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Contents

Article

A New Choice for Marketing Mode of Medical Devices: Mobile Phone Media

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ABSTRACT

Since the release of Chinese economic reform, the industry of medical devices has gained a rapid development in China and has been one of the important supports for national economy. The marketing of medical devices is facing problems such as white hot market competition, large amount of medical device products, severe blind marketing, single marketing mode and incomplete marketing network. Limited by the traditional marketing mode, the advertisements input by the medical device enterprises produce low economic benefits, suggesting the traditional marketing mode for medical devices has not been able to keep pace with the rapidly developed digital age. The emergence of mobile phone media solves the deficiencies of the traditional marketing mode in the aspects of creativity, interactivity, accuracy, service and marketing network and becomes a new marketing mode for medical devices. Mobile phone media based marketing improves the popularity of medical device enterprises, help establish good corporate image, enhances the sales volume of medical device products, and increase profits, which attributes to its advantages that is distinguished it with traditional media. Moreover, it also improves the grade and intangible value of commodities and brings about more economic benefits to enterprises.

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Keywords: medical devices; mobile phone media; marketing; mobile demand side platform

INTRODUCTION

With the rapid development of science and technology and the intensive competition of medical device market, Chinese customers have gradually generated new understanding on the consumption of medical devices. As a result, traditional marketing mode has not been able to adapt to the situation, and transformation is imperative. Liu QF, a Chinese scholar, mentioned in his article that, medical device industry is a multidisciplinary-cross, knowledge-intensive and capital-intensive high-tech industry. [1] He thought, the marketing of medical devices in accordance with customer perception could center on the strategies of product development and design, sales promotion and pricing. The development speed of intelligent mobile phones has far beyond the estimation of people. Because of the popularity and flexibility of mobile phone and the timeliness of network, mobile phone media is featured by strong interaction, high transmission speed, wide scope and small limitation, but few studies concerns about mobile phone media based marketing. [2] Pearson pointed out in his article that, mobile social technologies changed not only the communication pattern between people but also the communication pattern between advertisers, marketing staffs and customers. [3] Dialogue mining and emotional analysis in multiple social channels can help create strategies, attract new clients, and moreover display the important understanding of enterprises on their products, thereby providing a huge opportunity for any enterprises which want to enter the world of mobile and social media marketing. Zhang LP held that, the effects of mobile phone on human should not be ignored under the background of mobile internet, and enterprises could get a part of benefits from the industry if getting good command of mobile phone marketing strategies. [4] This study aims at discussing the economic benefits that mobile phone based marketing can bring to the marketing of medical devices based on the status of medical device market in China and related marketing problems and specific mobile demand side platform (DSP) cases.

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BACKGROUND

With the constant development of economy, continuous growth of population, the deepening of aging and the improvement of health care consciousness, demands for global medical devices has been in sustainable growth. It has been one of the industries with the fastest development in the world today.

Medical device industry is a multidisciplinary cross, knowledge-intensive and capital-intensive high-tech industry.[5] As to the global medical device market share, America accounts for more than 40%, Europe for 30%, Japan for 15% ~ 18%, and China for 2%.

Though the medical device industry in China which started lately has a great gap with the developed countries, its development speed is attractive. With the development of Chinese economy and higher requirements on health, the demands of both high-end medical devices and convenient domestic medical devices have achieved substantial increase, which creates a broad development prospect for the domestic medical device industry. The medical device market in China is excessively active. The policies released by Chinese government and the requirement for updating of equipment in Chinese medical and health organizations both make China be a huge market for medical device consumption and sales. The 13th five-year plan which concerns medicine industry and health care has confirmed high-performance medical devices as one of the key breakthrough fields, which undoubtedly brings hopes for the future development of medical device industry in China.

ANALYSIS OF MEDICAL DEVICE MARKET IN CHINA AND RELATED MARKETING PROBLEMS

Since Chinese economic reform, the development of the medical device industry as one of the supports of medical and health cause is attractive.[6] Especially at the beginning of 21st century, the medical device industry has entered a rapid-growth stage. Between 2000 and 2009, the overall scale of Chinese medical device industry increased for 6 times, and the proportion of the industrial growth value in the national Gross Domestic Product (GDP) went up steadily.

The medical device industry in China has experienced introduction, absorption, digestion and independent development and innovation. Moreover, the system with complete variety, broad coverage, perfect industrial chain and advanced technologies has been established. It has been the pioneer and basic industry in the process of economic transition of China.

