GLOBAL BENCHMARKING SURVEY 2020

Benchmarking the competitiveness of the global animal health industry

CHINA

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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, to continue to commercialise existing products and be competitive.

This report is the second for China. It summarises the data from 9 China-based international companies that mainly import veterinary medicines for registration in China.

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 7 separate sections.

The company representatives that participated for this survey are regulatory affairs managers from international companies, working for imported products in China. For Imported products, all of the development data in the dossier is obtained outside of China except some of the local studies or testing required by Chinese authorities during the registration process.

Section A - Economics of the animal health sector

The global animal healthcare (i.e. medicines and ancillary healthcare products) industry continues to grow ($24 billion in 2015 and $41.5 billion in 2018); as part of this, 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 Chinese regulatory environment on ability to innovate

Over the past five years, the evolution of China's regulatory framework has had both positive and negative effects on innovation. Broadly speaking, Chinese authorities and officials have demonstrated greater transparency in the policy making process by allowing companies to comment on new regulatory provisions.

Some revisions or new regulations have had a positive contribution for the relatively healthier development of the animal health sector, while some of the updates of regulations have been implemented without enough rationale or transition period to cushion the effects on compliant businesses. Some of them caused the cost and timeline increase of innovative products introduction to the market, or negative impact on the business continuity.

More and more multinational animal health corporations set up their R&D and or manufacturing activities or facilities in China. This is largely due to government's efforts in bolstering China's veterinary pharmaceutical industry which has allowed in the past 5 years for more domestic players from multinational companies to emerge as a driving force for investments in those areas.

When it comes to innovation, the most important tasks faced by policymakers is to put in place a regulatory framework that could withstand industry and technological progress. Factors below are examples of key obstacles faced by the multinational companies in the past and currently:

- unclear regulatory requirements,
- import ban on modified live virus (MLV) vaccines against class A diseases and/or vaccines from class A pathogens,
- market access allowance for domestic generics earlier than their import pharmaceutical equivalents/original import pharmaceuticals,
- consequent restriction of the timing of application of original pharmaceuticals during monitoring periods of domestic generics,
- different regulatory data requirements from other countries
- stricter and stricter data requirements or their explanations on the same regulation.

In the last five years, only a small number of import biologicals were registered in China.

There is an increase in time and cost for product registration. GMO live vaccines took the longest time with averagely 8.7-8.8 years to register with sometimes unpredictable approval timelines.

For pharmaceuticals, local residue testing method validations, new GCP regulations implementation for the local confirmatory clinical studies etc contributed to the registration cost and time increase.

Participants also highlighted the importance for foreign companies to respect the cultural and organisational specificities of the Chinese business and regulatory environment to create a balance between expectations and perceived outcomes in regulatory affairs procedures while navigating new market or regulatory changes.

Section C - Commercialisation of existing product

As China continues its move towards greater conformity with international benchmarks in its regulatory practices, multinational companies are facing more and more competition from local companies.

Consequently, pressure increase for multinational companies to maintain their existing products portfolio. International corporations must delay the renewal of the brand-name product or discontinue its license for some specific cases. Deletion of growth promotion claims for medicated feed additives into the market can pose a threat to some business sections continuity for some multinational and domestic companies, while the trend is similar to that of US and EU and the global practice. New GCP and residue testing method validations requirements significantly affected the extension or maintenance of the license timeline for pharmaceuticals.

Higher standards for finished product quality and traceability have also impacted the cost and timelines to commercialize a product in the market. Some examples include:

- Serialisation outside of China
- Running additional local residue testing validations to comply with revisions of regulations
- Update finished product quality specifications based on up to date regulatory requirements
- Additional/different testing based on the Chinese Veterinary Pharmacopeia (not yet harmonised internationally)
- Non-flexible post-approval variations regulatory processes
- Specific requirements on the qualifications of API suppliers from China
- Updated new requirement on the facilities, especially for the local production in China
- *Other new and/or unclear regulatory requirements.*

Section D - Regulatory predictability and quality

Veterinary medicines registration pathways have significantly improved the past years.

Attendees recognized a considerable improvement in the quality of the technical reviews and supports provided by the Chinese authorities and would like to see China more involved in international regulatory cooperative or convergence initiatives. They also want the authorities' support throughout the development or pre-submission phase, and further develop a risk-based system (pharmacovigilance based) for renewal of marketing authorization, instead of the regular renewals of the import marketing authorizations every 5 years. Multinational companies would also like to be involved earlier in the law-making process to help design better regulations and expect optimized regulation updates frequency for positive sides reflecting industry and technology developments.

Both domestic and imported product registrations are generally subjected to increasingly strict rules and guidelines but travel some different bureaucratic processes: e.g. foreign manufacturers importing veterinary pharmaceuticals will be asked to conduct local confirmatory clinical trial studies in China.

Section E - Regulatory trends

Some beneficial changes have occurred in the Chinese regulatory framework since 2015:

- Reduction of the number of animals included in biological clinical trials
- General priority Review guideline was initiated for some specific product types based on the Chinese market needs
- Exemption of registration fees and confirmatory quality testing fees
- More public consultations on draft of regulations.

Others have significantly impacted on the access to the market or business continuity. These include new requirements on good clinical procedures, residue testing method validation, GMO...

Section F - Hopes and Expectations for the next 5 years

The most helpful trends identified by participants were:

- The shift from a zero-risk to a benefit-risk assessment approach
- Broader involvement of industry in the regulatory process through public consultations
- Increasing transparency regarding the disclosure of data.

The most unhelpful identified by participants were:

- The increasing requirements for post-market surveillance and pharmacovigilance

Section G - Regulatory cooperation and special product categories

There are no joint review or parallel assessment between China and other countries. Chinese authorities will usually refer to US/EU or VICH, if there are no specific guidelines or regulations in China.

There are no special simplified processes for imported products, but for local products, there are special approaches e.g. generics, local production permission, green channel etc. for some specific cases.

Summary and recommendations

The Chinese animal health industry has been undergoing rapid transformation for the past 10 years, while the regulatory environment evolves relatively slowly. Challenges for multinational companies still abound especially when it comes to imported products, and of those, especially for biological products. Many of the issues, hopes and expectations have been listed previously.

In China, we are at a milestone moment, on the eve of the announcement of new draft regulations, which is anticipated to bring some hopes towards increased support for innovation, facilitation to availability of drugs in the market but also a concern that more strict requirements may have an impact on our business continuity or access to the market.

The Chinese regulatory environment is unique. When a new veterinary drug regulation is drafted, it usually refers to EU or US regulation requirements and Chinese human side requirements, considering China animal health industry specific environment, while usually it will mix up and end up with specific requirements.

Key recommendations

- Regulatory requirements and standards harmonisation with other countries
- In-parallel registration with other countries
- CMO and MAH policy introduction
- Flexible various variation procedures requirements
- Priority registration clarification via a detailed regulation
- MUMs registration facilitation via set up of corresponding regulations
- Clear specification of reasonable transition period for multinational companies to implement regulation
- Clear review and approval timeline set-up and facilitation measures for GMOs
- Quality verification testing of the regulating authorities to reduce inefficient internal communications
- Finished product quality specification issues settlement process including direct, efficient communications with the industry
- Earlier and deeper involvement of all stakeholders, including multinational companies, in the consultations on draft regulations
- More efficient and transparent communication mechanisms
- Speed up the authority testing process

2. Introduction and background

The purpose of the HealthforAnimals Global Benchmarking Survey is to examine the interactions between industry and regulatory systems, particularly the impact of regulations on the animal health industry's ability to be innovative and competitive. This includes the ability to bring new products to the market, as well as to retain existing products on 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 and grown to include 11 countries in the 2020 survey (see box 1).

Box 1

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

With the cooperation and involvement of the HealthforAnimals member national associations, the survey is run every 5 years. 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 second for China. It summarizes the data from **9 Chinese based international companies**.

3. Outline methodology

The previous Benchmarking Survey **questionnaire** 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 survey was divided into two parts. Part 1 covered financial data and product development costs and was sent to the headquarters of each company (so regional offices were not involved). Part 2 covered the regulatory environment and its impact on innovation and competitiveness. The Part 2 questionnaire was adapted to the situation in each of the 11 surveyed markets and was completed by the country offices of companies active in those markets.

The national associations were responsible for requesting their membership to complete the questionnaires, to collect and collate the results using a standard template, and to organize 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 questions are reflected in the subheadings and are reproduced at the beginning of each section in a box below each sub-heading.

The GBS2020 survey covers 11 markets: Europe, United States of America, Japan, Canada, Australia, China, Brazil, India, Russia, South Africa and Mexico.

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

Details for China

Kellen collected filled questionnaires from **9 HealthforAnimals companies in China** during September and October 2019. Subsequently, a workshop was held on 6 December 2019 wherein the participants could discuss their answers to the questionnaire and add supporting comments and narrative to further explain the findings.

This is only the second year that China has participated in the survey and, therefore, there is limited data to track or predict trends.

4. The findings for China

Section A – ECONOMICS OF THE ANIMAL HEALTH SECTOR

Global context

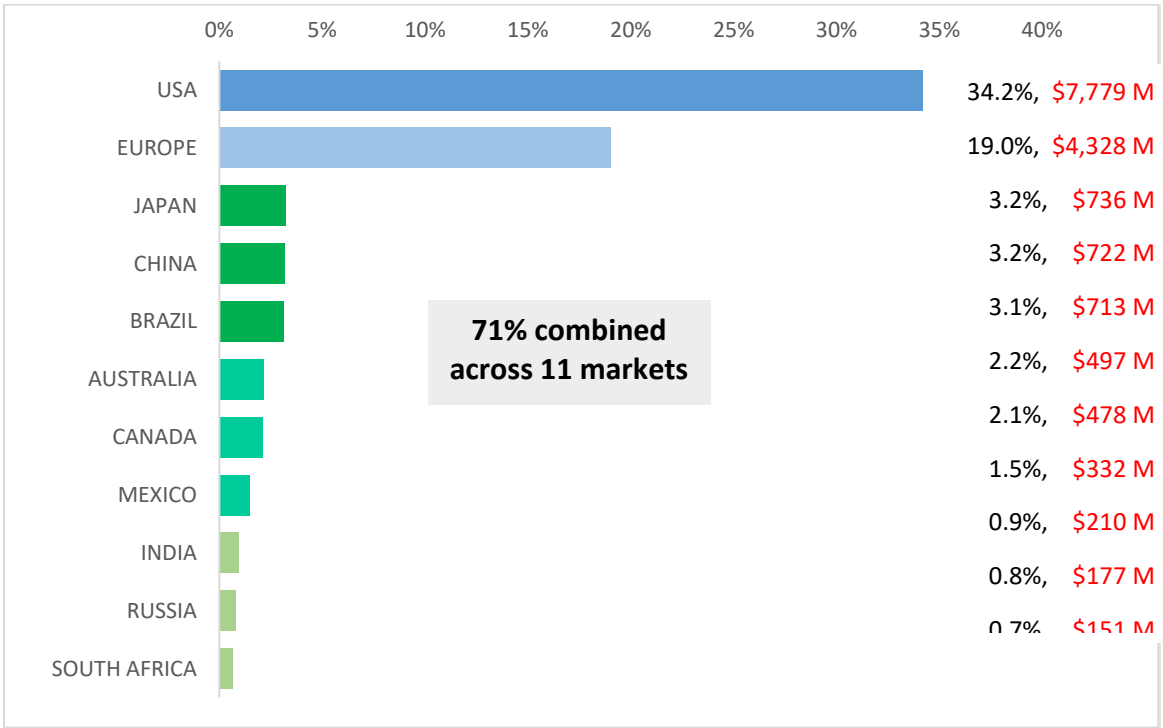
The financial data covers the 2018 full financial year. All data is presented in US dollars ($).

The GBS2020 Part 1 report on financial data is published separately. Key findings from that report are cross-referenced where relevant in this report for Europe, 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 China representing 3.2% of that revenue.

Figure 1: Revenue distribution of HealthforAnimals 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%). The R&D share for the two principle animal segments was 51% for companion animals and 49% for major food animal species.

