of regulations on business

Do government regulations in India have any of the following effects on your business?

Participants acknowledged the fact that, in the last two years, government has created newer regulations, which have increased the development cost, approval time as well as the associated expenses. The industry is in the phase of adjusting to the newer and increased expectations of the regulators.

The regulators are also in the phase of regularizing the requirement of animal health care sector and treating them differently from human healthcare. This segmentation is expected to be beneficial to the sector in the long run.

We expect the concept of predictability in the approval of globally approved molecules and their entry into the Indian market. But the concepts of innovation and exclusiveness remain un-predictable.

Table 4: Impact of regulations on business

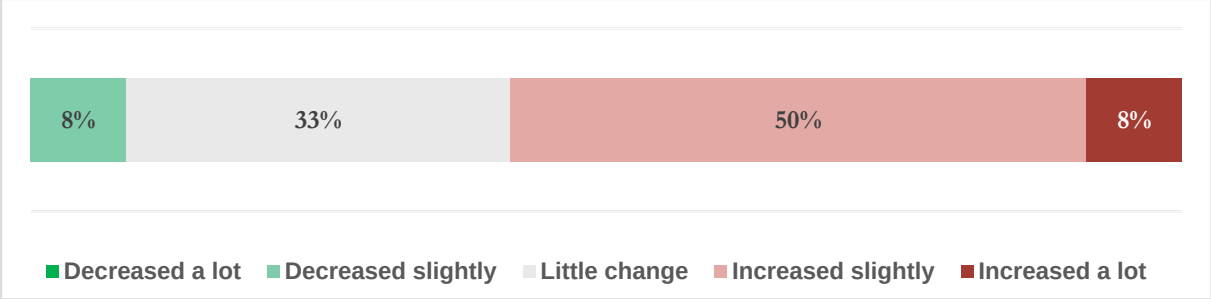
Business Impact	Importance Average ranking score
Increase development time	2
Increase costs of development	3
Other (Specify: Bureaucratic regulatory framework)	4
Divert management time	5
Re-direct resources into defensive R&D	5
Reduce cash flows from existing products	6
Reduce access to new ideas, particularly in biotechnology	7
Create significant uncertainty or unpredictability	7
Restrict collaborative R&D ventures	7
Close markets for specific products	8
Limit the use of innovative marketing methods	8

5. Expenditure on mandatory defensive R&D

Which of the following statements best indicates how your expenditure on mandatory defensive R&D in India has changed since 2015?

The workshop participants reported that their mandatory defensive R&D (MD-R&D) expenditure had changed a little since 2015 (Figure 3), primarily because of changes in the regulation outlines for both existing and new products.

Figure 3: Companies' perception of the burden of mandatory defensive R&D spending since 2015



Respondents were asked to report the percentage of their local R&D budget that was spent on MD-R&D. Across all 11 markets included in the GBS2020 survey the level of MD-R&D spend ranged from 14%-41% of the local R&D budget, with an average global MD-R&D of 27.7% (which is consistent with previous surveys). India had one of the highest rates, at 40% of the local R&D budget.

6. Factors causing the change in expenditure on mandatory defensive R&D

Table 5: Factors causing a change in expenditure on mandatory defensive R&D

Factors causing a decrease in expenditure on mandatory defensive R&D
The group in general felt that newer initiatives such as specific guidelines for veterinary biologicals and those in discussion guidelines for veterinary pharmaceuticals will assist the Indian animal healthcare industry in standardizing the requirements and will improve predictability.
Factors causing an increase in expenditure on mandatory defensive R&D
The participants believed that the recent changes in regulations and upward revision of fee structures haves led to the increased timelines and factors are as follows: • The ten-fold increase in treasury/ registration fees for product registrations and import renewals has impacted the change. • The Zone IVB stability studies requirement has increased the timelines of developing the products and for renewal of licenses. • For imported biologicals, the condition of three batch testing at IVRI has impacted the timelines of registration and import of products. Frequently in case of biologicals there are series of communications and discussions on viral strains and its correlation with Indian field strains. This increases timeline of approval.

7. TIME to gain registration for a major new product in India

Please state the AVERAGE LENGTH OF TIME it takes you to gain registration for a major new product in India, from submission of the marketing authorization dossier to first-market product approval. Please make separate estimates for major livestock species, companion animals and minor species and for the product types of pharmaceuticals and biologicals.

The participants overall expressed the view that the average length of time for registration of products has increased in the last three years. The group also agreed that therapeutics and biologicals for minor species is not an area of focus because of the extremely small size of the market. Major food animals and major companion animals remain the prime focus areas of product development and registration.

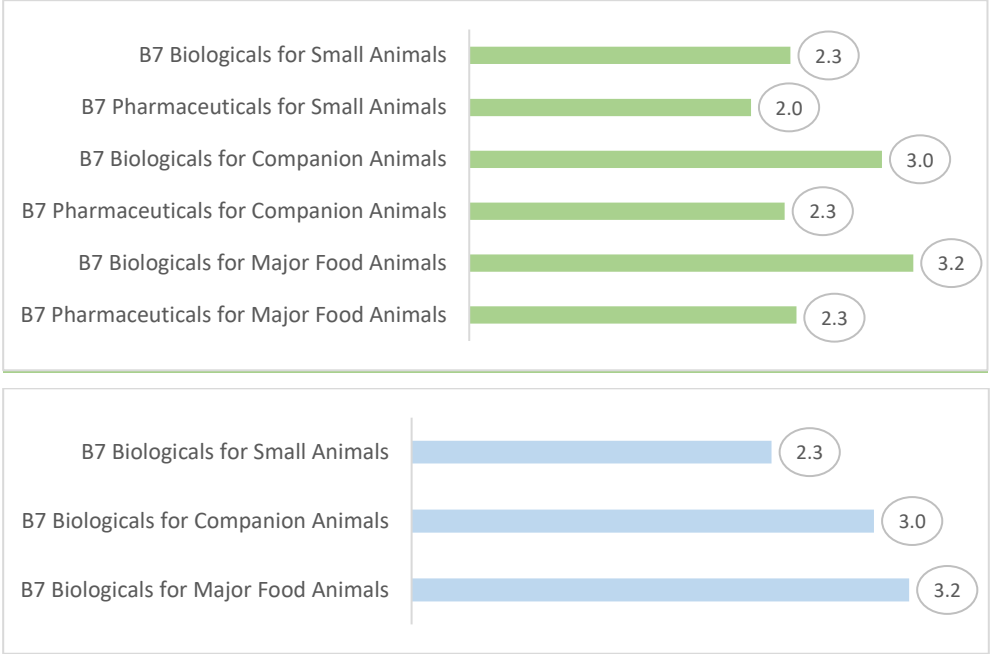
For pharmaceuticals, until 2015 the typical registration timelines were 2.5 years. These timelines have increased by 20 percent in the last three years and is currently averaging at 3 years for food animals and 2.5 years for companion animals. These increases are primarily because of validation of the active and finished products, growing concerns of residues and AMR (for food-producing animals), as well as the multi departmental review process.

For biologicals, the average timelines for food and companion animals product registration was 3.0 years and 2.5 years for the Indian market until 2015. During the last three years, the group felt that the timelines have increased to 3.5 years and 3 years respectively. This is because of increased validation of the process and pre-approval testing of biologicals.

Table 6: Time to gain registration for a major new product in India

Target species category	Product category	Average time (years)	N
Major Food Animals	Pharmaceuticals	2.3	12
	Biologicals	3.2	15
Companion Animals	Pharmaceuticals	2.3	10
	Biologicals	3.0	12
Minor species	Pharmaceuticals	2.0	12
	Biologicals	2.3	10

Figure 4: Time (years) to gain registration for a major new product in India



8. Impact of Regulations on TIME to develop a major new product

Have regulatory factors caused a change in the average length of time it takes you to develop a major new pharmaceutical product (from initial research to final market authorization), compared to 2015? Please make separate estimates for major livestock, companion animals and minor species.

Have regulatory factors caused a change in the average length of time it takes you to develop a major new biological product (from initial research to final market authorization), compared to 2015? Please make separate estimates for major livestock species, companion animals and minor species.

The majority of the participants perceive that overall there is increase (≥ 1 year) in the average length of time it takes to develop and commercialise (market authorization) a new pharmaceutical product in India. This increase is across all segments.

Most respondents agreed that there is an increase in average length of time of 6 months to 1.0 year due to regulatory factors. However, some participants also felt that the increase is more significant, up to 1.5 to 2.0 years.

The participants agreed that the delays are mainly due to the multistage and multi-department evaluation process, which is often not well synchronized, makes the process and response cycle a little complicated and delayed, and a process of simultaneous evaluation is not in place.

There are typically three sequential stages and each has its own lead time. First is technical evaluation by subject expert committee (DAHD), followed by CMC data evaluation (CDSCO) and finally testing of three consecutive batches (commercial size) at the National laboratory (IVRI/IPC).