The medical device manufacture industry in China with huge potential is becoming a new global center for medical device manufacture; however, there are still many problems in the medical device market.

1. With the reformation and openness of medical policies, the market is further opened; medical device enterprises from other countries come in, and the domestic medical device enterprises rise sharply, which intensifies market competition.
2. The technical levels used in producing medical devices differ significantly; limited by financial strength, low-end market clients usually purchase domestic medical devices.
3. The rapid development of medical device industry has attracted a large amount of investment and the participation of enterprises. They blindly follow market tendency, resulting in the severe repetition of categories of medical devices and the aggravation of competitive pressure between products of same kind.
4. The marketing network of medical device enterprises has not kept up with the rapidly developed industry. The single marketing tool, shallow channel construction and narrow marketing convergence greatly limit the marketing towards final-end clients.

The limitations caused by the single marketing mode and traditional marketing mode lead to the lower conversion rate of advertisement and economic benefits as well as the following marketing related problems.

1. Lack of creativity.[7] Limited by the traditional marketing mode, the marketing tool used by medical device enterprises is single, and the marketing content is dull, which is difficult to attract the attentions of clients, leading to general marketing effect and weak response. Nowadays, many users read messages using fragmented time.[8] Only the advertisement that can trigger the interest of customers at a glance can attract them and inspire purchasing desire.
2. Weak interaction. In the traditional marketing mode, users receive marketing information passively, with little independent option and less opportunities for communicating with enterprises. Medical device enterprises are in no interaction relationship with the advertisement audience, which fails to connect them by marketing and moreover weakens the effect of marketing.

3. Low precision. Due to the support deficiency of a large amount of user data, advertisement of medical devices may not be put precisely according to user information such as job category, consumption capacity, financial situation, family status, interest and hobbies, leading to overgeneralization.[9] The putting of medical devices advertisement makes up precision deficiency by enlarging the scope, resulting in the waste of advertisement funds.
4. Poor service. Due to the lack of guarantee of convenient communication, enterprises are difficult to provide timely and accurate pre-sales and after-sales services after the marketing content of medical devices are released in the traditional marketing mode. The improvement of sales volume depends on consumers. Therefore, the important role of users in marketing should be paid attention to.[10]
5. Incomplete sales network. The marketing platform of many medical device enterprises is so single that customers cannot purchase products conveniently, which reduces the purchasing rate.

The emergence of mobile phone media marketing,[11] a novel marketing mode, solves the aforementioned problems. It brings huge economic benefits to the medical device enterprises which launch advertisement, with extremely high conversion rate.

ECONOMIC BENEFITS BROUGHT BY MOBILE PHONE MEDIA MARKETING TO MEDICAL DEVICE ENTERPRISES

Nowadays, advertisement has taken over the APP information flow of mobile phone. The development of intelligent mobile phone and new media technology, the extension of network ecological platform and the growth of mobile phone media have forced a large number of putting opportunities of mobile phone advertisement and also enriched the putting modes and channels such as microblog corporate account, WeChat public plat and various APP.[12,13]

The huge mobile phone APP market provides broader support for the transmission benefits of advertisement. The conversion rate of such a kind of scenario proactive trigger is extremely high. Moreover, the conscious or unconscious secondary transmission of users brings huge economic benefits.

To improve sales volume of products and create economic benefits, enterprises appeal consumers to pay attention to and actively understand their brands through releasing advertisement in mobile phone. In observation process, consumers may produce favorable impression on the brands and then purchase their products.

Users can directly skip to the purchasing pages to pay through clicking the advertisement on mobile phone.[14] Advertisers adjust putting strategies to obtain higher input-output ratio and improve economic benefits by precisely calculating promotion channels and data motivated running.

Advertisement marketing based on mobile phone media can improve the popularity of medical device enterprises, help build good corporate image, enhance sales volume of medical device products, and bring profits for enterprises, which are affected by its advantages which distinguishes it with the traditional media. Moreover, advertisement via mobile phone can improve the grade and intangible value of commodities and bring more economic benefits to medical device enterprises.

TAKING MOBILE DEMAND SIDE PLATFORM (DSP) AS AN EXAMPLE

Mobile DSP refers to the advertisement putting platform that crosses media and mobile terminal applications.[15] Advertisers can pay for the right of displaying advertisement based on real-time data analysis.

For example, a medical device enterprise expects to increase the visitor volume on its official website, phone consultations and sales volume of products.