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

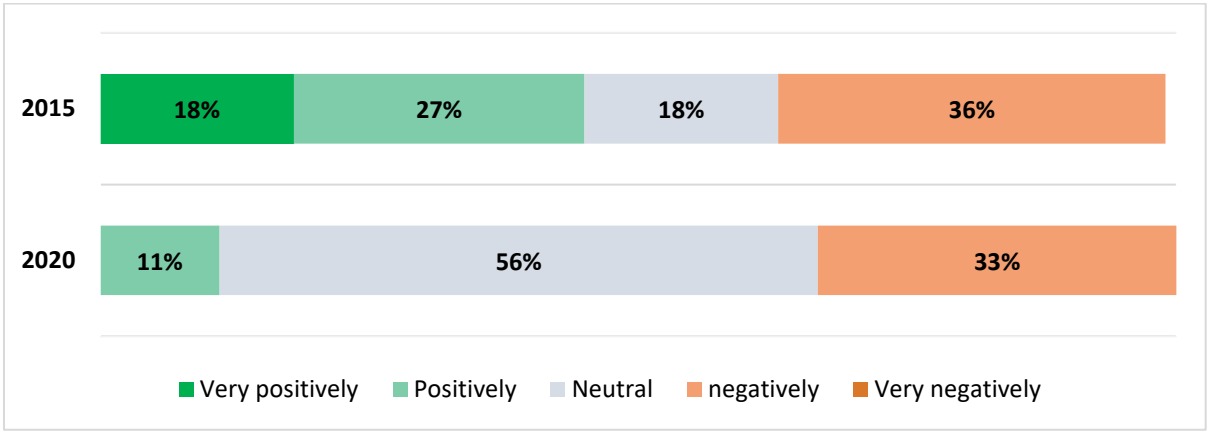
Section B – IMPACT OF REGULATIONS ON INNOVATION

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

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

There has been a definite shift in the opinion of companies on the impact of the Chinese regulatory environment on their ability to innovate since the previous survey in 2015. Many of the previous positive responses have become neutral, while the negative responses are still a third of the total (see Figure 2). Related regulations are still awaited. The latest registration regulation is from 2004. Additionally, intellectual property is not complete, and the innovative environment needs to be improved. The new regulation (e.g. GCP 2018) does not have related supporting regulations to implement it successfully for transient periods. Lastly, the registration speed is slow especially for imported biologicals.

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



However companies do report an improvement within the authorities in areas such as the registration environment, open mindedness from officers, good available communication channels, new rational requirements of reduction of animal numbers for biological field studies, and reasonable commenting periods.

One of the main challenges that occurs is the impact of cultural differences on the internal communications within international companies.

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 China?

The overall ranking of the factors relevant to innovation are shown in Table 1. Unclear Chinese regulatory requirements remain the biggest challenge for companies looking to place veterinary medicinal products on the Chinese market.

Table 1: Ranking of factors relevant to innovation

Factors relevant to innovation	Average ranking score
Unclear Chinese regulatory requirements	3.1
Closure of China and/or other geographic markets for certain products	3.7
Inadequate intellectual property protection (for patents or commercial data)	4.3
Accessibility of officers/experts for enquiries	5.4
Internal company organizational or cultural barriers	6.3
Small size of market segments	6.6
Negative consumer attitudes	6.9
Poor technology transfer mechanisms between academia and business	6.9
Lack of access to specialist biotechnology companies	7.8
Lack of skilled staff	8.1
Lack of availability of financial resources	8.6
Other: No harmonized guidelines, e.g. EP/USP vs. CVP	not ranked

The topmost important factors relevant to innovation have stayed relatively the same since the previous survey in 2015 with one major exception: 'Closure of China and/or other geographic markets for certain products' has nearly doubled in importance (from 36% ranking it very important in 2015 to 66% in 2020.)

3. Regulations that have improved competitiveness

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

All respondents ranked the factors individually and the average ranking scores for each factor are given in Table 2. The 3 most helpful factors where: Improved product quality; Prevented dangerous products entering the market; and Reassured the public about the safety of animal health products.

However, during the workshop discussion, all attendees thought that "Provided a fair, regulated environment", "Provided a stable business environment" and "Provided confidence to invest (added to certainty and predictability)" should be the top 3 factors for helping to improve the competitiveness of business resulting in the additional column, 'NEW RANKING'. Multi-national companies in China increased investment or achieved growth of the business because of relatively fair and stable regulatory environment.

Regulations in China also have had some negative impacts, as indicated in the next question below, illustrating the complicated and sometimes contradictory relationship businesses have with regulations.

Table 2: Government regulations that have improved competitiveness

Competitive Factors	*Average ranking score*	*NEW RANKING*
Improved product quality	2.4	4
Prevented dangerous products entering the market	3.4	5
Reassured the public about the safety of animal health products	3.7	6
Provided a stable business environment	5.8	2
Provided a fair, regulated environment	5.9	1
Provided confidence to invest (added to certainty and predictability)	5.9	3
Triggered innovation in new production processes	6.4	7
Helped redirect resources to innovation	6.9	8
Protected investments in innovation	7.9	9
Created alignment with other countries' regulatory processes	8.2	10
Speeded up time-to-market	8.2	11
Improved access to other geographic markets	8.4	12
Created new market segments	8.6	13

4. Other effects of regulations

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

Despite the positive impact of regulations on competitiveness, as reported above, regulations in China are also considered to adversely impact continuity of business as a result of new updated regulations, that cause problems due to limited transition time to implement new requirements, and increase costs of product development.

The regulations also have an impact, to a lesser degree, by closing the market for specific products, by creating significant uncertainty or unpredictability and by increasing product development time in the past 5 years.

Table 3: Effects of regulations on Chinese businesses

Impact	Average ranking score
Adversely impact continuity of business due to new updated regulations	4.0
Cause problems due to limited transition time to implement new requirements	4.0
Increase costs of development	5.0
Close markets for specific products	5.3
Create significant uncertainty or unpredictability	5.4
Increase development time	5.8
Re-direct resources into defensive R&D	6.8
Limit the use of innovative marketing methods	7.1
Restrict collaborative R&D ventures	8.1
Reduce access to new ideas, particularly in biotechnology	8.6
Divert management time	9.8
Reduce cash flows from existing products	9.9

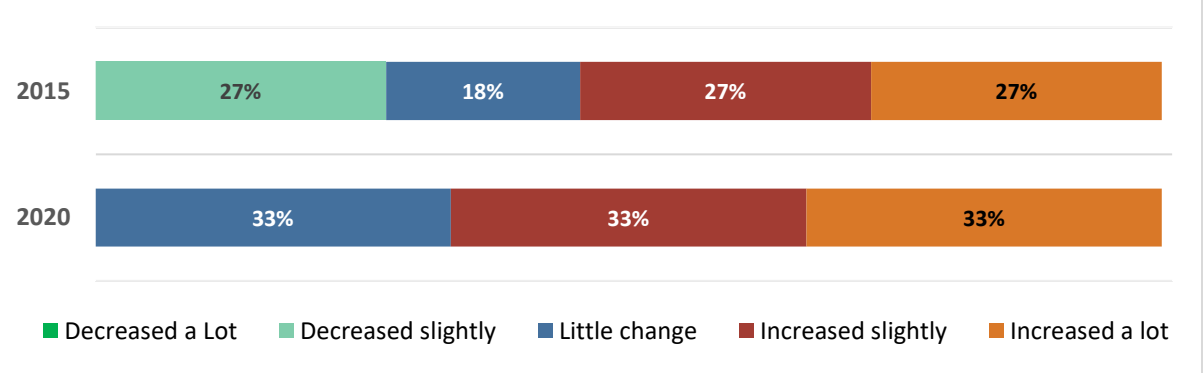
5. Expenditure on mandatory defensive R&D

Which of the following statements best indicates how your expenditure on MANDATORY DEFENSIVE R&D in China has changed since 2015?

Mandatory defensive R&D (MDR&D) is defined as the cost of additional studies to maintain a product on the market, demanded by the regulatory authority, either at renewal, or during other regulatory activity (such as product reviews or referrals).

The situation in China seems to have deteriorated since the previous report (2015). Report of decreasing MDR&D costs has disappeared altogether in 2020 and the majority of companies now report increasing costs. The results are summarized in Figure 3 and reasons for these changes are explored in the next section.

Figure 3: Changes in Mandatory Defensive R&D costs



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

The main factors causing a change in expenditure on mandatory defensive R&D are listed in Table 4. Decreases in expenditure were related to the removal of fees, while increases in expenditure were triggered by new regulations.

Table 4: Factors causing a change in expenditure on mandatory defensive R&D

Factors causing a *decrease* in expenditure on mandatory defensive R&D
• No registration or testing fee to be charged from the authorities
Factors causing an *increase* in expenditure on mandatory defensive R&D
• Clinical study expenditure was increased because of new GCP, GLP regulation, etc. • Residue analytical method validations expenditure was increased because of new regulations

Other factors, not specifically related to MDR&D, but that will affect overall R&D and commercialization are:

- Field study animal number reduction
- Increase in the cost of local clinical trials, such as new GCP regulations
- New regulations on production facility requirements, mainly for local production sites
- High requirement for registration: even if the regulation is not changed, the explanations from IVDC are changed requiring additional study data; these stricter explanations may cause challenges of implementations because of lack of more practical regulations

- New updated regulation on vaccine development, such as GCP requirements, and a lack of qualified Specific Pathogen Free animals for vaccine development, e.g. feline vaccines
- The costs of sourcing experimental pigs for animal studies are much higher due to the sharp decrease in pig numbers caused by the ASF outbreak
- New explanation on the old regulation e.g. production, assay set up development parameters
- New GCP and GLP requirements increased the study costs
- 2D bar-code implementation increased the production cost, timeline, and overseas manufacturers met various implementation challenges.

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

Please state the AVERAGE LENGTH OF TIME it takes you to gain registration for a major new product in CHINA, from submission of the marketing authorisation dossier to first-market product approval.

This question looks at the product registration step, separately from the product development phase (which is covered in the next question). Companies were asked to provide their product registration times for 8 different product categories. The average product registration times and the sample size (N) are shown in Table 6.

Table 5: TIME to gain registration for a major new product in CHINA

	Average years	N
Pharmaceuticals for Major Food Animals	3.9	8
Biologicals for Major Food Animals（Normal）	4.3	6
Biologicals for Major Food Animals （GMO）	8.7	5
Pharmaceuticals for Companion Animals	3.8	8
Biologicals for Companion Animals （Normal）	4.3	4
Biologicals for Companion Animals （GMO）	8.8	3
Pharmaceuticals for Minor species	NA	NA
Biologicals for Minor species	NA	NA

The situation has become more complex since the 2015 survey because GMO strains have been added to both Major Food Animals and Companion Animals in the Biologicals Category.

In general, there has been very little or no change in the last 5 years, and registration times for non-GMO products remain in the region of 4 years, which is significantly longer than the majority of countries in the Global Benchmarking Survey.

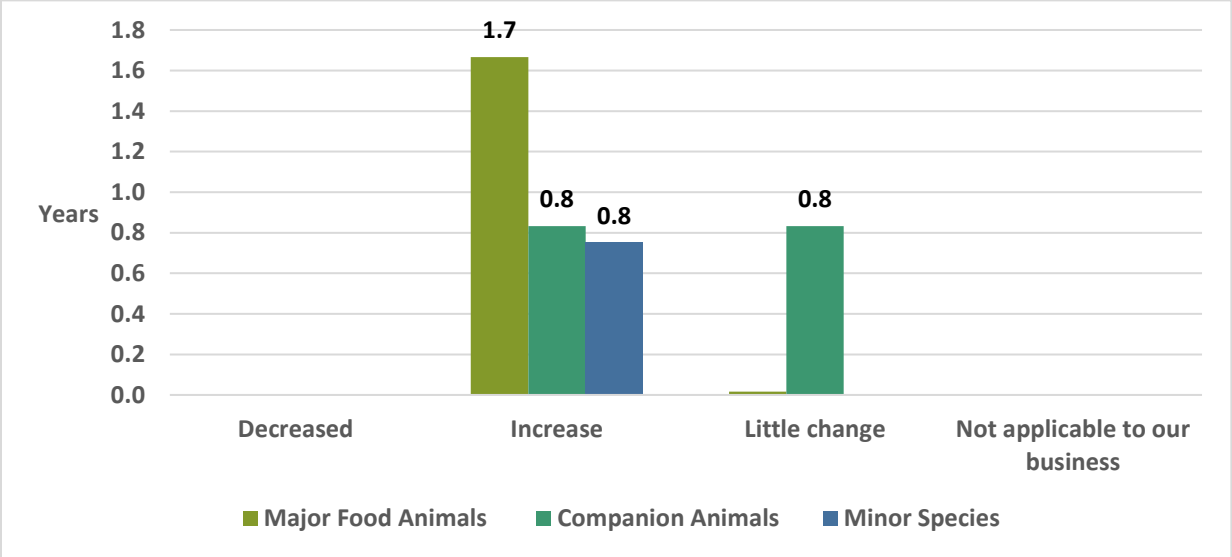
The GMO category, however, has a very long lead time, more than double that of the non-GMO products.