However, in recent times the authorities are working to formalize the process and bring more transparency and clarity, and it is expected that these delays might be minimized.

Biologicals are primarily impacted as the regulations are guided by government policies related to infectious disease prevention and control. Many times, there is less clarity / data in this regard for newer biologicals.

Table 7: Impact of Regulations on TIME to develop a major new product since 2015

Product category	Target species category	Little change (average years)	Increase (average years)	N
Biologicals	Minor Species	n.a	1.0	5
	Companion Animals	0.9	1.0	8
	Major Food Animals	0.9	0.9	8
Pharmaceuticals	Minor Species	n.a	1.0	5
	Companion Animals	0.6	1.0	6
	Major Food Animals	0.4	1.0	13

9. COST of developing a major new PHARMACEUTICAL product

Thinking about the AVERAGE COST of developing a major new PHARMACEUTICAL product in IN (from initial research to approval) for all possible species and indications for that product, compared to 2015 have REGULATORY FACTORS caused this cost to change in real terms? Make separate estimates for major livestock species, companion animals, and minor species.

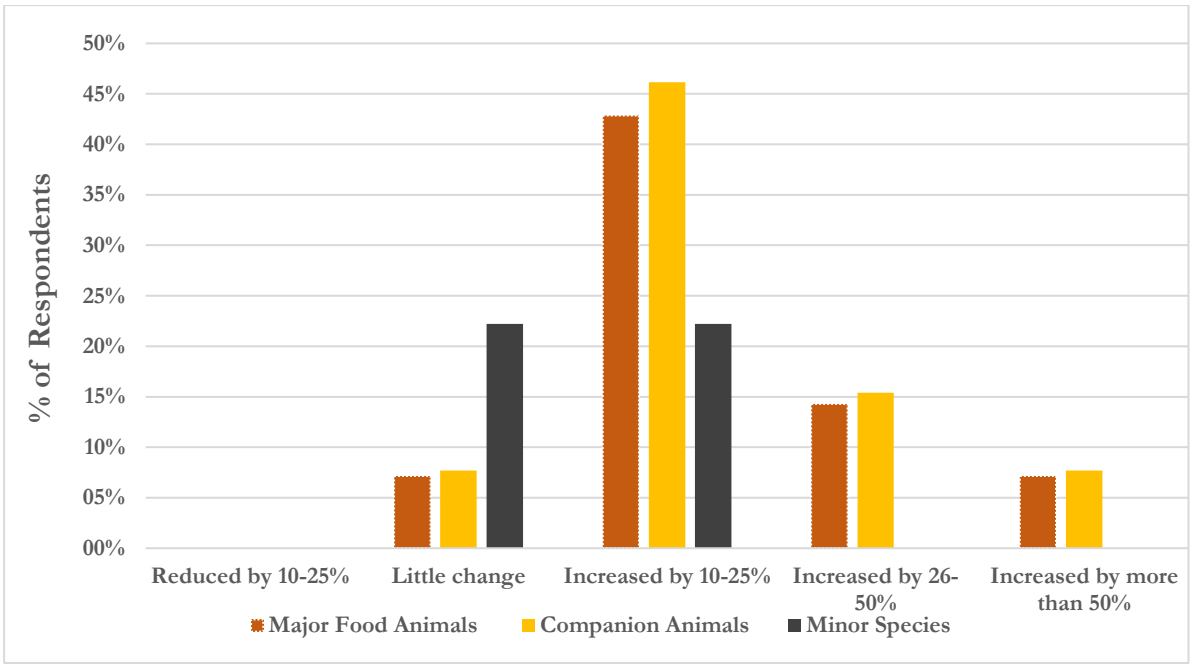
The majority agreed that there is increase in the cost of pharmaceutical product development (from initial research to approval). The majority felt that there is increase in research costs of 10-25% due to new regulatory factors after 2015, mainly due to increasing compliances and regular inflation.

On the other hand, there is also an increase in regulatory fees. This increase is several fold for import registration and moderate for approval for local manufacturing.

However, some participants feel that this increase is 26-50% and the perception is mostly linked to increased registration fee for import approval as all import sites and product registration cost have increased by tenfold.

No companies reported a decrease in costs for any of the product categories.

Figure 5: Perceived change in cost to develop new PHARMACEUTICAL product



10. COST of developing a major new BIOLOGICAL product

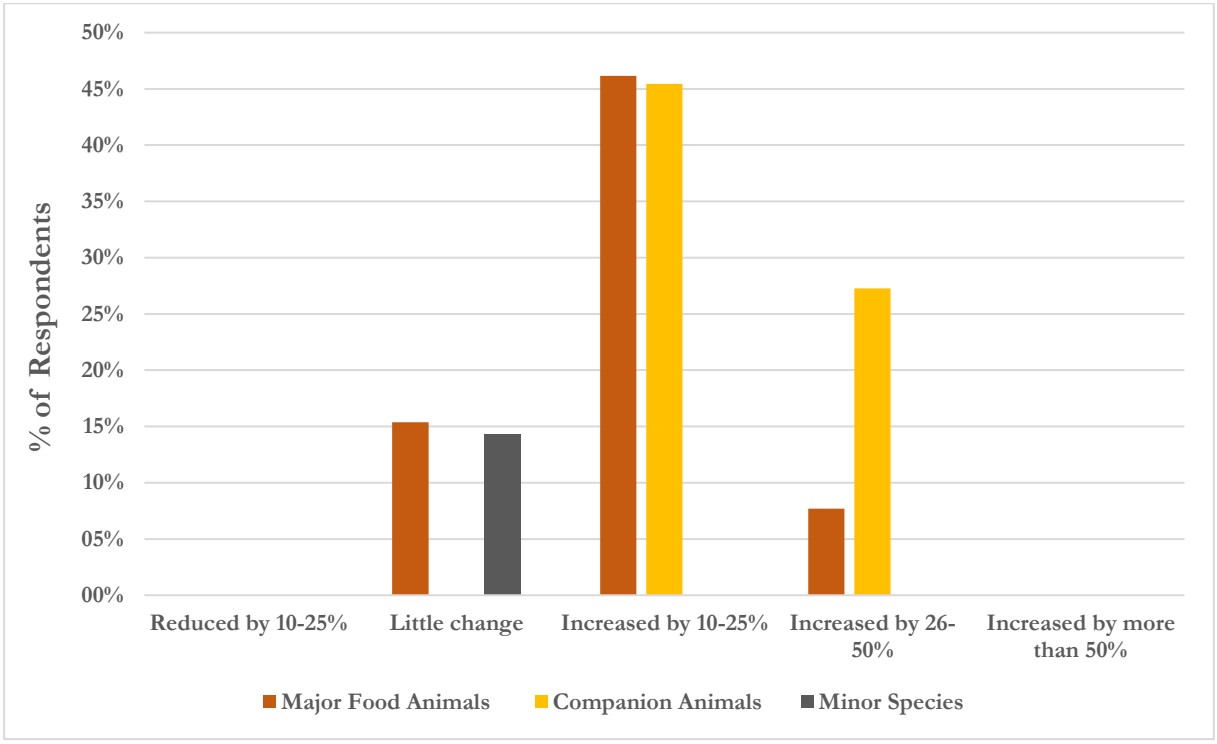
Thinking about the AVERAGE COST of developing a major new BIOLOGICAL product in IN (from initial research to final market authorization) for all possible species and indications for that product, compared to 2015, have REGULATORY FACTORS caused this cost to change in real terms? Make separate estimates for major livestock species, companion animals, and minor species.

Overall there is agreement that there is increase in cost of development new biological products, which is primarily due to new compliance requirements for testing of biologicals and secondarily due to increase in registration fees, which is very significant for import registration.

The majority believed that there is an increase of 10-25% in the cost of development due to new regulatory factors after 2015. However, some participants felt that this increase is 26-50% and here the perception is mostly linked to increased registration fees for manufacturing sites and import product approval.

No companies reported a decrease in costs for any of the product categories.

Figure 6: Perceived change in cost to develop new BIOLOGICAL product



11. COST of developing a major new PESTICIDAL product

Thinking about the AVERAGE COST of developing a major new PESTICIDE product in IN (from initial research to final market authorization) for all possible species and indications for that product, compared to 2015, have REGULATORY FACTORS caused this cost to change in real terms? Make separate estimates for major livestock species, companion animals, and minor species.

Pesticidal products are approved by CIBRC. The animal healthcare industry has been primarily having a few topicals approved as topical anti-tick formulations. No significant products have been introduced in this sector.

12. Incentives from Indian Authorities driving innovation due to data protection

Considering the length of data protection (market exclusivity) given by the Patent Law and Innovative Drug Registry in India, to what extent do you consider it to be an incentive?

Most of the participants felt that the current length of data protection / market exclusivity provided by the law and drug registration system in India is helpful and can be considered as an incentive for the business.