Firstly, the advertisement delivery strategy was formulated.

a. regional orientation: geographical location was confirmed based on the distribution of population which is in demand of medical devices and location based service (LBS), mainly covering shopping mall and office area.
b. media orientation: APP which was highly adhered to medical devices was selected as the major platform for advertisement according to the analysis results of attributes of consumers.
c. Population orientation: people who aged from 35 to 50 years old or were interested in sports or health preservation or ordinary white-collar workers were regarded as the target population.

Figure 1: The diagram of an advertisement of a sphygmomanometer in the form of insert screen

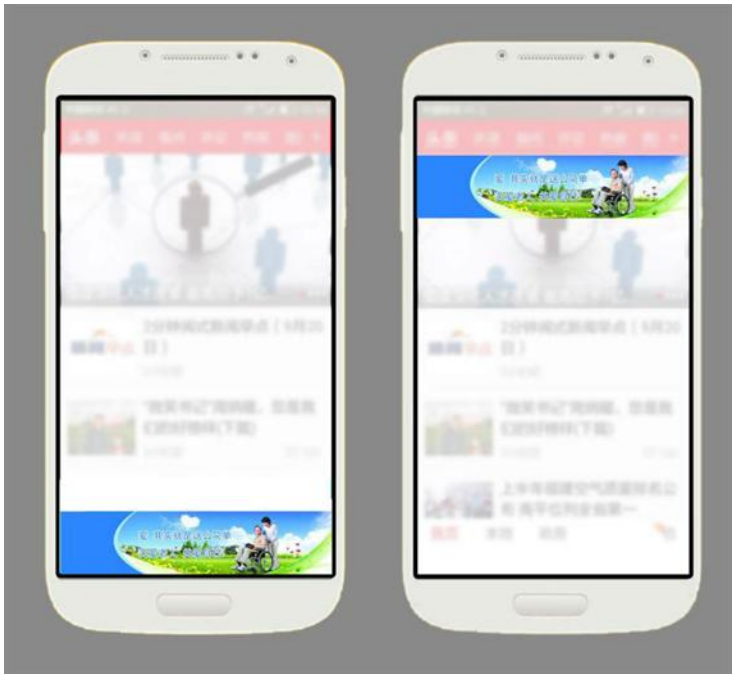

Figure 2: The diagram of a wheelchair in the form of banner

d. Time frame orientation: advertisement were displayed from 8:00 am to 6:00 pm.

The medical device advertisement was displayed in the form of insert screen and banner (Figure 1 and 2) for four days according to the formulated strategy. The size was not limited.

The background operation interface is shown in figure 3.

After the putting of advertisement, the data were compared. It was found that, the click volume mainly concentrated on the period from 9 am to 16 pm, and from 21 pm to 24 pm. The detailed distribution is shown in table 1. The analysis and observation of data in different periods directly reflected the behavioral habits of users. Increasing the input ratio of advertisement in the two periods could improve the effect of advertisement and conversion ratio of advertisement putting to click.

Besides the putting period, we found that, the major click volume was from China Mobile (55.7%), followed by China Unicom (11.49%), China Telecom (6.87%) and other (26.47%). Therefore, the putting volume of advertisement for China Mobile users can be increased.

In addition, by comparing the click volume of advertisement in different sizes, we found that, the click volume of the insert screen advertisement in a size of 320 * 480 accounted for 61.54%, that of the advertisement in a

Figure 3: A diagram of advertisement putting operation platform in DSP

Table 1: A report for the analysis of click volume in different periods

Period	Percentage of click volume
0:00–4:00	1.15%
5:00–8:00	2.46%
9:00–12:00	26.39%
13:00–16:00	25.65%
17:00–20:00	19.17%
21:00–24:00	25.18%

size of 640 * 100 accounted for 29.14%, and the advertisement in other size only accounted for a few percentages.

The advertisement put in this test achieved 102456 clicks. At the end of advertisement putting, the visitor volume on the official website, the phone consultations and the sales volume of the products all suggested remarkable improvement. More than 10 thousand clicks were achieved within the controllable cost. Moreover, the cost was 28.18% lower than that of the other traditional marketing means, and its conversion rate was 3 to 4 times that of the other means.

With the increase of the scale, online time and online frequency of intelligent mobile phone users, mobile terminal has gradually become an important platform for advertisement development, and mobile DSP is facing with a development opportunity and its growth speed has been far more than the development speed of DSP market and the overall advertisement market. Mobile terminal has been a new driving force for industrial development. Medical device enterprises as the advertisers can precisely put DSP advertisement via mobile

phone media, which can yield twice the result with half of the effort.