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

Have REGULATORY FACTORS caused a change in the AVERAGE LENGTH OF TIME it takes you to develop a major new PHARMACEUTICAL product in China (from initial research to final market authorization), compared to 2015?

Local product development, except for additional local studies necessary for registration in China, is not applicable for multi-national companies for imported products in China; local generic development is shorter than global (EU, U.S.) innovative development. However, hand-in-hand with the increase in requirements comes an increase in the time it takes to prepare the data dossier for China, including for multi-national companies. The data in Figure 4 mainly covers the initiation of registration to final market authorization in China for imported products.

Figure 4: Change in the average length of time it takes to develop a pharmaceutical product



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

Have REGULATORY FACTORS caused a change in the AVERAGE LENGTH OF TIME it takes you to develop a major new BIOLOGICAL product in China (from initial research to final market authorization), compared to 2015?

The data in Table 6 mainly covers the initiation of registration to final market authorization in China for imported products.

Changes in Regulations can have an impact on the time it takes to develop a product. The average increase in product development time for biologicals for the 3 main categories of animals is shown in Table 6. Only data with at least 3 data-points is shown. No companies reported a decrease in product development time, and no companies had examples for minor species products.

For Major Food Animals, while more companies claim that the time to develop biological products has increased (56% in 2020 vs. 22% in 2015) the increase is slightly lower (1.5 years in 2020 vs 2 years in 2015). For both categories (Major Food Animals & Companion Animals), there is a considerable number of respondents (33%) who mark this as not applicable for their business.

Table 6: Change in average length of TIME to develop a major new BIOLOGICAL product

Species		Decreased	Little change		Increased		Not applicable
			Av. years	N	Av. years	N	
BIOLOGICAL	Major Food Animals	0	No valid number	1 company	1.5 Y	5 companies	3 companies
	Companion Animals	0	No valid number	2 companies	1.3 Y	4 companies	3 companies
	Minor Species	NA	NA	NA	NA	NA	NA

10. Change in AVERAGE COST of developing a major new PHARMACEUTICAL product

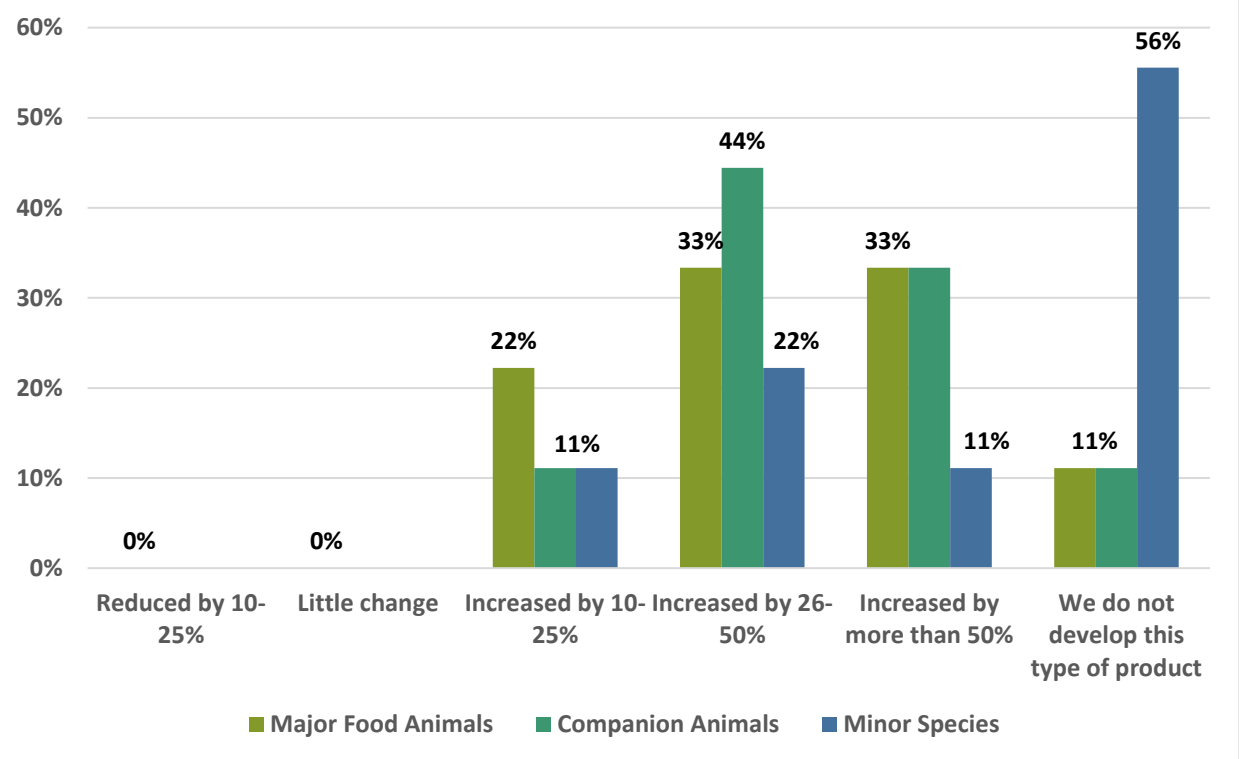
Have REGULATORY FACTORS caused change in the AVERAGE COST of developing a major new product in China (from initial research to final market authorization) for all possible species and indications for that product, compared to 2015, in real terms?

The data in Figure 5 mainly covers the initiation of registration to final market authorization in China for imported products.

All companies report that product development costs for a major new pharmaceutical product have increased, with the majority reporting a significant increase (greater than 26% since the previous report in 2015).

More than half of the companies do not develop pharmaceutical products for minor species.

Figure 5: Change in Average COST of developing a major new PHARMACEUTICAL product



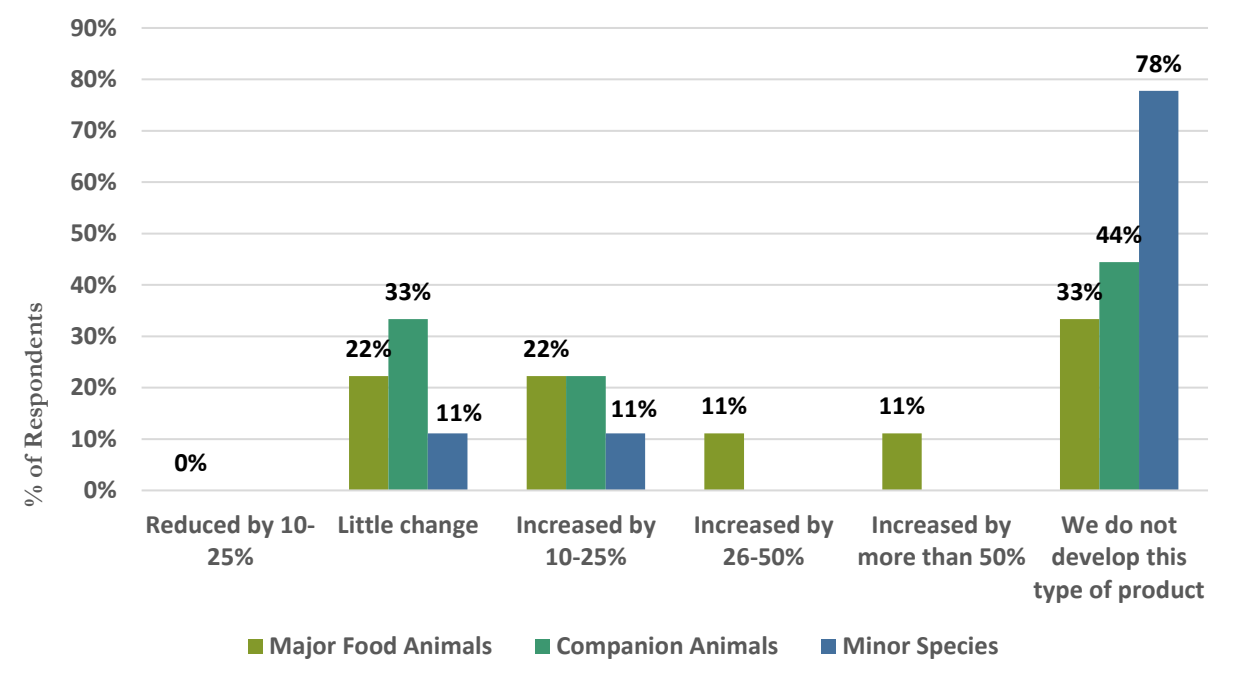
11. Change in AVERAGE COST of developing a major new BIOLOGICAL product

Thinking about the AVERAGE COST of developing a major new BIOLOGICAL product in CHINA (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.

The data below mainly covers the initiation of registration to final market authorization in China for imported products.

All companies report that product development costs for a major new biological product have not increased in the same way as the development of a pharmaceutical product (Figure 6). The majority of companies report that the cost of product development for a biological product has changed a little or up to 25%. A significant minority (33 to 44%) of the companies do not develop biological products for food or companion animals, and the great majority (78%) do not develop biological products for minor species.

Figure 6: Changes in Average COST of developing a major new BIOLOGICAL product



12. Impact of Government Regulations on ABILITY TO INNOVATE

Thinking about Government Regulations in China, how would you assess the impact of each of the areas of regulation listed below on your ABILITY TO INNOVATE successfully?

The impact of a range of government regulations in China on the ability of companies to innovate is shown in Figure 7. The companies were asked to rank the regulations on a scale from very helpful to very unhelpful.

The three most ***helpful*** regulations are:

(1) Market Authorizations,
(2) Maximum Residue Limits and
(3) National policy on access to documents of government bodies.

The three most ***unhelpful*** government regulations are:

(1) Protection of IP patents,
(2) Protection of IP commercial data and
(3) Biotechnology regulations.

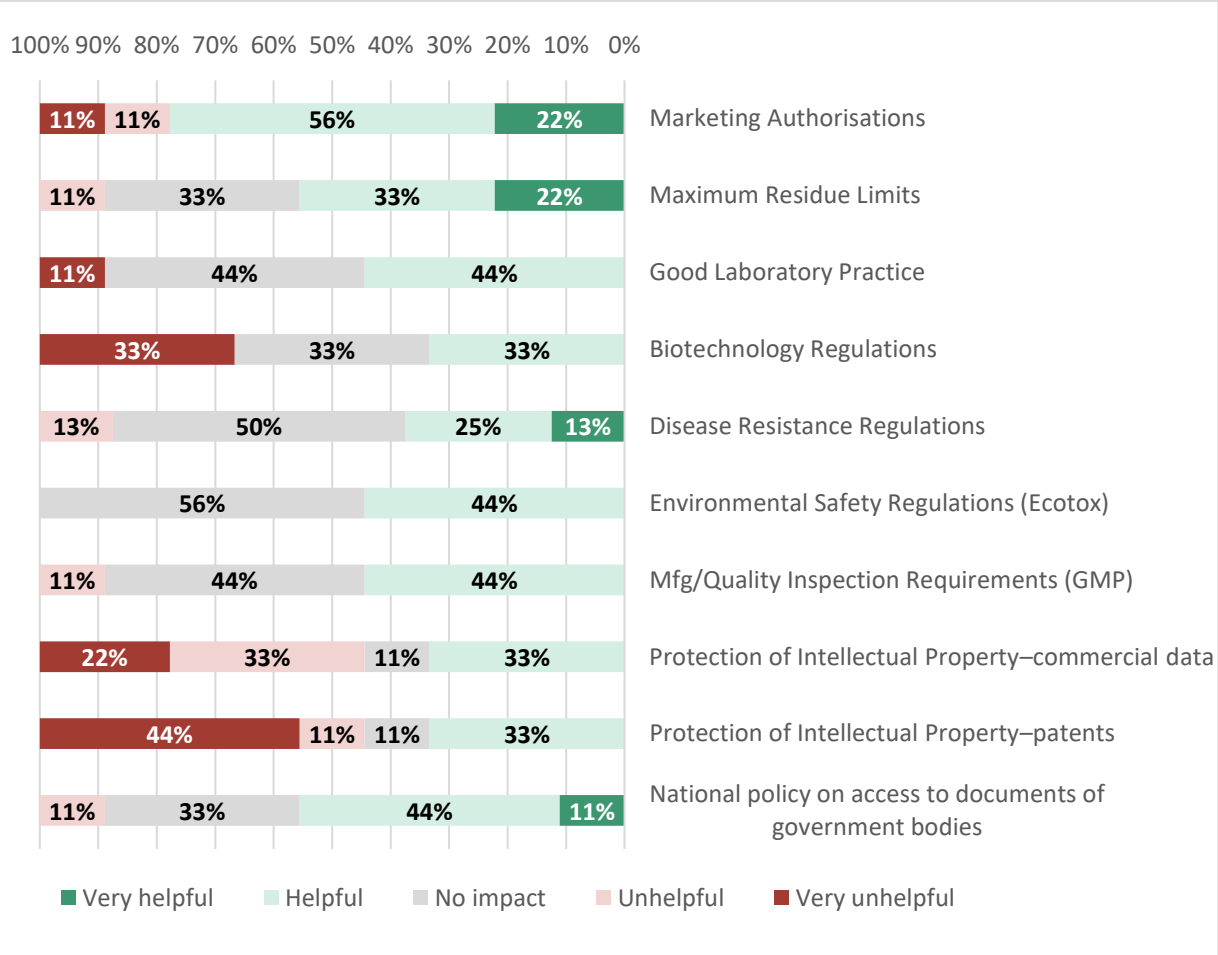
Disease Resistance Regulations (covering antimicrobial resistance and antiparasitic resistance) were also seen as relatively helpful.