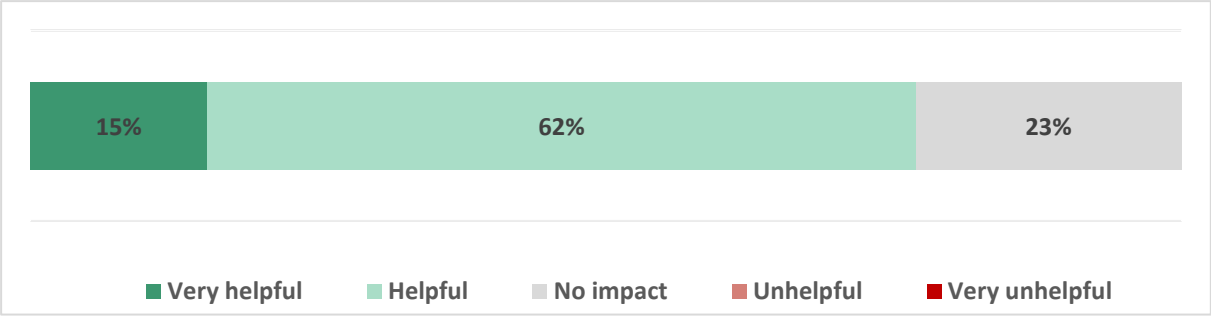
- 77% participants feel that it is very helpful / helpful.
- 23% participants do not see any positive or negative impact and remain neutral.

All participants agreed that the patent law in India is quite robust and helpful in the provision of market exclusivity for enough length of time for innovative developments. No alternative to patented product can be launched unless the patent expires.

Participants also felt that the new drug registration (first time in India) is also protected, with the submitted data package protected for 4 years. Any second market entrant can be introduced after registration with CDSCO with compliance to the entire drug regulatory processes. However, no new generic can be launched with authorization from regional / state Drug authorities before 4 years.

However, some participants felt that this protection is not sufficiently robust.

Figure 7: Helpfulness of data protection (market exclusivity) given by the Patent Law and innovative Drug Registry



Section C - COMMERCIALISATION OF EXISTING PRODUCT

1. Factors relevant to the commercialisation of existing products

Below is a list of potential factors relevant to the exploitation of existing products in the animal health industry in IN. Which of these, if any, are significant for the exploitation of your existing products? (Please rank from 1 for 'most important' to 12 for 'least important)'.

The workshop group felt that there are 3 factors that can be considered significant for the exploitation of existing products. One of the most important factors is the regulatory framework for maintenance/extension of licences. This is more relevant for products that have import registration. This is mainly due to the significant increase in fees for renewal and maintenance works (variations) of the licence. This issue is further amplified by the short three years period of the renewal requirements. It limits the exploitation of existing products.

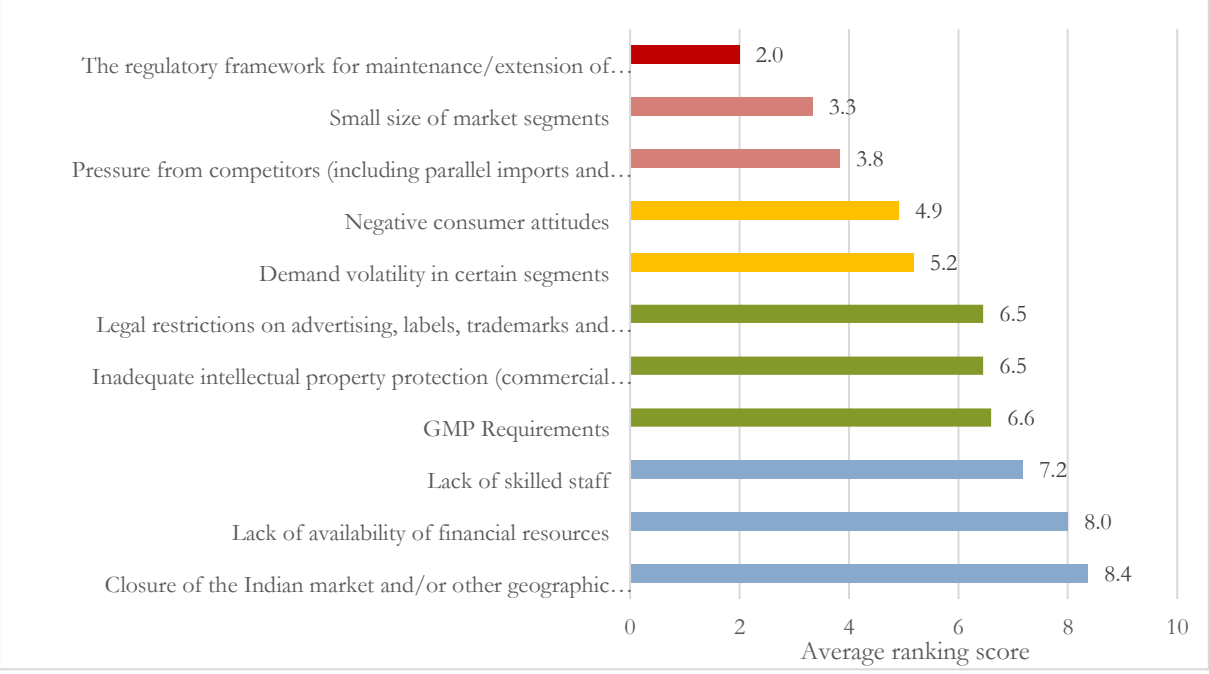
The other two top factors are mall size of market segments (the market for veterinary medicines is highly fragmented), and pressure from competitors (including parallel imports and generics)

Other relevant factors are GMP compliance leading to increased manufacturing cost and smaller size of some market segments. Demand volatility (season, government policy…etc.) is also an important factor limiting the exploitation existing product. Some members also feel that inadequate intellectual property protection (commercial data and patents) and negative consumer attitudes also to some extent relevant for the exploitation of existing data.

Table 8: Ranking most important factors relevant to the exploitation of existing products

List of potential factors	Average ranking
1. Regulatory Framework for maintenance/extension of licenses	2.0
2. Small size of market segments; the market for veterinary medicines is highly fragmented	3.2
3. Pressure from competitors (including parallel imports and generics)	3.8

Figure 8: Ranking of all factors relevant to the exploitation of existing products (low score = most important)



2. Impact of regulation on ability to commercialise existing products

Do government REGULATIONS in India have any of the following effects on your business?

In the view of the participants, government regulations in India creating disproportionate costs for maintaining/extending marketing authorization is considered as the top ranked issue. It has been rated high because of the implementation of regulatory fee hike during the year 2019, which was an exorbitant rise owing to lower business volume of many segments of animal healthcare.

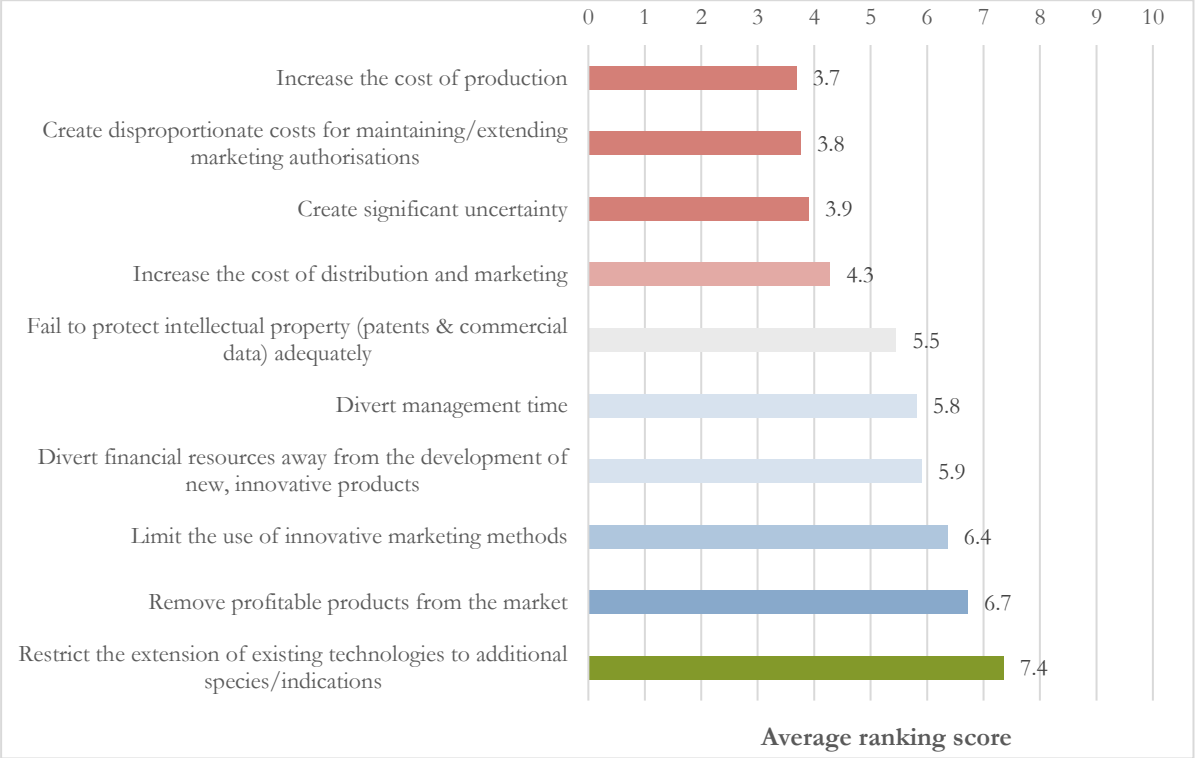
For example, the registration fee or renewal of registration fee for manufacturing site located outside India has been increased from 1500 USD to 10000 USD; the registration fee of each product has been increased from 1000 USD to 5000 USD. The said fee is applicable to both human and veterinary formulations. Some marketers find it unjustifiable to maintain the market authorization (MA) for products of niche segments or for a product where the market is not fully developed (e.g. products for companion animals or small ruminants or others).