CONCLUSION

Throughout our life, consumption via mobile phone has exceeded consumption via the traditional PC. Mobile terminal advertisement tends to be account an increasingly more proportion in enterprise marketing budget. Motivating sales via advertisement can improve rate of return on investment and maximize the economic benefits of advertisement. With the further development of Internet, medical device enterprises must realize the changes caused by the reformation. The changes in the marketing mode and concepts of the medical device industry are imperative. In the we-media age, information transmission is featured by higher speed, better quality, larger amount, wider scope and more patterns. Compared to the traditional marketing ways, marketing via mobile phone media can integrate multiple media resources together, trigger the interests of audience through creative marketing means, recycle user information while transmitting advertisement information to provide data support for marketing next time. Enterprises should pay high attention to mobile phone marketing tools, improve brand exposure rate by formulating marketing strategies taking creativity, interaction, preciseness and service as key elements, and expand sales platforms and marketing development space with network, thus to obtain more economic returns and create more economic benefits with less advertisement investment.

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Article

Venture Investment Assessment of the Biotechnology Industry

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ABSTRACT

The biotechnology industry has been the leading industry among various high-tech industries since the mid- and late stage of 20th century and has applied in many fields. Venture investment originates from the same stage. This study evaluated the value of venture investment programs through qualitatively analyzing the venture investment of the biotechnology industry. According to the characteristics of biotechnology industry, a biotechnology industry venture investment assessment indicator system was established firstly. Then a cluster-radial basis function (RBF) neural network comprehensive evaluation model was established. The comprehensive evaluation value of the biotechnology industry venture investment programs was obtained through analyzing the relational expression with regard to biotechnology industry production value and venture investment. The above models and relational expression were verified. The fitting coefficient of the model empirical results suggested that reached 0.912, and the error in the comprehensive evaluation model test was 0.052. The dynamic simulation result ranking was highly identical with the practical operation results. The empirical results of the relational expression suggested every 1% of increase in the logarithmic value of biotechnology industry venture investment could result in 0.727% of increase in the industry program production value. Therefore, the models and relational expression obtained were verified with practical operability and certain accuracy. Venture investment can effectively promote the development of the biotechnology industry and produce positive impact on the development of venture investment in the biotechnology industry in China.

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Keywords: Biotechnology, venture investment, evaluation

INTRODUCTION

Biotechnology industry is a practical technology which integrates modern biological science and engineering technology and creates new biological function. As an important part in high-tech industry, it is featured by high input, high yield and high risk. Biotechnology industry which develops rapidly in the worldwide has become a new economic growth point;[1] it is a commanding point which makes all countries race to control in the strategic emerging industry. The release of a series of policies by the Chinese government for the biotechnology industry indicates its importance, which is also a symbol that biotechnology in China has entered the rapid development period. Venture investment is an innovative financial mode with high risk and high yield, and its investment concept is extremely consistent with the development demand of high-tech industry.[2] The biotechnology industry requires capital input, while venture investment is ready to undertake high risks to support the development of biotechnology for the pursuit of high yield.[3] Thus biotechnology venture investment is the combination of the two matters. Sohn B.K. et al.[4] investigated the influence of venture investment on the corporation and innovation of small enterprises in the biotechnology industry. Vida P.[5] drew a conclusion from the published publications that eastern European countries should adapt to the venture capital market of domestic biotechnology industry, adjust relevant policies and regulations, and improve investment environment. In biotechnology industry venture investment, the application of biotechnology venture investment comprehensive assessment model can effectively simplify the complexity of program investment risk assessment, improve accuracy, reduce error and enhance pertinence. This study found that, every 1% of increase in the logarithmic value of biotechnology industry venture investment could result in

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0.727% of increase in the industry program production value, suggesting the model can effectively evaluate the venture investment of the biotechnology industry.

INDUSTRY VENTURE INVESTMENT PROMOTING BIOTECHNOLOGY

Venture Investment Mechanism of the Biotechnology Industry

The venture investment mechanism of the biotechnology industry is consistent with the common venture investment mechanism,[6] but it focuses on the investment on the biotechnology industry. Venture investment mechanism is composed of financing,[7] funding and capital withdrawal,[8] and the subjects involved include fund provider, fund operator and venture investment enterprise. Fund firstly flows from the fund provider to fund operator and then flows to potential venture investment enterprises after the selection decision made by the fund operation institute. The value of the fund is increased after the fund operation institute invests the venture investment enterprise. The fund flows back, and the investors obtain the benefits. It is the whole fund circle chain.