This perspective of companies in China is very different to that in other regions of the world, where intellectual property protection, in the form of patents or protection of the data in marketing authorisation dossiers, is regarded as an essential element in supporting and stimulating innovation.

The answers to this question are also contradictory to the answers to the first question in section C (Commercialization factors for exploiting existing products), where "Inadequate intellectual property protection (commercial data & patents)" is ranked as an important factor.

The unhelpful 'Biotechnology regulations' is presumably related to the issue with GMOs.

Figure 7: Impact of Government Regulations on ABILITY TO INNOVATE



Section C - COMMERCIALISATION OF EXISTING PRODUCT

1. Commercialization factors for exploiting EXISTING PRODUCTS

Below is a list of factors relevant to the commercialization of existing products in the animal health industry in China. Which of these, if any, are significant for the exploitation of your existing products?

The respondents were asked to rank, from 1 to 11, a list of factors relevant to the commercialization of existing products (Table 7).

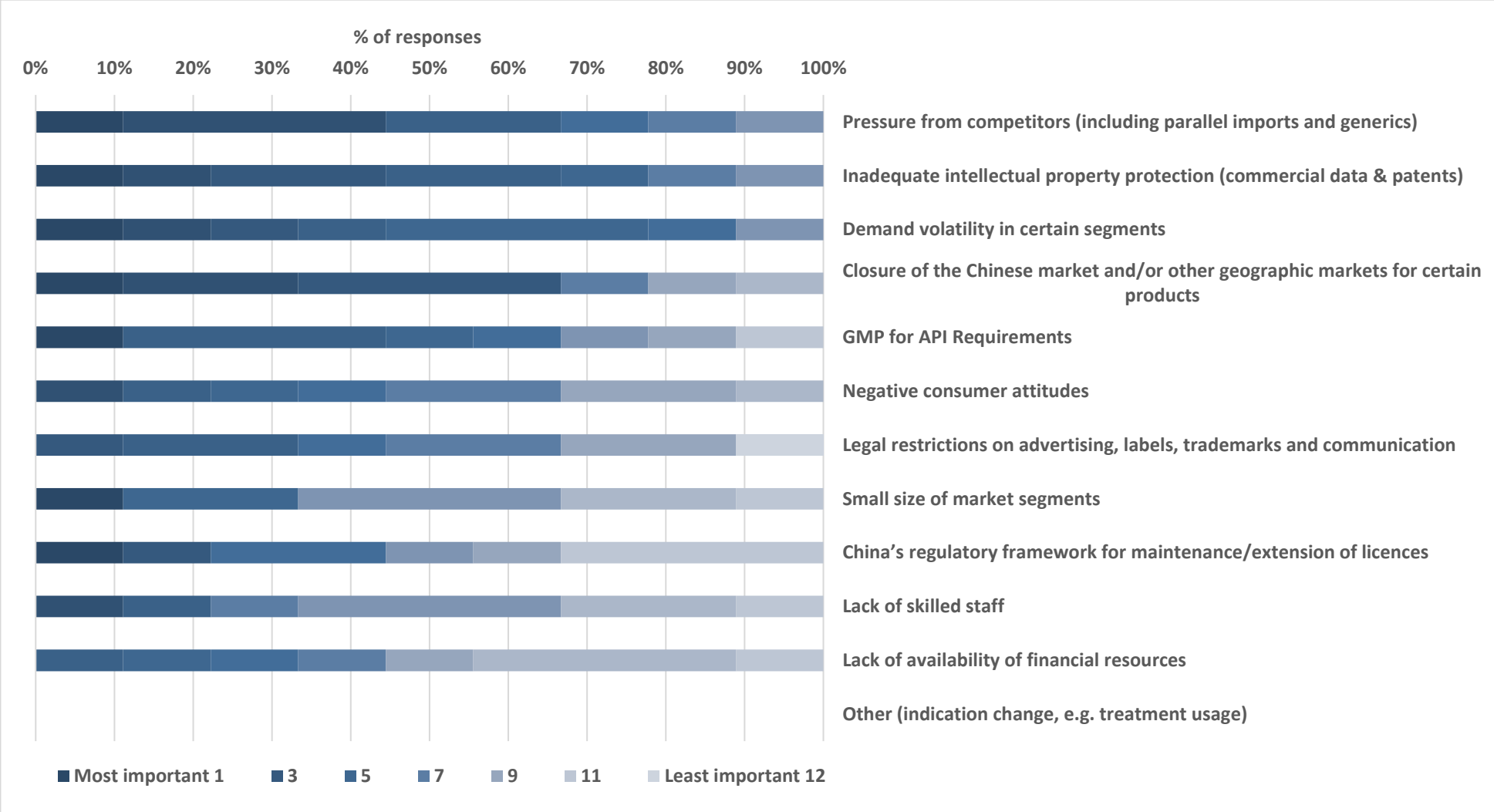
Table 7: Commercialization factors for exploiting EXISTING products

Factor	Average Ranking Score
Pressure from competitors (including parallel imports and generics)	4.0
Inadequate intellectual property protection (commercial data & patents)	4.1
Demand volatility in certain segments	4.3
Closure of the Chinese market and/or other geographic markets for certain products	4.4
GMP for active pharmaceutical ingredient requirements	5.8
Negative consumer attitudes	6.6
Legal restrictions on advertising, labels, trademarks and communication	6.8
Small size of market segments	7.3
China's regulatory framework for maintenance/extension of licences	7.3
Lack of skilled staff	7.6
Lack of availability of financial resources	8.0
Other: indication change, e.g. treatment usage	0.0

Pressure from competitors (including parallel imports and generics) remains one of the top factors affecting commercialization of existing products (Figure 8). In fact, it rose from the second-most important factor in 2015 to the most important in 2020. It is important to note that not only GMP certification but also production permission is required for APIs and other materials produced and exported from China.

Additionally, some items of this question are not suitable for the products imported into China. Multi-national companies in China are required to introduce and maintain the licenses of imported products, based on the data developed or produced outside of China and approved by the relevant regulatory authorities in other countries.

Figure 8: Commercialization factors for exploiting EXISTING products



2. Impact of regulation on business

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

The respondents were asked to rank, from 1 to 11, a list of 'effects on your business' that regulations in China might cause (Table 8). Pressure from generic competition was by far the highest-ranking factor. This is probably linked to the next highest factor - 'Fail to protect intellectual property (patents & commercial data) adequately'.

The other high-ranking factors are more related to changes in government regulations:

- Increase the cost of production, and
- Create significant uncertainty.

Table 8: Impact of regulation on business

Factor	*Average Ranking Score*
Other: Generics Pressure	1.0
Fail to protect intellectual property (patents & commercial data) adequately	4.1
Increase the cost of production	4.3
Create significant uncertainty	4.9
Restrict the extension of existing technologies to additional species/indications	5.2
Remove profitable products from the market	5.9
Increase the cost of distribution and marketing	6.0
Limit the use of innovative marketing methods	6.4
Create disproportionate costs for maintaining/extending marketing authorizations	6.7
Divert financial resources away from the development of new, innovative products	7.2
Divert management time	8.0

3. Impact of regulation on ability to commercialize existing products

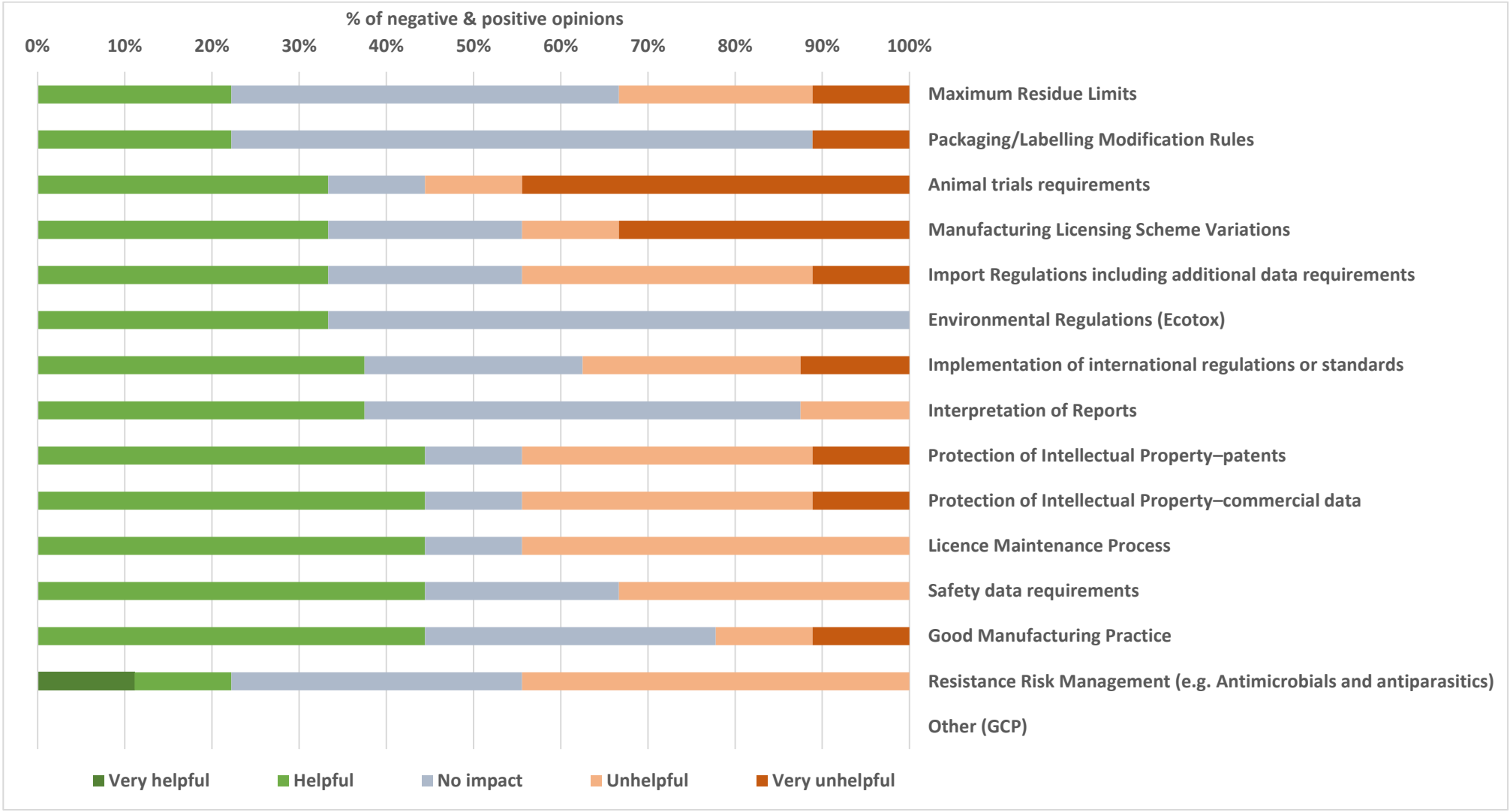
Thinking about Government Regulations in China, how would you assess the impact of each of the areas of regulation listed below on your ABILITY TO commercialize EXISTING PRODUCTS successfully?