An increased cost of production and diverting financial resources away from the development of new, innovative products are also ranked in the top three impacting existing products.

The response of participants on 'Divert financial resources away from the development of new, innovative products' is given importance due to the lower return on investment owing to smaller market size as compared to human pharmaceuticals.

Increased cost of distribution and marketing has been ranked as the fourth important issue.

Figure 9: Impact of regulation on ability to commercialise existing products (low score = most important)



3. Impact of regulation on ability to commercialise existing products

Thinking about Regulations in India, how would you assess the impact of each of the areas of regulation listed below on your ABILITY TO COMMERCIALISE EXISTING PRODUCTS successfully?

The survey participants were presented with 13 areas of regulation to rank in order of impact on a company's ability to successfully commercialise existing products. The top 5 most helpful and most unhelpful areas of regulation are summarised in the Table below and are shown ranked from most to least helpful in Figure 10.

It is noticeable that many of the areas of regulation received a mixed response, with some respondents regarding them as helpful, while other respondents regarded them as unhelpful. This may be based on personal experience, or may be due to experiences with different types of product (e.g. imported versus locally manufactured).

Table 9: The top 5 most helpful and most unhelpful areas of regulation for commercialising existing products

Rankings for most helpful	Rankings for most unhelpful:
Good Manufacturing Practice	Trade and Customs requirements and rules
Animal Drug User Fee rules (ADUFA)	Packaging/Labelling Changes
Environmental safety regulations	Disease resistance regulations (e.g. Antimicrobials)
Protection of Intellectual Property – patents	License Maintenance
Pharmacovigilance	Manufacturing Changes Rules

Three areas of regulation did not attract any "unhelpful" scores: Good Manufacturing Practice, Animal Drug User Fee rules (ADUFA) and pharmacovigilance.

Good manufacturing practice rules receive a positive response as they are seen as good business practice by providing assurance of the quality of a company's products and is a standard that is generally accepted worldwide, giving a good balance between inputs and outcomes.

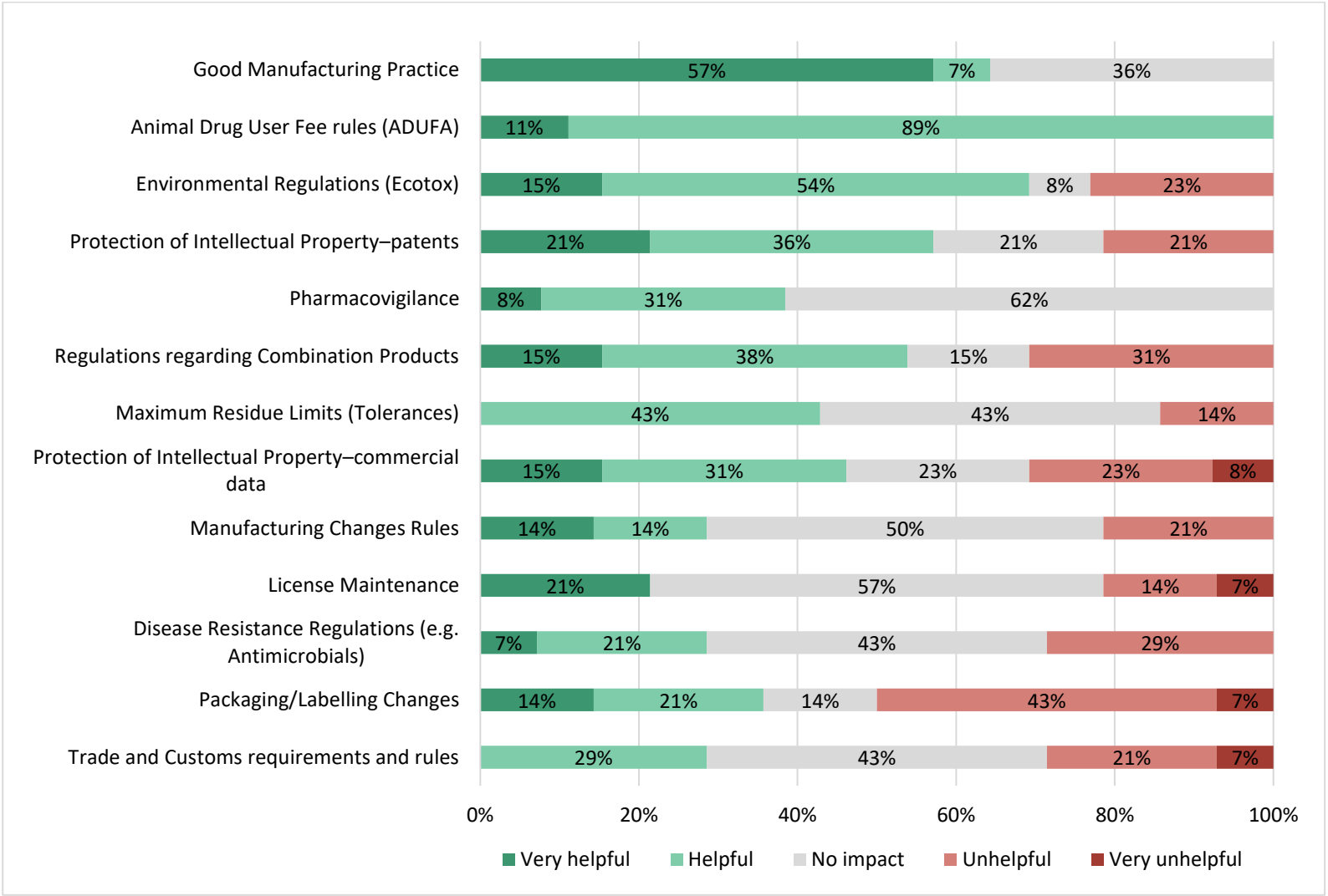
License maintenance is a good example of an area of regulation that received a mixed response, with an equal number of people regarding is a very helpful or unhelpful, and a majority regarding it as having no impact. However after discussion in the workshop 50% respondents expressed in favour of very helpful and helpful while those considering it of no impact for the existing product dropped to 25%, with the remaining continued to regard it as unhelpful.

After deliberation it was clarified that maintenance cost of imported product is high whereas for domestic manufacturer maintenance cost it is low. The regulatory fee hike has mostly impacted imported products, while impact on domestic manufacturing is minimal.

Maximum Residue Limits (Tolerances) was seen as helpful or no impact by the large majority. Food Safety Standards Association of India (FSSAI) has established a list of veterinary drugs and their MRLs and made it mandatory to comply a withdrawal period accordingly.

For Packaging / Labelling Changes the majority of the responses were 'unhelpful'. In the recent past, there has been some amendments in the labelling rules, such as more prominence to the generic name than the trade name or highlight of drugs (Schedule H/H1) which can be sold only through prescription. However, there are a few positive responses mentioning useful information for the customers.

Figure 10: Impact of regulations on ability to commercialise existing products



Section D - REGULATORY PREDICTABILITY & QUALITY

1. Predictability of regulatory procedures

Does the Indian regulatory agency as currently managed provide you with the regulatory predictability that you need and the regulatory quality you expect?

What are the top issues and what might be done about them?

Three regulatory authorities are considered:

1. Central Drug Standard Control Organization (CDSCO), MOHFW: The prime authority that regulates drugs & biological (both human & Veterinary)

2. Dept. of Animal Husbandry & Dairying (DAHD), MOFAHD: Evaluates the technicality and suitability of animal health products for Indian condition and accordingly issues NOC for further evaluation at CDSCO.

3. Genetic Engineering Appraisal Committee (GEAC), MOEF & CC: Examines the biotech and genetically engineered products for their effect on the environment or non-target species.

The regulatory predictability for the three regulatory authorities has been recorded as 'mostly to always' predictable. A few respondents also mentioned predictability as 'sometimes'.