The regulations deemed most unhelpful in commercialization of existing products were Animal Trial requirements and Manufacturing Process/CMC requirements (Figure 9). Manufacturing Licensing Scheme Variations were also ranked as unhelpful.

The regulations that were most helpful were the safety data requirements and Good Manufacturing Practice. Respondents were almost evenly split on both the License Maintenance Process and IP protection (commercial data and patents) with an equal number of rankings as unhelpful and helpful.

Good clinical practice (GCP) was mentioned as an 'Other' factor that was generally seen from the unhelpful perspective.

Figure 9: Impact of regulation on ability to commercialize existing products



Section D - REGULATORY PREDICTABILITY & QUALITY

1. Predictability and quality of regulatory procedures in China

(a) Does the China regulatory agency as currently managed provide you with the regulatory predictability that you need and the regulatory quality you expect? (b) If not, please tell us what the top issues are and what might be done about them (your proposed solutions moving forward).

The perception of the multi-national companies of the regulatory predictability and quality of their national regulatory agencies is reasonably positive, while acknowledging that there is room for improvement (Figures 10 and 11).

The issues affecting regulatory predictability and quality are reported in Table 10, together with suggestions for improvement. Several of these revolve around more efficient and transparent communication, and more transparency on the requirements. Other common themes are the need for transition periods when requirements change, the need for clear guidance and clear timeframes for the work of the regulatory agencies.

In general, there is a lack of internal trust, so more work is needed to persuade Global HQ of multi-national companies to build more trust in China's regulatory environment.

Figure 10: Regulatory Predictability

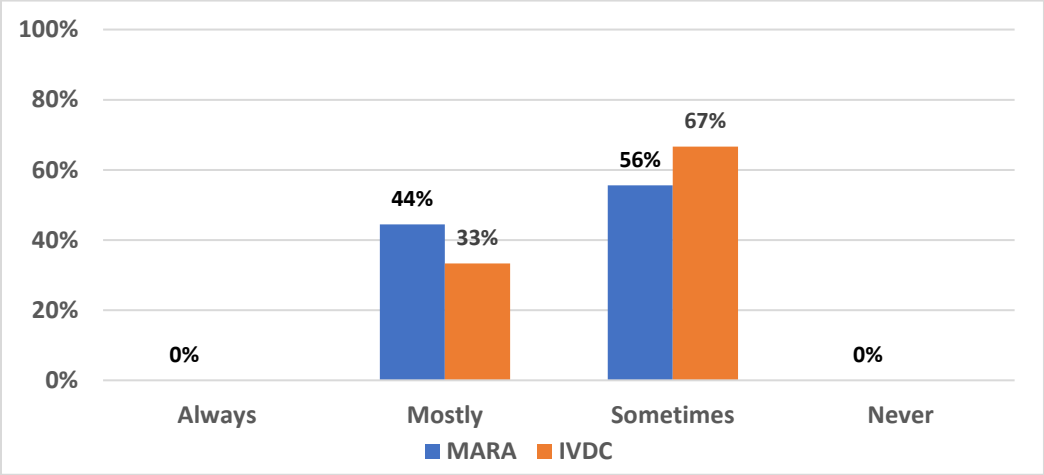


Figure 11: Regulatory Quality

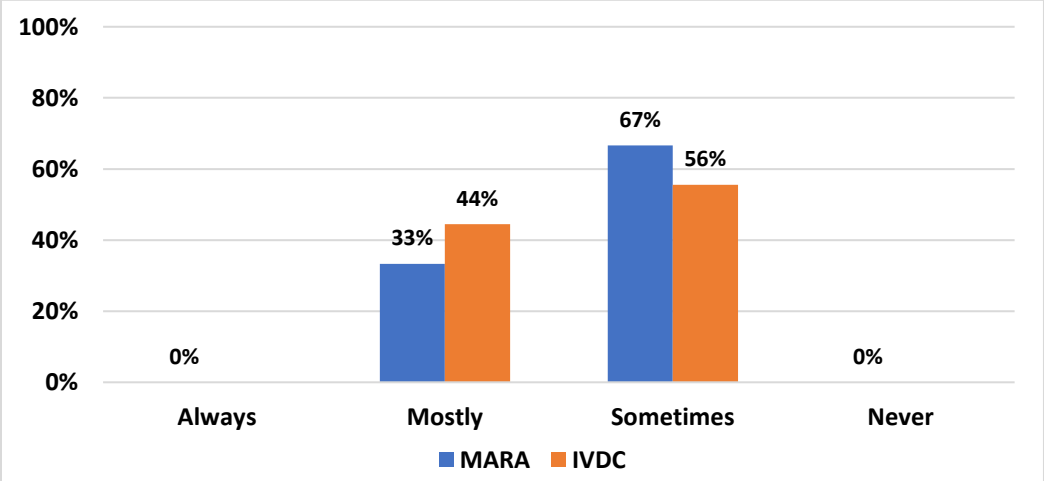


Table 9: Top Issues Affecting Regulatory Predictability & Quality and Suggestions for Improvement

Regulating Authority	Issue / Suggestion for Improvement
MARA	• Site transfer to different countries is considered as new imported products; • Regulation regarding variation needs to be optimized with more flexibility based on production practice; • Category classification and differentiate the requirement for disinfectants and aqua vaccines; • MAH system (e.g. veterinary drug company hold the license), CMO is suggested to be implemented; • Involve multi-national companies more when drafting the new regulation; • More efficient and transparent communication; • Transition time for new regulation implementation should be extended; • No clearly specified grace period in regulation/registration; • Set up a formal communication system such as consultation process with experts on the scientific perspective in China.
IVDC	• Harmonize CVP, EP/USP; • Manufacturer should be the responsible body for its own specification and test procedures. Proposed solution: IVDC is suggested to proceed with the test according to the technical registration documents; • Increase regulation training organized by IVDC; • For quality control testing related to target animal testing conducted by IVDC, they could spend more than the legalized timeframe (maximum 150 working days) to complete the testing and issue the report due to multiple reasons (such as no sufficient budget or difficulty to source quality animals). Proposed solution: there should be an increased involvement of IVDC on the review/confirmation of quality standard to make sure the minimal/proper use of animal for the confirmatory testing; • During the conducting phase of confirmatory testing at IVDC, there is no "direct" communication channel between officers at IVDC lab and industry. The current "indirect" communication channel needs to go through IVDC's administrative department that couldn't facilitate a timely communication between IVDC lab and industry. Proposed solution: there should be a direct and reasonable communication channel between IVDC lab and industry.
CVDE	• There is no legalized timeframe of Quality Standards confirmation process between CVDE and Committee experts. For example, after the Committee hearing, CVDE will still send new questions (different from the queries from Committee hearing) raised from different experts on quality standard, that results in multiple query cycles between CVDE and firms. Proposed solution: there should be a clear and legalized timeframe for every step involving CVDE, committee experts, and firm on confirmation of quality standard; • For the regulation of Priority Review released in no.2599 announcement, there is no clear guideline for industry to apply and receive feedback/result of application. For example, if a firm submitted the application of priority review, the firm didn't receive any feedback on if CVDE has reviewed/accepted or rejected the application. It seems the Priority Review is not really implemented. Proposed solution: CVDE provides a clear guidance/process with details to industry on how to apply for priority review and how CVDE will evaluate the application and give feedback to firms. • For the official queries received after committee hearing, there is no clear clarification and details on each query. For example, the query would simply state "lack of relevant document/research data", but didn't specify what the "relevant document/research data" they were really looking for. Proposed solution: CVDE should provide details of each query and specify what additional documents are missing/required for the related section number in the submission.

2. Procedures for registering NEW products

Consider the current IVDC/CVDE procedures for registering new products. To what extent does the process meet the criteria as listed in Figures 12a & 12b.

The IVDC/CVDE are generally viewed as practical, competent, rigorous and not excessively bureaucratic (see Figures 12a & 12b). Although in previous questions companies have reported challenges arising from changing and more strict interpretations of regulations, the situation appears to be improving for new product registrations. In response to this question, companies believe the applications are being reviewed with a consistent interpretation of regulatory guidelines, risk analysis and available science. The only slight concern voiced by a third of all companies was whether the scientific assessment of risks and benefits is clear and respected by other international regulators.

The two standout findings are:

- The positive attitude towards the fact that final registration of new products is based on the expert assessment of safety, quality and efficacy;
- However, there is a slight concern that there may not be recognition by other international regulators of China's scientific assessment of risks and benefits.

3. Procedures for registering EXISTING products

Consider the current IVDC/CVDE procedures for registering existing products. To what extent does the process meet the following criteria?

The perception of the IVDC/CVDE processes for existing products, shown in Figure 13, are generally positive and mirror, in general, those for new products (practical, competent, rigorous, etc.) The divergences or concerns are mostly related to risk analysis. Specifically, there is concern that the scientific assessment of risks and benefits is not clear nor respected by international regulators; and, doubt remains as to whether there is a clear distinction between risk assessment and risk management decisions.

Additionally, there is concern that science-based analysis of pharmacovigilance data and/or best available science is not conducted consistently.

Figure 12a: New Product Registration Criteria – Scientific Basis

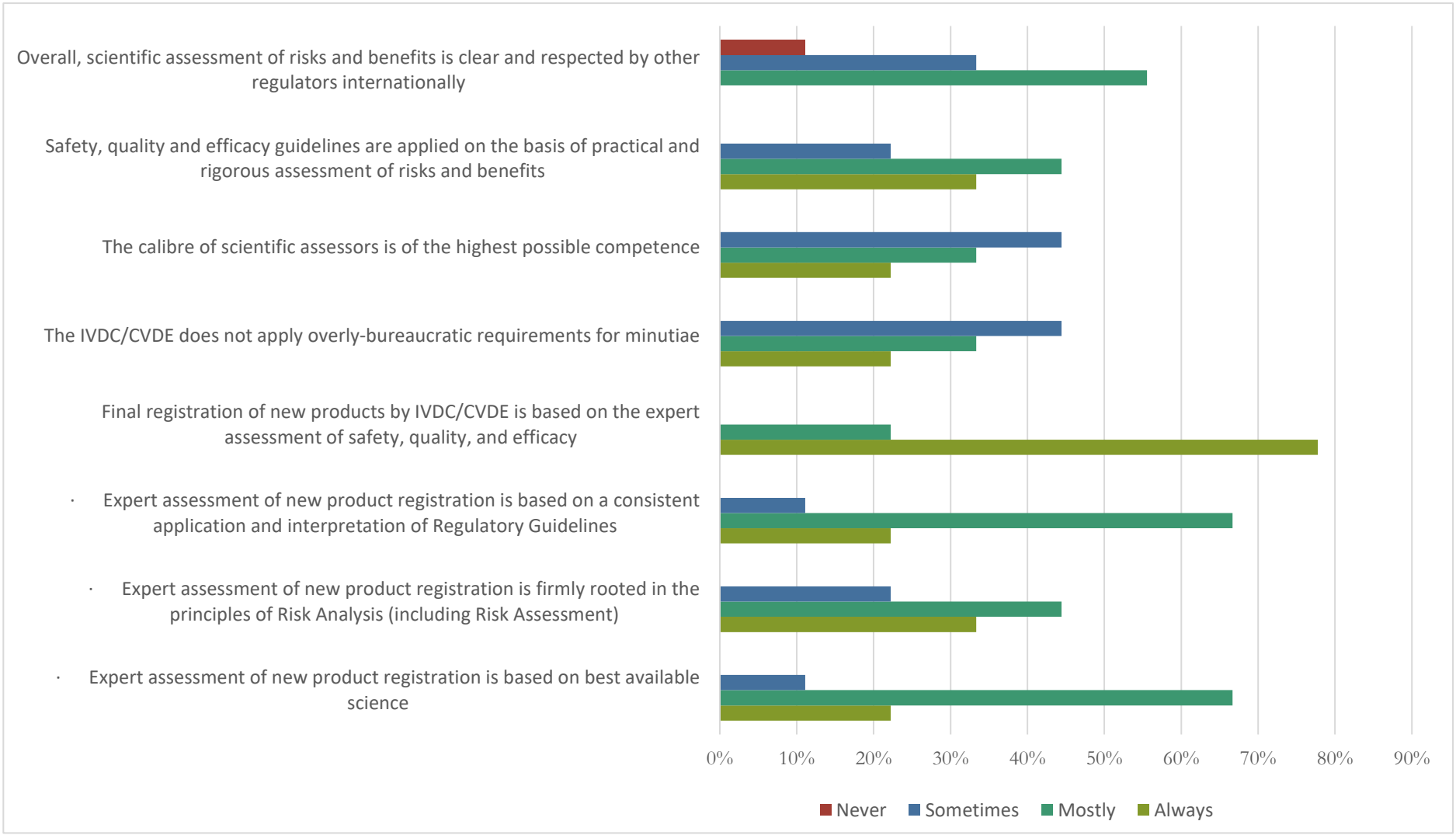


Figure 12b: New Product Registration Criteria – Process Basis

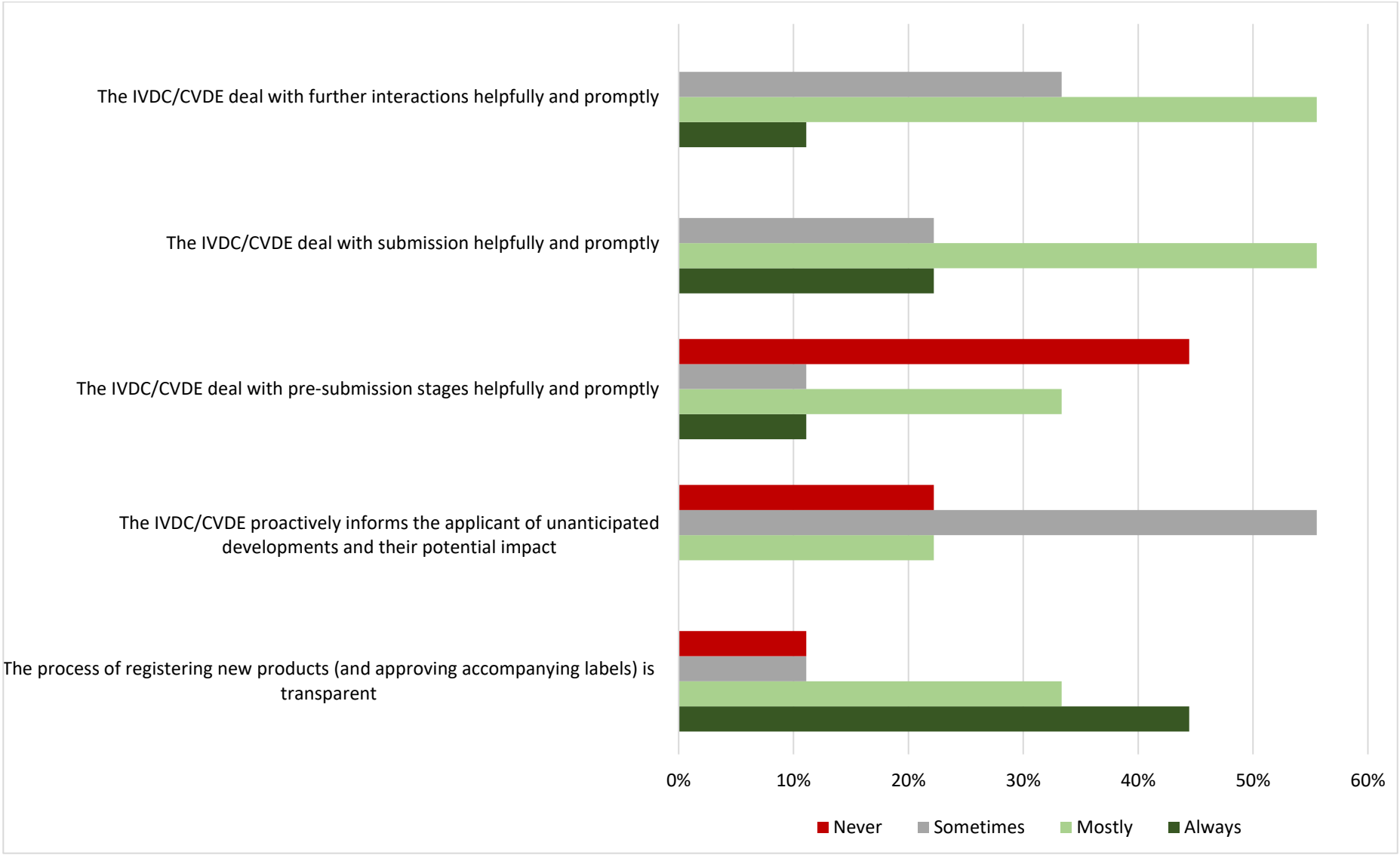
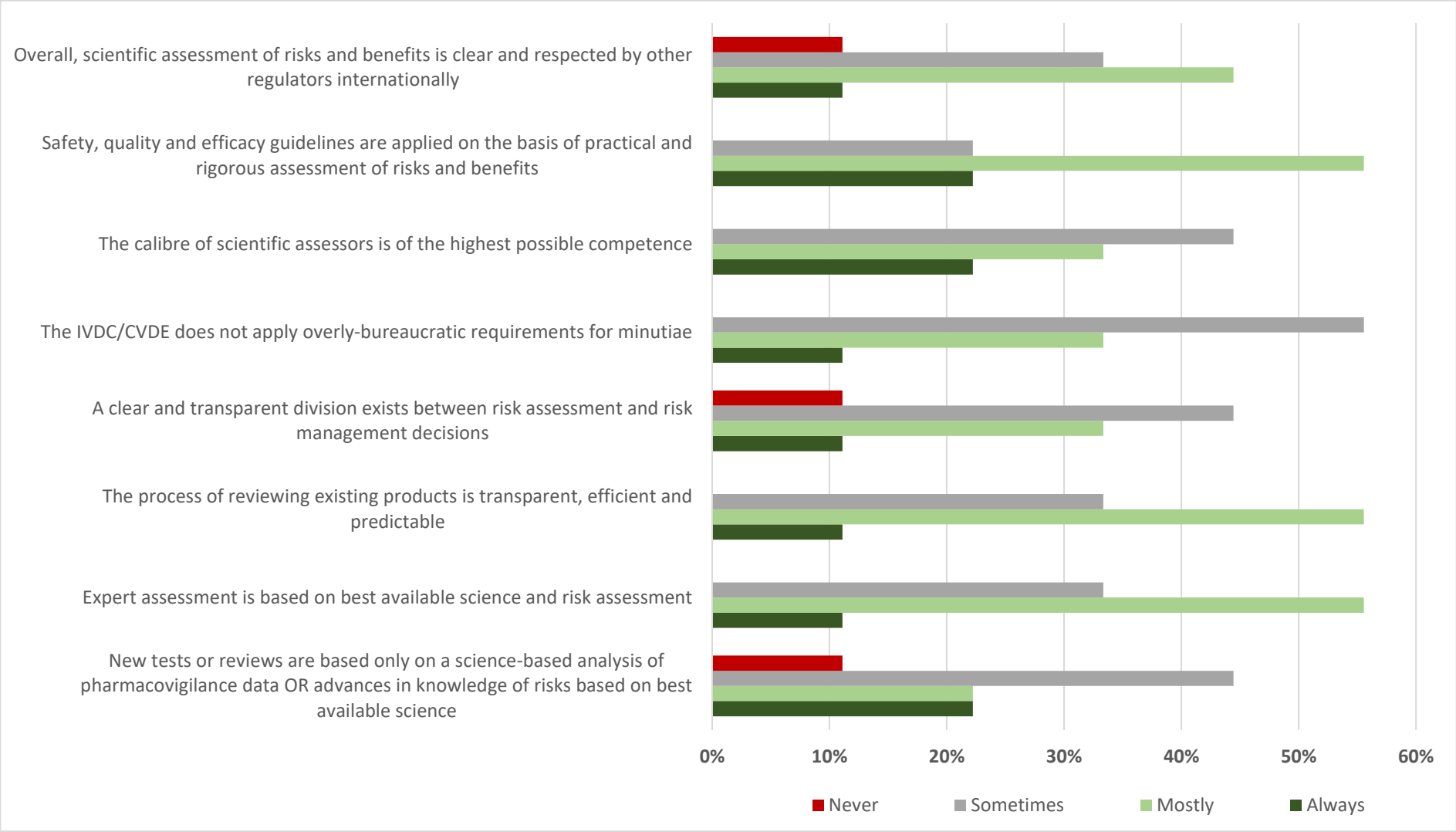


Figure 13: EXISTING Product Registration Criteria

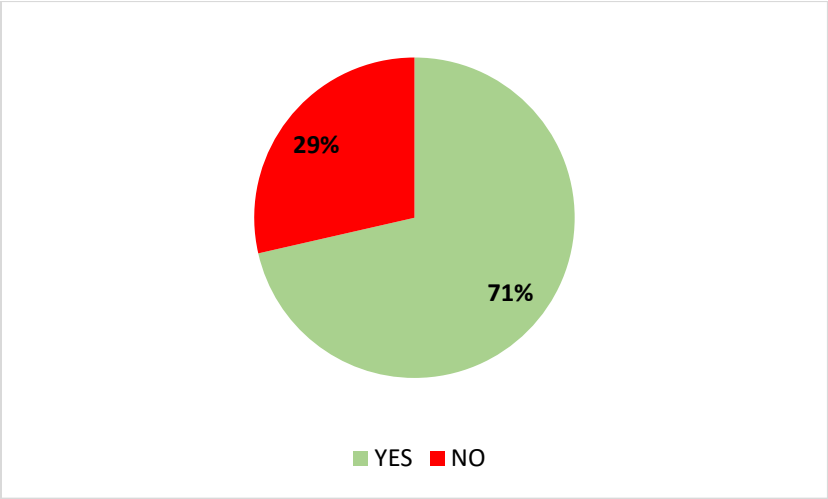


4. Procedures for registering NEW and EXISTING products

The process for registering new products is similar for existing products; if 'no', please explain.

The majority of respondents considered that the process for registering new products is similar for existing products (Figure 14). The variation process for existing products was also considered to be similar to new products, however the renewal process was thought to be different.