Figure 11: Regulatory predictability under CDSCO, Department of Animal Husbandry and Dairying & CIBRC

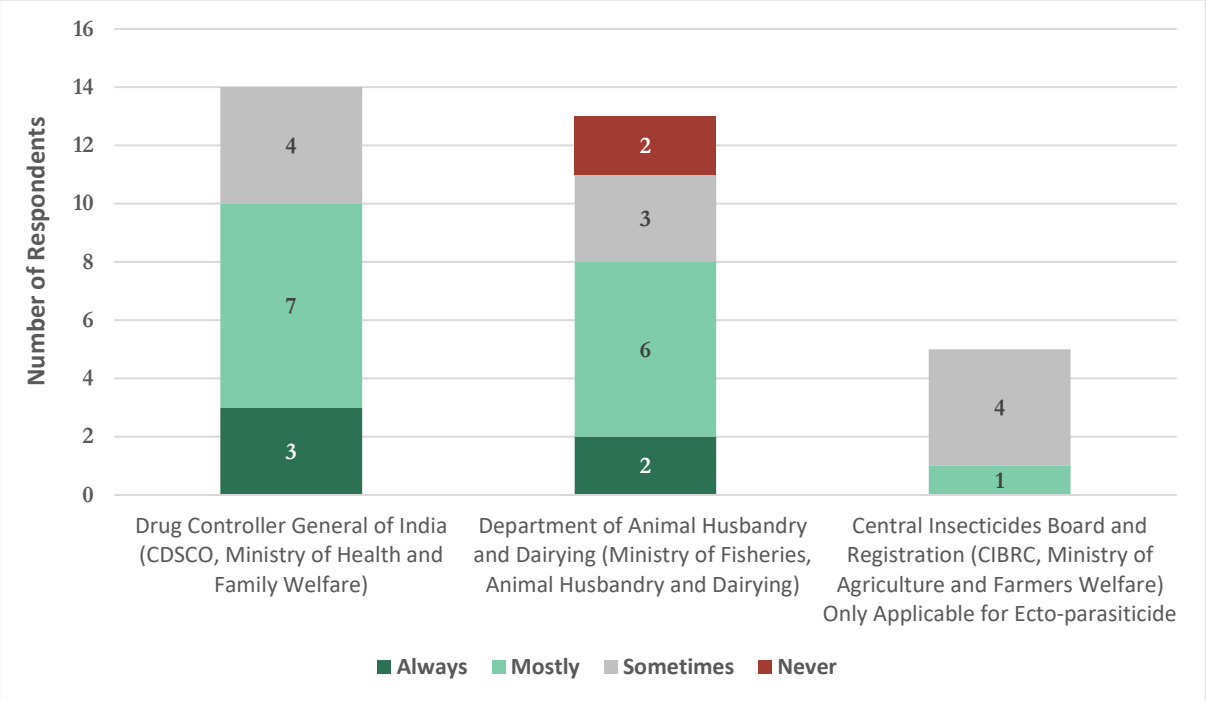
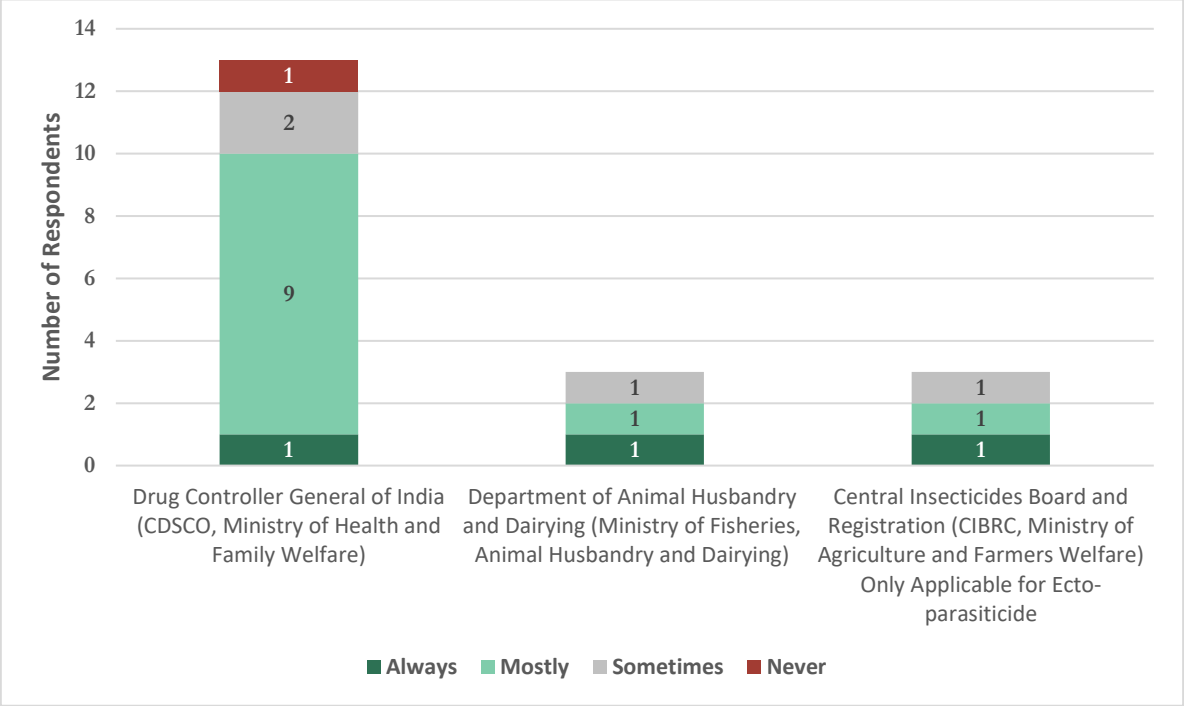


Figure 12: Regulatory quality under CDSCO, Department of Animal Husbandry and Dairying & CIBRC



Participants discussed the issues faced by them including the regulatory fee hike, validity period of the marketing authorization, longer time duration of approval, frequent testing of biological products etc.

It was felt that there is need for improvement in a few regulatory processes to harmonize with the global regulatory norms. For example, the validity of registration and import license need to be increased to five years from the existing norms of three years.

The regulatory fee for registration and imports of veterinary pharmaceuticals and biologicals should be abridged owing to the lower market size of the animal health sector and the reduced opportunity to obtain a return-on-investment.

The batch safety testing of veterinary biologicals needs to be harmonized as per the global standards (e.g. the VICH guidelines for target animal batch safety testing (TABST)) to reduced unnecessary costs and align to animal welfare norms ('3Rs).

A single technical committee should be created with more technical experts to regulate the veterinary products with involvement of DAHD and IVRI experts.

Transparency would be improved with the publication of approved veterinary medicinal products and biological strains.

2. CDSCO procedures for new product registration

Consider the current CDSCO procedures for registering new products. To what extent does the process meet the following criteria?

Part A Scientific basis:

After discussion in the workshop, the responses are recorded as 'mostly' on the question of whether the scientific basis for evaluation of new products has been uniform as per the norms and guidelines.

Part B Process:

Participants discussed the regulatory process and found that there has been improvement in terms of transparency and predictability. However, it is also noted that the approval process takes longer time especially for new product approval due to involvement of multiple regulatory agencies (DAHD & CDSCO). The responses are noted as mostly, however few respondents felt as 'sometimes'.

Figure 13: Scientific basis (Part A)