Figure 14: Company opinion if registration process is similar for NEW and EXISTING products



5. Effectiveness of regulation and policy-making processes

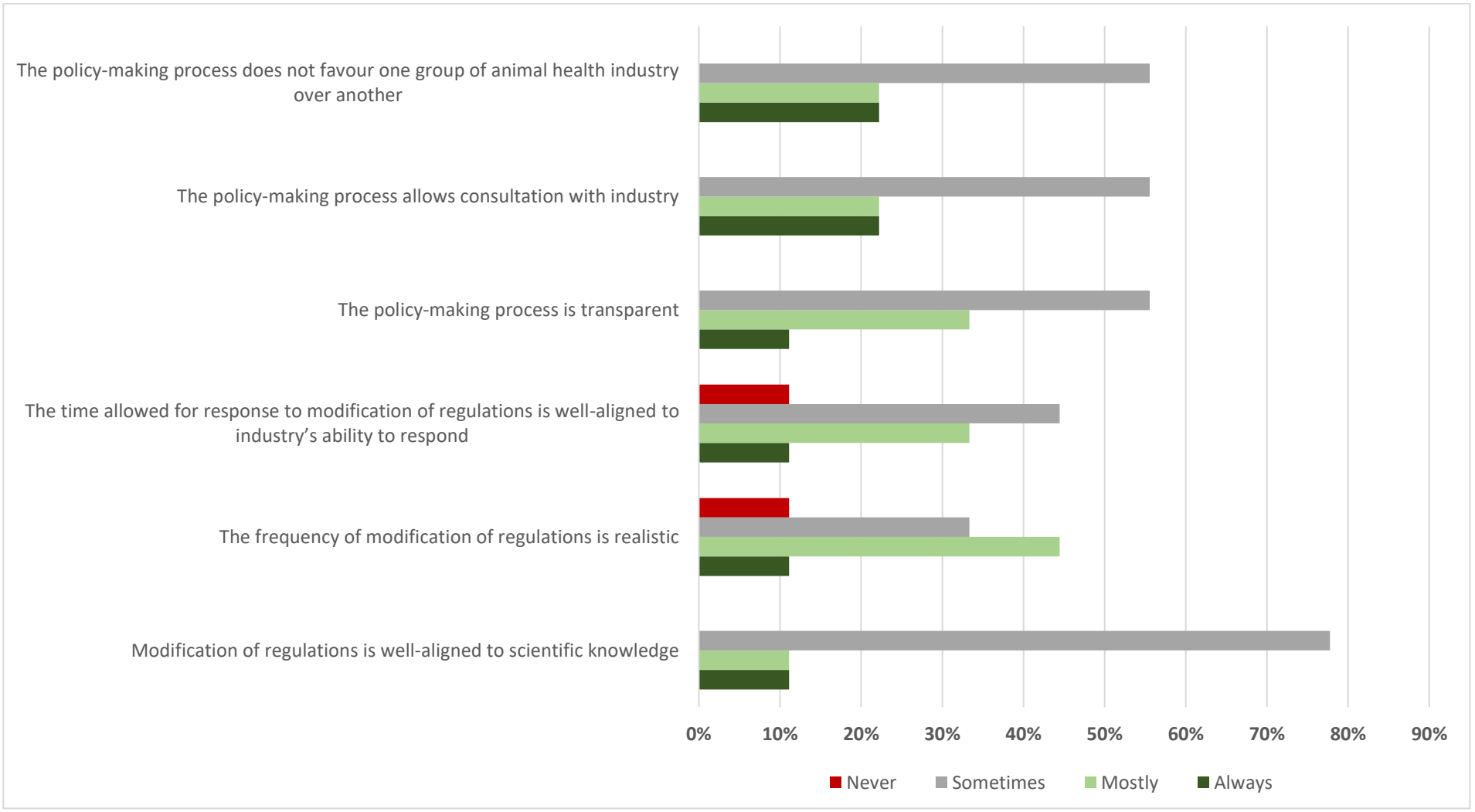
Consider the current MOA Veterinary Bureau policies. To what extent does VB's approach meet the criteria listed in Figure 15?

The companies were asked to consider (by scoring never/sometimes/mostly/always) the effectiveness of MOA Veterinary Bureau regulation and policy-making processes against a set of criteria statements (Figure 15).

The MOA Veterinary Bureau is generally viewed as effective in that the policy-making process is transparent, allows consultation with industry and does not favor one group of animal health industry over others.

However, there are two concerns: whether the frequency of regulation modifications is realistic and if such modifications take into account the industry's ability to respond to them.

Figure 15: Effectiveness of MOA Veterinary Bureau regulation and policy-making processes



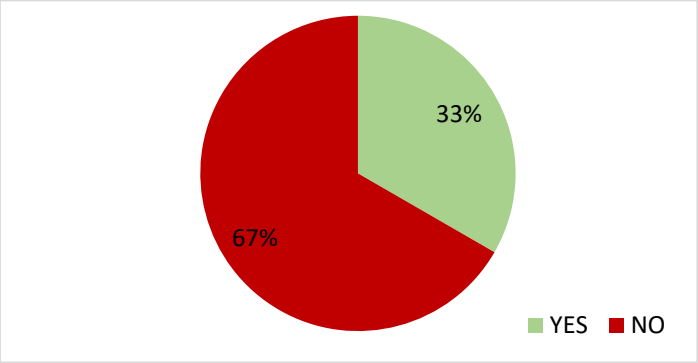
6. Bias towards indigenous Chinese companies vs. foreign companies

Some have commented that China's regulatory processes operate on a two-speed system, one for foreign companies and a faster speed for indigenous Chinese companies. Do you share this feeling?

Previously, the majority opinion was that China's regulatory process operated faster for indigenous Chinese companies than for foreign companies. In the 2020 survey, this opinion has migrated away from the belief that the regulatory system operates on two different speeds with two-thirds of companies rejecting that assertion.

The main reason for one-third of the companies still believing the two-speed regulatory process exists relates to imported products, which typically take longer to gain market authorization.

Figure 16: Opinion regarding potential two-speed regulatory system (Chinese vs. foreign companies)



Why is this statement TRUE?
• Imported products must repeat local efficacy trials even though this product has conducted trials oversea or are not new in China (e.g. in CVP already). • The two-speed system is mainly caused by additional regulatory requirement to the registration of imported products. For example, the registration of imported pharmaceutical products, the foreign companies need to conduct an "extra" local clinical confirmatory study in China, and this local clinical confirmatory study can only be initiated until the dossier/submission was reviewed by Committee hearing. However, for local companies, they can simply use the clinical data generated during research & development phase (prior to submission) to substitute the local clinical confirmatory study without conducing any extra clinical study. • For the regulatory process related to importation of biological samples and reagents, it currently only allows firms to import sample and reagents to be used for Quality Confirmatory testing by IVDC after the confirmation of Quality Standard. The current process does not allow firms to import samples and reagents to be used for local method transfer prior to the confirmation of Quality Standard. However, this process has imposed the difficulty for foreign firms to ensure the Quality Standard will meet the local technical capacity in China without conducting a method transfer and evaluation.
Why is this statement FALSE?
• Same requirement between local and MNCs. • The regulations are the same. • Local companies took similar time length to get registration • It will also take a long time and require a lot of study data to get approval for the registration of new product from indigenous Chinese companies. But it's faster for indigenous companies to get approval number by applying CVP products / generic products. I would say the above mentioned point of view is partly right. • For domestic or foreign products, it is more and more difficult to register it. • Both imported product and local products share the same registration guidelines. • The speed system is the same to local site of foreign company and Chinese company

Section E - REGULATORY TRENDS

1. Recent beneficial changes to the regulatory frameworks in China

What beneficial changes have occurred in regulatory frameworks SINCE 2015?

- Release of more precise technical guidelines, such as No. 2326 of MARA on the number of target animals in clinical trials of new animal biologicals;
- The initiative of having a general Priority Review guideline for pet/aqua products;
- For bio clinical studies, reduced animal numbers, facilitated pet product registration;
- The registration fee and sample test is free, but the test procedure is slower;
- Companies had the chance to be involved in the commenting on draft regulations.

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

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

- Simplification of the Registration requirements, including variations;
- Home/original registration procedures prevent bringing innovative products fast into China;
- Recognition with international standards and guidelines, such as VICH;
- More transparency in the communication channel between industry and CVDE reviewers;
- Facilitation of Minor Use/Minor Species;
- New Registration regulation and the guideline and law have not been issued since 2015 including No. 442, 44, 683, 630, 1247, and 1425.

3. Problematic changes to the regulatory frameworks in China

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

- GMO products have no clear review and approval timeline; the process is delayed;
- Residue analytical method validation at 2 different qualified contract research organisations and authority confirmation in China/Residue requirement influence the product's new registration and renewal, causing delay and cost increase;
- On January 01, 2018, enforcement of Good Clinical Practice (GCP) for veterinary drugs began in China. Currently limited accredited GCP sites are available. The new requirement increased the cost, challenges and timelines;
- No cost required for quality testing review; however, this triggers longer time to finish the test;
- Regulation of QR code increased the challenge and costs for multi-national companies;
- For the local producers, more strict inspection requirements since publication of legislation on Punishment on Serious Illegal Practice.

4. Business decisions as influenced by regulations

Have regulations played a major role in influencing you to take any of the major decisions listed in Figures 17a and 17b over the last five years?

Regulations can have a significant impact on business decisions. The survey presented a set of typical major business investment decisions and asked respondents whether regulations influenced those decisions. The outcome is presented in Figures 17a and 17b.

The main observation arising from these results in Figure 17a is that the business decisions most influenced by regulations all tend to favor a domestic focus within China as opposed to exporting production and R&D outside of China. The companies highlighted four decisions in particular:

- Restricting market focus in China
- Increasing the product range in China
- Investing in production in China
- Switching R&D budgets to labs inside China

In Figure 17b it can be seen that the business decisions that have been most influenced by Regulations are:

- Reduce coverage of certain species or indications in China
- Develop or avoid certain product technologies

Figure 17a: Business decisions as influenced by regulations

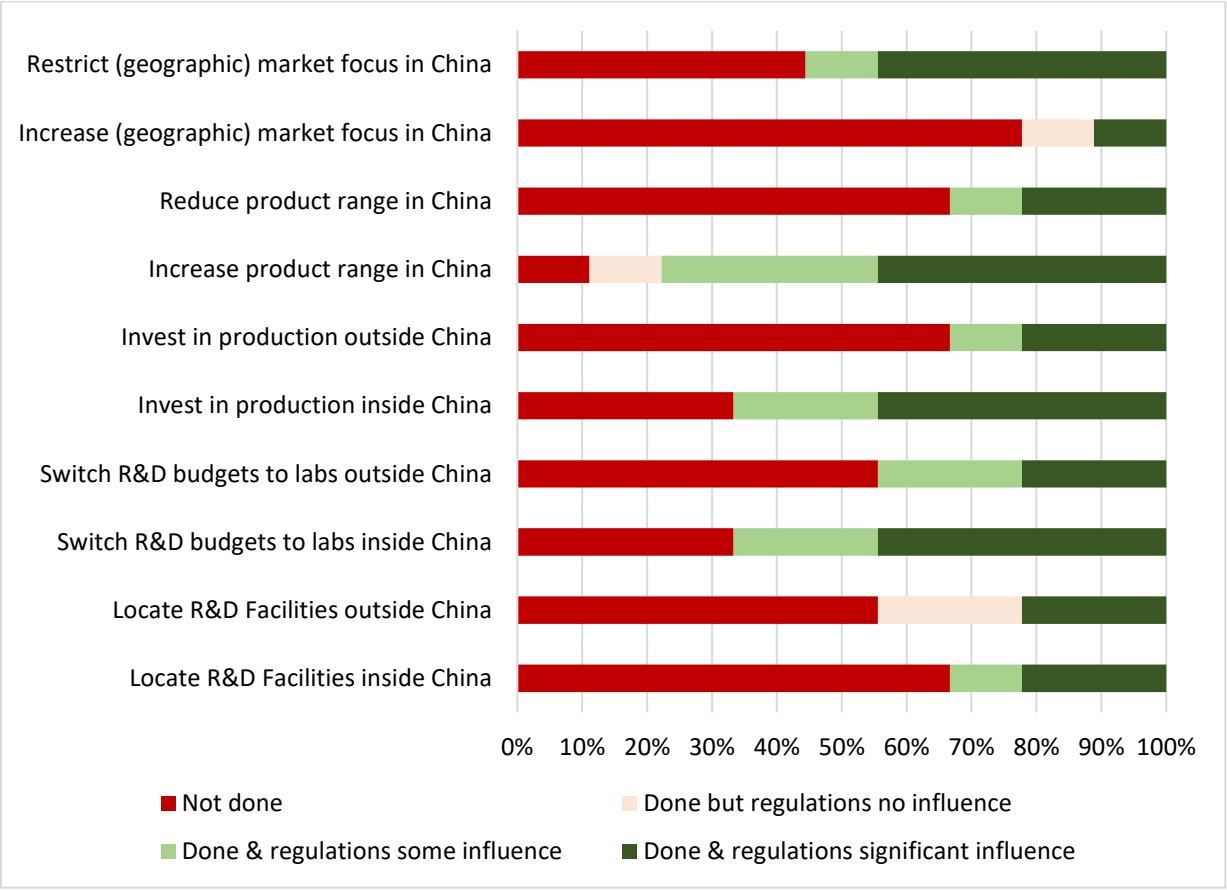
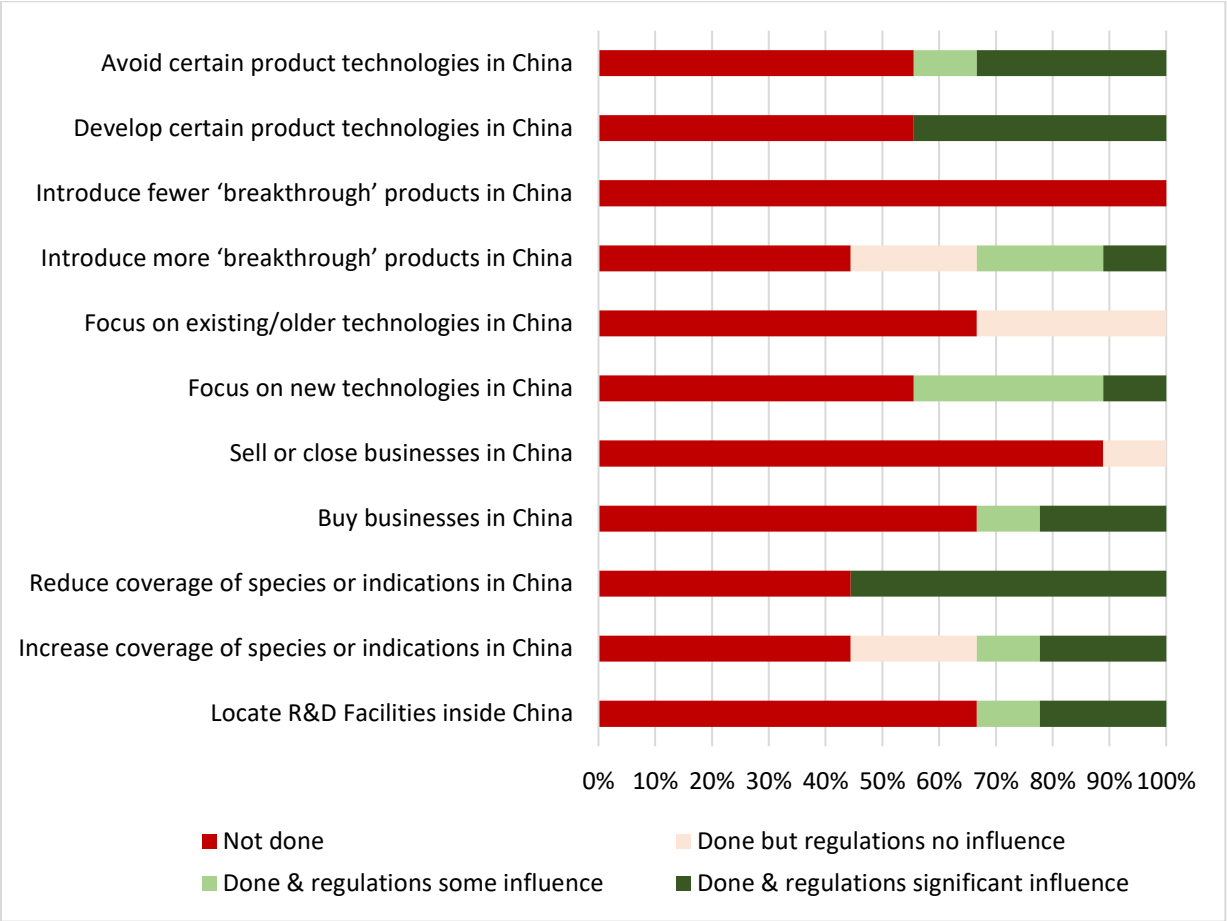


Figure 17b: Business decisions as influenced by regulations



Section F - HOPES AND EXPECTATIONS FOR THE NEXT 5 YEARS

1. Expected impacts of recent trends or changes in China's 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 changes to have on your business in the next 5 years?

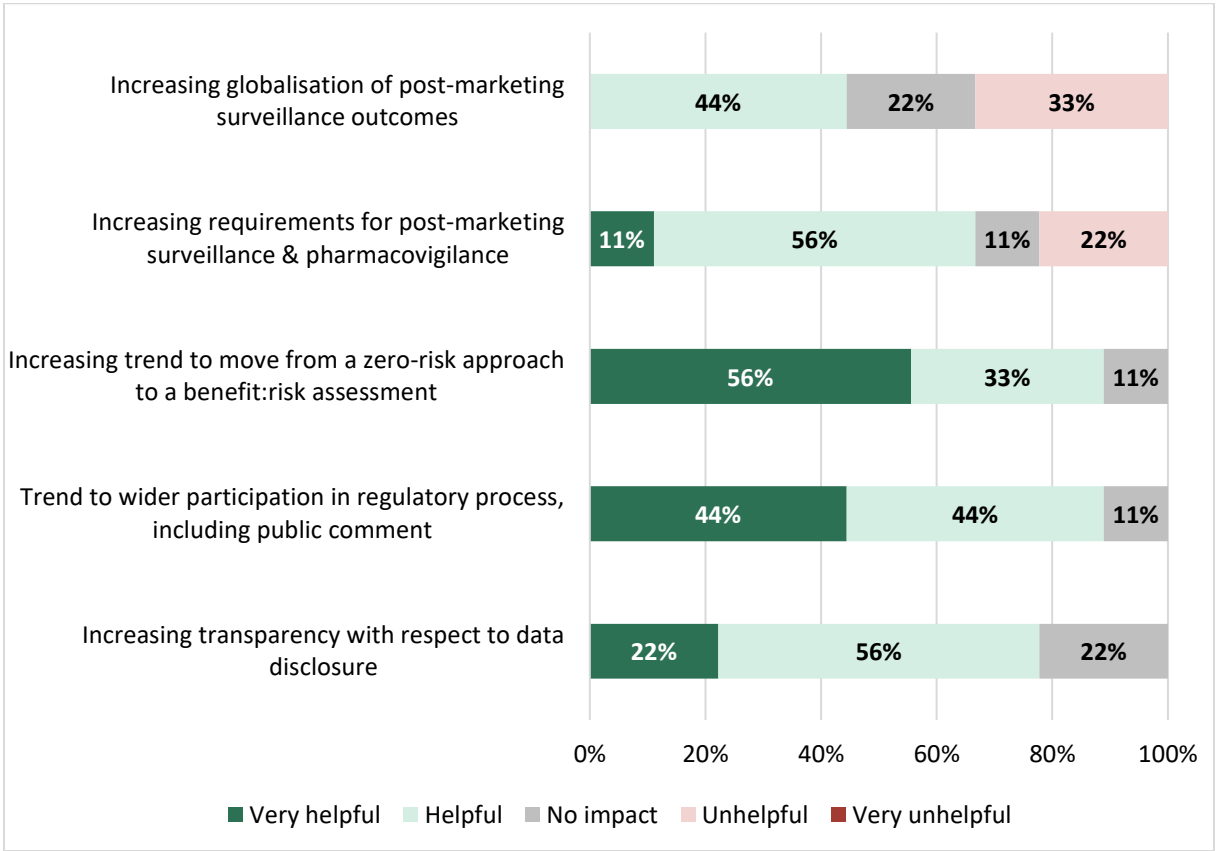
The companies' perceptions of the impact of China's regulatory approach are shown in Figure 18, and overall are extremely positive with none of the companies reporting any trends to be 'Very Unhelpful'.

The top three trends that companies perceived as Very 'Helpful' or 'Helpful' were:

- the transition from a zero-risk approach to a benefit-risk assessment,
- wider participation in the regulatory process including public comment and
- increasing transparency of data disclosure.

Two trends, both related to post-marketing surveillance and pharmacovigilance, did attract some negative responses.

Figure 18: Impacts of regulatory trends



2. Impact of foreign regulatory decisions on innovation

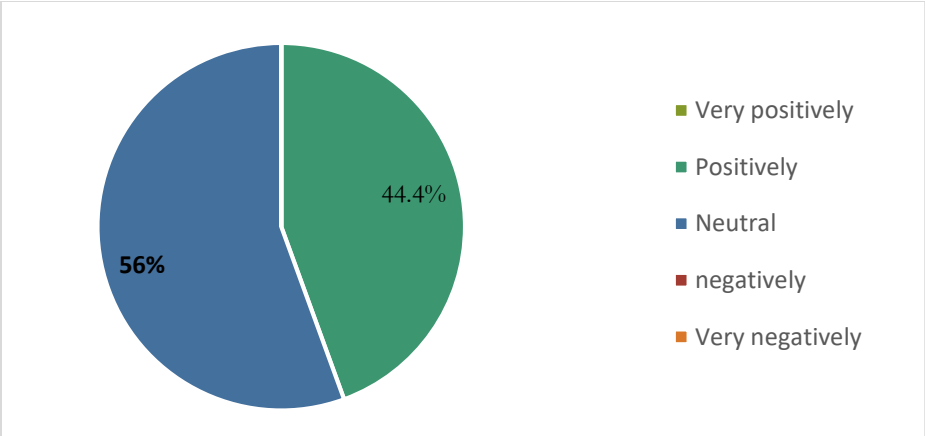
Does the use of foreign regulatory decisions in the Chinese review process impact your ability to innovate?

The use of foreign regulatory decisions in the Chinese review process may impact a company's ability to bring new products to the Chinese market by providing a level of assurance, particularly if the regulatory decisions have been issued by respected foreign regulatory agencies (such as those involved in the VICH initiative).

For multi-national companies, who are the main focus of this survey, it is important to be able to bring their products to global markets. Currently, these products are often first developed for the USA and/or EU markets, and thus a foreign regulatory decision will normally exist prior to bringing the product to the Chinese market.

In Figure 19 it can be seen that the existence of a foreign regulatory decision either has no impact or a positive impact on a company's ability to bring a new product to the Chinese market. It was also noted that there is no requirement to submit the foreign regulatory decision in China.

Figure 19: Impact of foreign regulatory decisions on innovation



3. What changes do you still want to see and why?

- Consulting system during development phase
- More transparency via communication and interaction between CVDE and applicant, IVDC lab and industry
- 'Home registration' or in parallel registration with other countries is suggested for the facilitation of registration
- Will draft the new management regulation, which was informed already
- To optimize registration process and clearly define the time frame for "EVERY" step in the process For applicants to get the GCP approval
- CVDE provide a clear guidance/process with details to industry on how to apply for priority review and how CVDE evaluate the application and give feedback to firms
- CVDE should provide details of each query and specify what additional documents are missing/required for the related section number in the submission
- There should be an increased involvement of IVDC on the review/confirmation of Quality standard to make sure the minimal/proper use of animal for the confirmatory testing.
- Global convergence
  See others from MARA and IVDC comments: D1 (b)

Section G - REGULATORY COOPERATION AND SPECIAL PRODUCT CATEGORIES

1. Regulatory trend for regional regulatory cooperation

(a) Does your regulatory authority engage in any forms of regulatory cooperation, such as joint reviews or parallel assessment, with another regulatory authority? (b) If yes, how do joint reviews or parallel assessment between CHINA and another country impact your ability to innovate?

All companies replied negatively to the query of potential regulatory cooperation. During the process of Review, the Chinese authority will refer to existing guidelines in China. If there are no related guidelines, they will then refer to guidelines of VICH or those from US/EU.

2. Special categories of products exempt from data requirements for registration

In your country do "special categories" of product exist, such as "minor species", or "generic" for which there is an exemption from certain data requirements (e.g. registration can be obtained with an abbreviated or abridged data dossier)?

One company reported the existence of "special categories" of products for the Chinese market. These were identified as: generics, local production license and green channel process e.g. on diagnostics for African Swine Fever (ASF).

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 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

ASF	African Swine Fever
API	Active pharmaceutical ingredient
CA, CAP	Companion Animal[s], CA Product[s]
CMC	Chemistry, Manufacture and Controls
CMO	Contract Manufacturing Organization
CP	Centralized Procedure
CRO	Contract research organization
CVDE	China's Center for Veterinary Drug Evaluation
CVP	Chinese Veterinary Pharmacopoeia
EP	European Pharmacopoeia
GBS	Global Benchmarking Survey
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GSP	Good Supply Practice
GMO	Genetically modified organism
IP	Intellectual Property
IVDC	China's Institute for Veterinary Drug Control
MAH	Marketing Authorization Holder
MARA	Ministry of Agriculture and Rural Affairs
MLV	Modified live virus
MOA	China's Ministry of Agriculture
MUMS	Minor Uses-Minor Species
MSPs	Minor Species products
R&D	Research and Development
TGA	Therapeutic Goods Administration, Australia
TPP	Trans-Pacific Partnership Agreement
VICH	Veterinary International Cooperation on Harmonization (of Technical Requirements for Registration of Veterinary Medicinal Products)

Report prepared with support of Kellen 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

Health for Animals
global animal health association