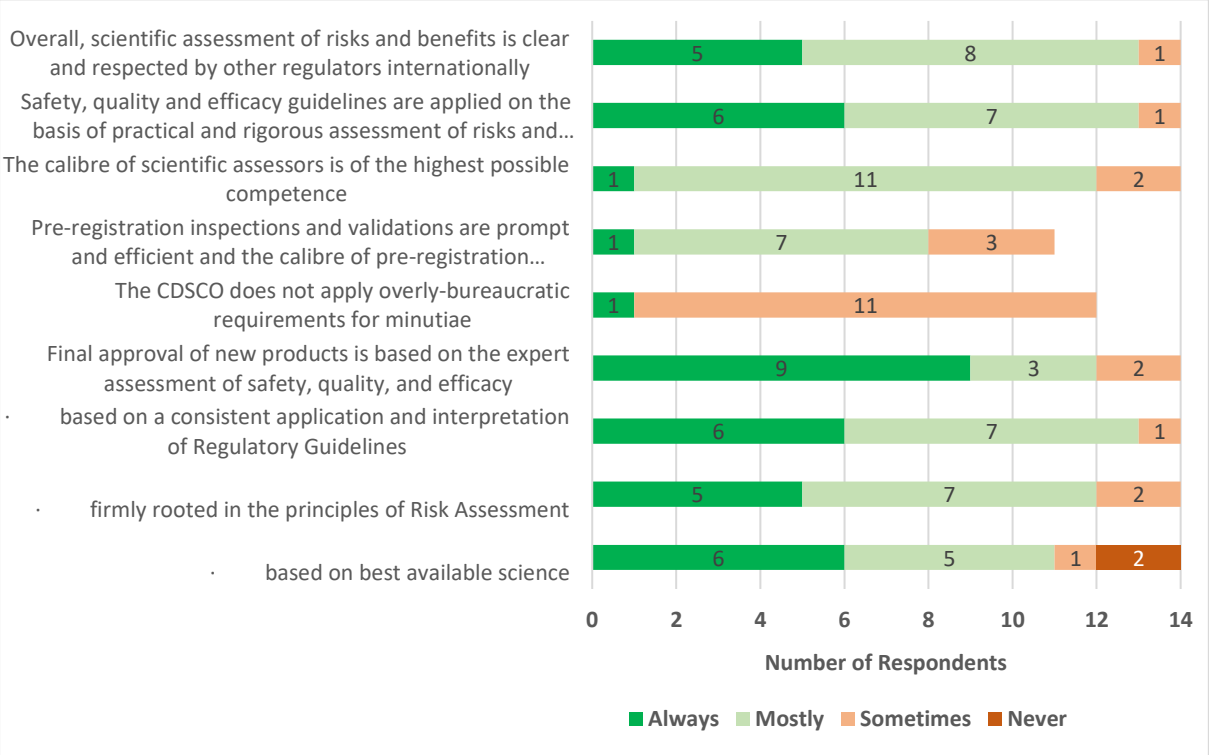
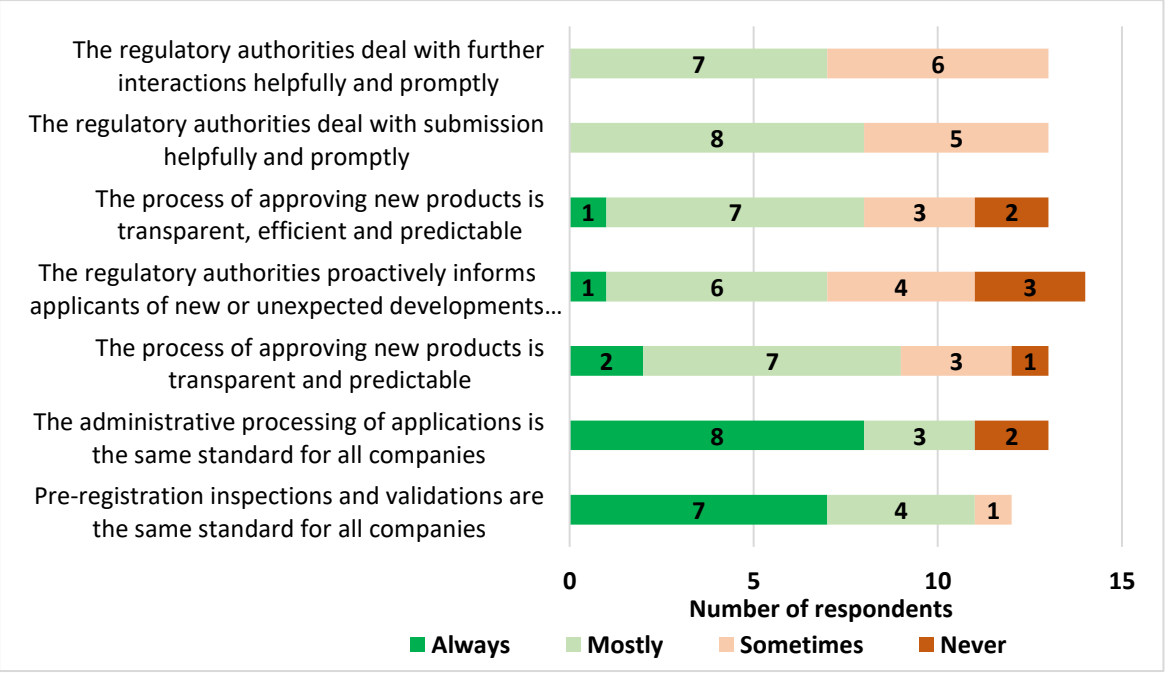


Figure 14: Process basis (Part B)



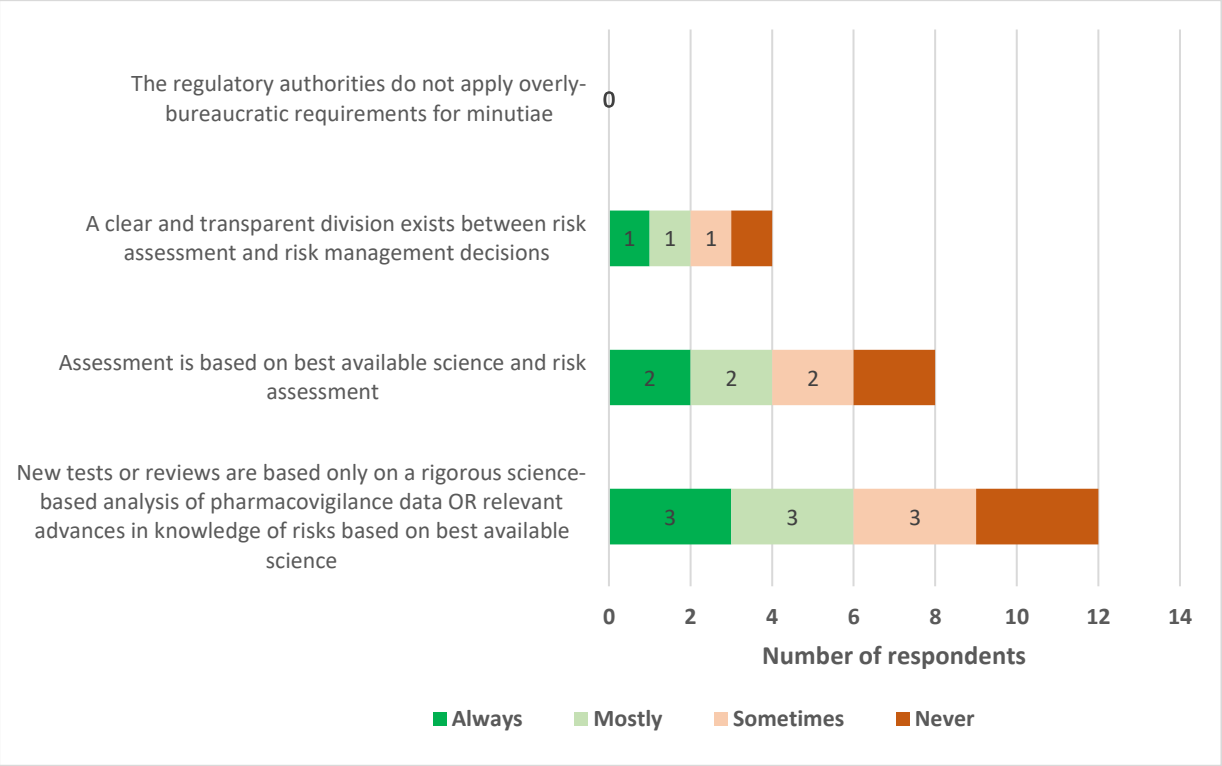
3. Current procedures for maintaining existing portfolio

Consider the current process for maintaining existing products on the market. To what extent does the process meet the following criteria?

Participants felt that maintenance of existing products for domestic manufacturer is appropriate and supportive to the industry, but for imported products, the regulation is more restrictive with a high registration fee.

The responses on the reviews of applications, scientific data assessment as well as risk-based analysis are recorded as 'Sometimes to Mostly' in meeting the specified criteria (Figure 15).

Figure 15: the extent to which the regulatory process for maintaining existing products meet the following criteria



Section E - REGULATORY TRENDS

1. Recent beneficial changes to Indian regulatory frameworks

What beneficial changes have occurred in regulatory frameworks SINCE 2015?

- Creation of a Veterinary Cell at CDSCO is the most important step taken
- Online submission through Sugum has improved the transparency and predictability of regulatory process
- Specific guidelines for veterinary biologicals have benefitted the industry
- H AND H_1 Schedule Classification
- Withdrawal period implementation.

2. Expected changes that have NOT occurred in Indian regulatory frameworks

What expected changes have NOT occurred in regulatory frameworks SINCE 2015 despite expectations of change?

- In India, the regulation of veterinary drugs and biologicals is same as that of human medicines.
- The authorities have initiated the process for separate regulatory guidelines for veterinary drugs and biologicals, but its impact on the animal health industry is still awaited.
- Representations from the industry were made for increasing the validity of registration and import licenses to five years. Currently these are valid for three years only.
- No decision has been taken till now following industry representation for reduction / abridged registration fee considering the small size of the animal health market and lower opportunities to obtain a return-on-investment on animal health products.

3. Recent changes to Indian regulatory frameworks causing the most problems

What regulatory changes SINCE 2015 have given you the most problems and why?

Key points from the discussion:

- Pre-registration testing of imported product samples at IVRI / IPC has been made mandatory for new products and is increasing timelines for the introduction of product onto the market
- Ten-fold increase of registration and renewal charges
- At times un-certainty due to involvement of multiple authorities in the approval process (CDSCO, DAHD, IVRI).

4. Impact of Indian regulatory frameworks on major business decisions

Have regulations played a major role in influencing you to take any of the following major decisions over the last five years?

Respondents were asked to consider a list of 20 potential major business decisions, and whether regulations played a major role in influencing these over the last five years. The options were often in pairs, looking at both the upside and the downside of a business decision. Many of these decisions have other multiple factors other than regulations, including other regulations related to business operations. The outcome is shown in Figure 16. For many (14/20) of the business decisions the majority of participants have not done such activity.

The most common activities (done by most of the participants) were to:

- Focus on existing/older technologies in India (done by 69% of the participants)
- Focus on new technologies in India (done by 64% of the participants)
- Restrict (geographic) market focus in India (done by 58% of the participants)
- Locate R&D Facilities inside India (done by 57% of the participants)

In these decisions regulations played a mixed role, ranging from no influence to significant influence.

The least common activities (not done by most of the participants) were to:

- Locate R&D Facilities outside India (not done by 92% of the participants)
- Increase (geographic) market focus in India (not done by 86% of the participants)
- Introduce more 'breakthrough' products in India (not done by 86% of the participants)
- Switch R&D budgets to labs inside India (not done by 86% of the participants)
- Sell or close businesses in India (not done by 85% of the participants)
- Increase product range in India (not done by 85% of the participants)

The top 4 decisions taken where regulations played a significant role were:

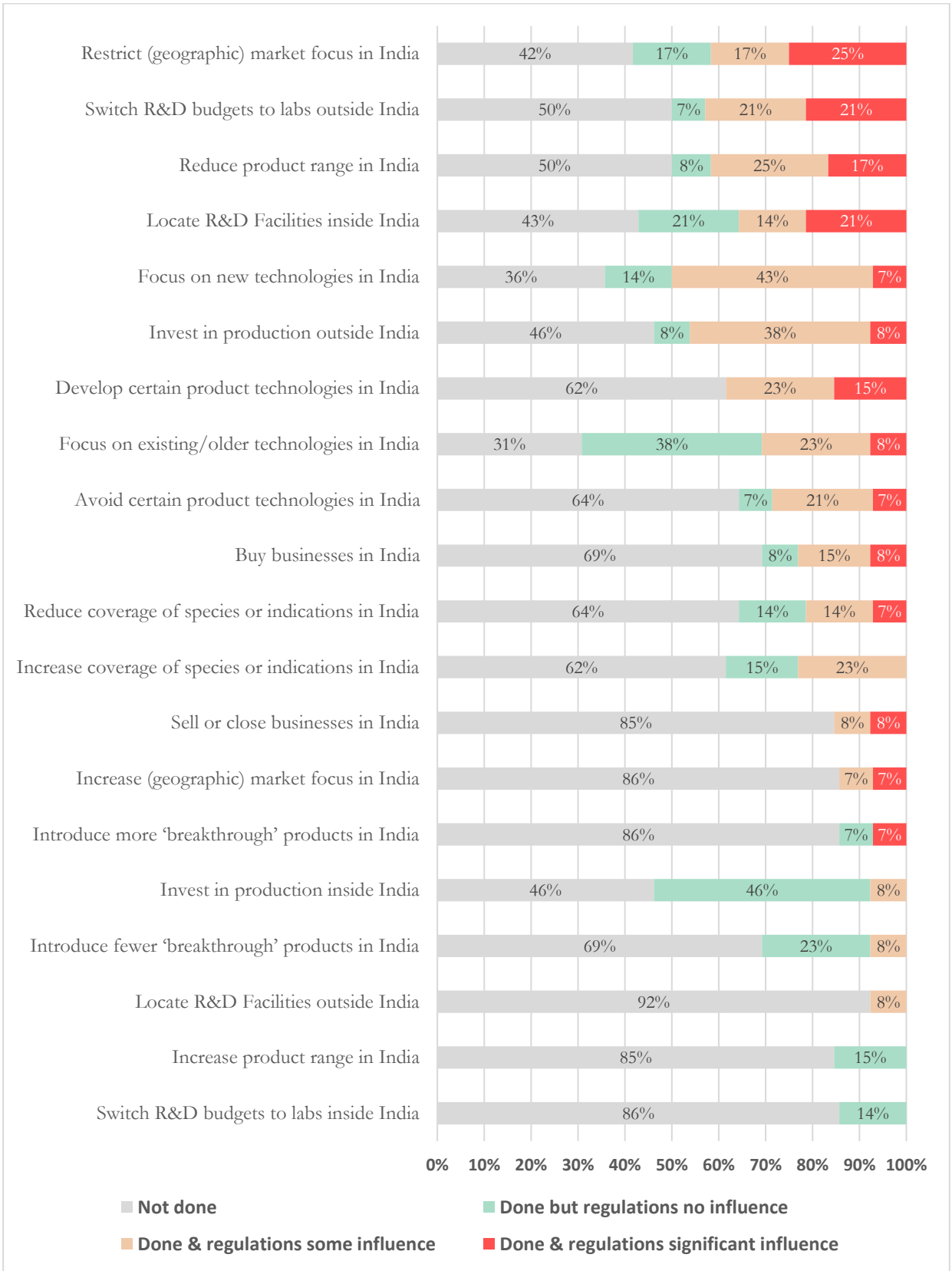
1. Restrict (geographic) market focus in India (significant role in 25% of decisions)
2. Switch R&D budgets to labs outside India (significant role in 21% of decisions)
3. Locate R&D Facilities inside India (significant role in 21% of decisions)
4. Reduce product range in India (significant role in 17% of decisions)

Regulations sometimes played a role in the following decisions:

- Focus on new technologies in India (50% said some or significant influence)
- Invest in production outside India (46% said some or significant influence)
- Develop certain product technologies in India (38% said some or significant influence)
- Avoid certain product technologies in India (29% said some or significant influence)

Invest in production inside India was the most common activity done where regulations played no role. Focus on existing/older technologies in India was the most common activity done where regulations played a mixed role, but with the majority reporting regulations played no role.

Figure 16: Major decisions taken in the last 5 years as influenced by regulations



Section F - HOPES AND EXPECTATIONS FOR THE NEXT 5 YEARS

1. Expected impacts of recent trends or changes in Indian regulatory approach

The following trends or changes in regulatory approach have been taking place recently and may well have an impact in future. What impacts do you expect these to have on your business in the next 5 years?

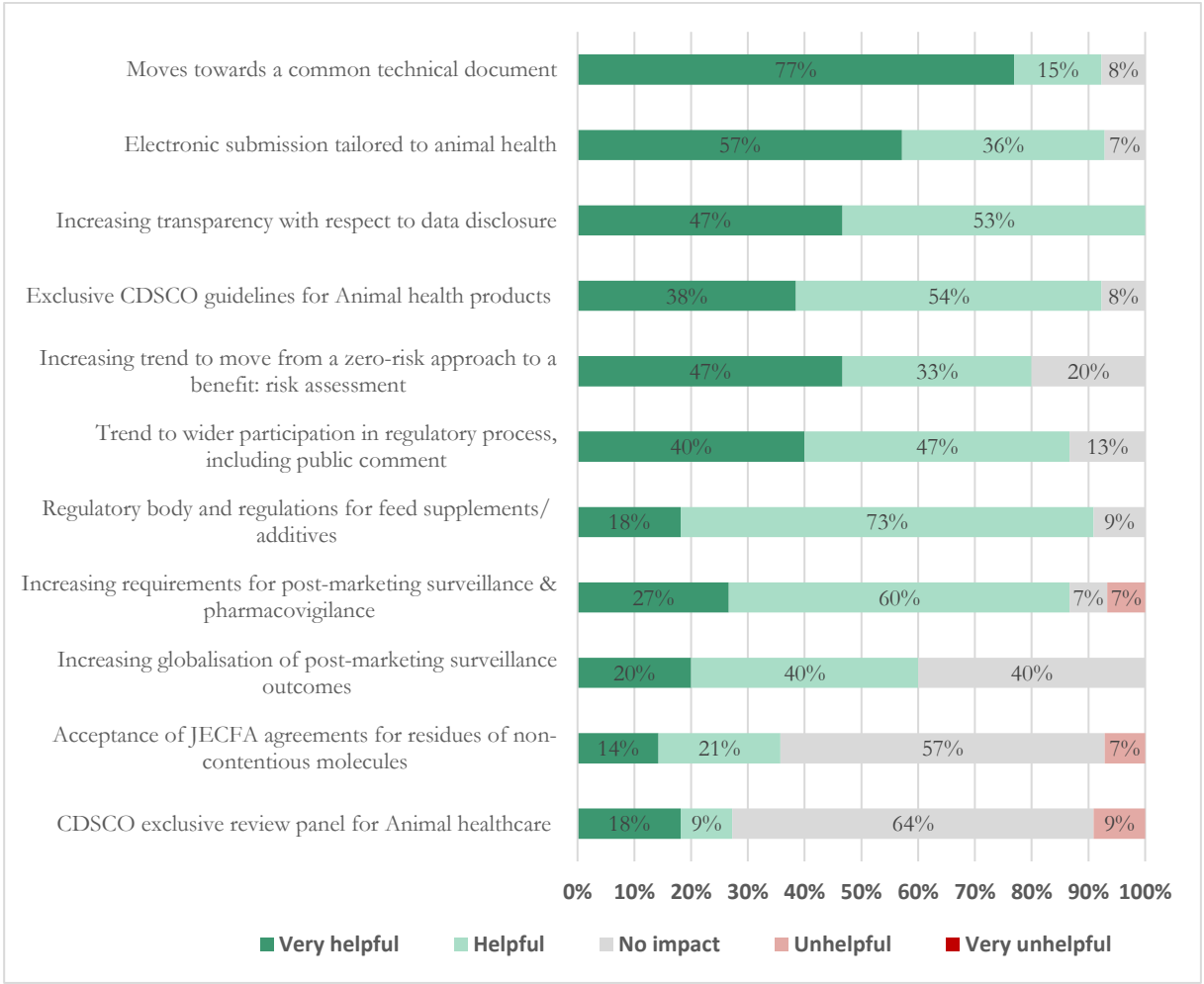
The top 5 most helpful and most unhelpful trends are summarised in the Table below and the responses to all the options are shown in Figure 17 ranked from most helpful to least helpful.

Perhaps the most significant outcome from this question is that there was no major dissention towards recent trends or changes in the Indian regulatory approach, with only isolated responses in the "unhelpful" bracket.

Table 10: Top 5 Helpful Trends in Indian regulatory approach

Top 5 Helpful Trends:
1. Moves towards a common technical document
2. Electronic submission tailored to animal health
3. Increasing transparency with respect to data disclosure
4. Exclusive CDSCO guidelines for animal health products
5. Increasing trend to move from a zero-risk approach to a benefit

Figure 17: Impacts of regulatory trends

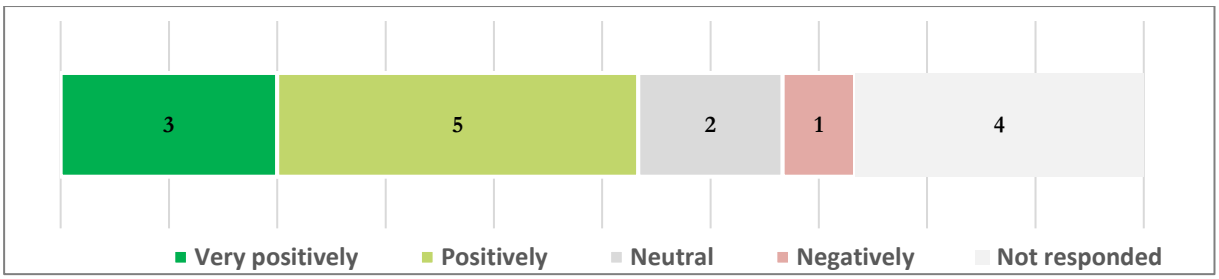


2. Foreign regulatory decisions impact on innovation

Does the use of foreign regulatory decisions in the Indian review process impact your ability to innovate?

Majority of participants believe that the use of foreign regulatory decisions in the Indian review process is positively impacting the ability to innovate.

Figure 18: Impacts of foreign regulatory decisions on innovation



3. Expected impacts of the NEW VETERINARY PRODUCT REGULATIONS

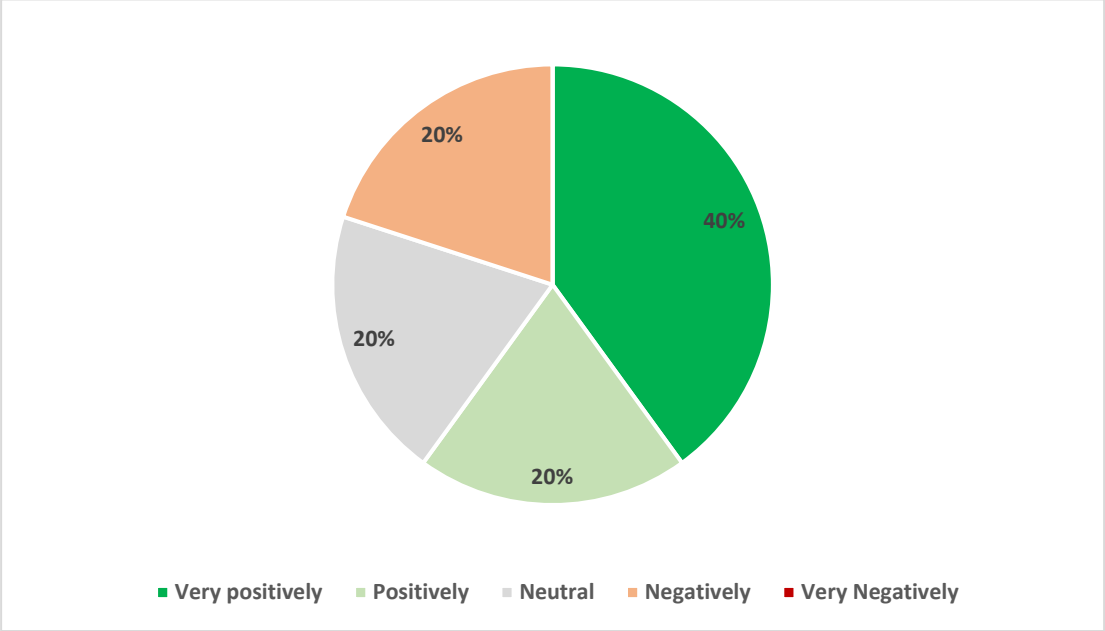
What impacts do you expect the new veterinary product regulations to have on your business and why?

Majority of participants feel that new veterinary product regulations there have a positive impact on business.

The reasons for the positive impact were:

- Focused approach towards veterinary drugs
- Veterinary specific guidelines (guidelines for biologicals have been finalized, while guidelines for pharmaceuticals are under development)
- Better and smoother co-ordination

Figure 19: Impacts of new veterinary product regulations



4. Changes still wanted in Indian regulatory approach

What changes do you still want to see and why?

- The registration validity of imported products should be equal to the validity of locally manufactured products, i.e. five years with renewal based on company declaration and payment of the registration fee
- Duplication of check list documents for market authorization and registration applications should be avoided
- More specific guidelines and check list for submissions of veterinary drugs
- India should have harmonization of requirements with global authorities and minimize registration timelines (e.g. VICH guidelines)
- The entire regulatory process should be predictable with continuous engagement of the Authority and applicant to clarify scientific issues with open dialogue.
- There needs to be a system for tracking the approval process as single window system with defined timelines
- Better coordination between CDSCO and DAHD with time bound response system
- Reduction of registration fee
- Published timelines for the assessment of marketing authorisation applications for veterinary drugs and biologicals
- One to one meeting with the stakeholders (CDSCO)
- Frequency of technical meetings at GEAC should be increased
- A specific Veterinary Experts panel for evaluation and NOC for veterinary product approvals.

Acknowledgements

A great deal of thanks and appreciation is offered to all the company personnel who had to find the time within their busy schedules to complete the questionnaire for the GBS2020 survey. A hearty thanks is also due to the dedicated staff within the Indian Federation of Animal Health Companies (INFAH) and HealthforAnimals national industry associations around the world, for the enormous effort in driving this project in their regions and delivering the data and analysis on time.

Glossary of abbreviations

ADUFA	Animal Drug User Fee rules
CDSCO	Central Drug Standard Control Organisation
CIBR	Central Insecticides Board and Registration
DAHD	Department of Animal Husbandry and Dairying
FSSAI	Food Safety Standards Association of India
GEAC	Genetic Engineering Appraisal Committee
IPC	Indian Pharmacopeia Commission
IVRI	Indian Veterinary Research Institute
MOEF & CC	Ministry of Environment, Forest and Climatic Change
MOFAHD	Ministry of Fisheries, Animal Husbandry and Dairying
MOHFW	Ministry of Health and Family Welfare
MRL	Maximum residue limit
NOC	No Objection Certificate

Report prepared by Vijay Teng of Infah (www.infah.org) as part of a HealthforAnimals initiative to support informed policy making in the animal health sector globally.

This report and reports on the other markets included in the benchmarking survey are available at: HealthforAnimals.org/GBS2020

Indian Federation of Animal Health Companies
INFAH

Health for Animals
global animal health association