Benign Interaction Between the Biotechnology Industry and Venture Investment

The biotechnology and venture investment are mutually interactive.[9] The biotechnology industry can satisfy the requirement of venture investment for pursuit of high return. They need each other and have consistent interest. Venture investment can effectively solve the problems of large financial input and difficult fund procurement in the biotechnology industry and ensure the innovative achievements in the industry to be transformed into products rapidly. The development of the biotechnology industry also can promote the development of venture investment in turn to provide a space for the development of venture investment. Therefore, they are interactive.

RELEVANT THEORIES

Cluster Analysis Method

Cluster analysis method which originates from Analytic Hierarchy Process method is a multi-element statistical analysis method that classifies indicators.[10,11,12] The method, in nature, classifies elements based on the statistics which can objectively represent the relationship between elements.

The comments of experts were converged using cluster analysis method. The first convergence generated elimination criteria according to the evaluation indicators of experts and practical conditions, while the second convergence weighted the remaining comments to obtain the final weight. The two convergences could obtain relatively scientific weights.

Radial Basis Function Neural Network (RBF Neural Network)

Neural network is a brand-new information processing means which can simulate human brain neurons.[13] There are two kinds of neural network, RBF neural network and BP neural network.[14] The former has generalization ability; therefore, it is advantageous in venture investment assessment. RBF neural network is a feed forward neural network containing RBF neuron hidden layers and linear neuron output layers.[15]

A COMPREHENSIVE EVALUATION MODEL FOR BIOTECHNOLOGY VENTURE INVESTMENT

Modeling of Cluster-RBF Neural Network Investment Assessment

Design of the input layer

The biotechnology industry venture investment assessment indicator system was established based on impacts of external environment, the competitive ability of enterprises and the characteristics of programs. Firstly, the weight of each indicator was determined according to scores given by the experts, i.e., the judgment matrix of the main criterion layer to the target layer was established. Then the judgment matrix of the main criterion layer to sub-criterion layer was established according to the same principle. Finally, the least important

Table 1: Summary of indicator values of five biotechnology programs in Xiaman, Fujian

Program Indicator	First	Second	Third	Fourth	Fifth
Uniqueness of products	0.8	1	0.8	0.6	1
Replaceability of products	0.6	0.8	0.8	0.6	0.6
Market scale	0.8	0.6	1	0.8	0.8
Market acceptance of products	0.6	0.8	0.6	0.6	0.6
Development period	0.6	0.8	0.6	0.6	0.6
Expected yield rate of investment	0.8	0.8	0.8	0.6	0.8
Organizational structure	0.6	0.8	0.6	0.6	0.6
Technical level	0.8	1	0.8	0.6	0.8
Intellectual property	0.8	0.8	0.6	0.8	0.6
Marketing group	0.4	0.8	0.6	0.8	0.8
Sales policy	0.6	0.8	0.4	0.4	0.6
Local policy support	0.2	0.4	0.4	0.2	0.4

indicators, i.e., the indicators with the lowest weight in the sub-criterion layer, were removed on the condition that there is no influence on assessment. The indicators left after the above procedures were taken as the input layer of the investment evaluation model.

Design of the output layer

The output layer of the model was the comprehensive assessment value of biotechnology industry venture investment. To make the output values of the model correspond to the program assessment results, a venture investment assessment result corresponding table was designed according to the practical situation of the biotechnology industry and the experience of the experts. The results were divided into five grades, the first grade for extremely higher investment value, the second grade for high investment value, the third grade for the medium investment value, the fourth grade for the low investment value and the fifth grade for the extremely low investment value.

MatLab2008 statistical software is capable of analyzing neural network system. Therefore, the model was realized by MatLab2008 statistical software.

The Actual Measurement of Venture Investment Program

The selection of venture evaluation indicators

Biotechnology industry venture investment combines the characteristics of both the biotechnology industry and venture investment, i.e., high return rate and high risk. However, the biotechnology industry also has uniqueness, for example, strong dependence on resources, long returning cycle and large investment. Therefore, when the system of biotechnology venture investment program evaluation indicators is designed, the uniqueness of the biotechnology and venture investment should be both considered to ensure the scientificity of results. Therefore, the biotechnology industry venture investment evaluation indicator system is mainly based on the target layer, i.e., influence from external environment, competitive capacity of enterprises and program characteristics. The main criterion layer includes program characteristics, market characteristics, program development stage, economic benefits, social and environmental benefits, management capability, technical level, production ability, marketing and financial capability and policy environment. Sub-criterion layer includes uniqueness

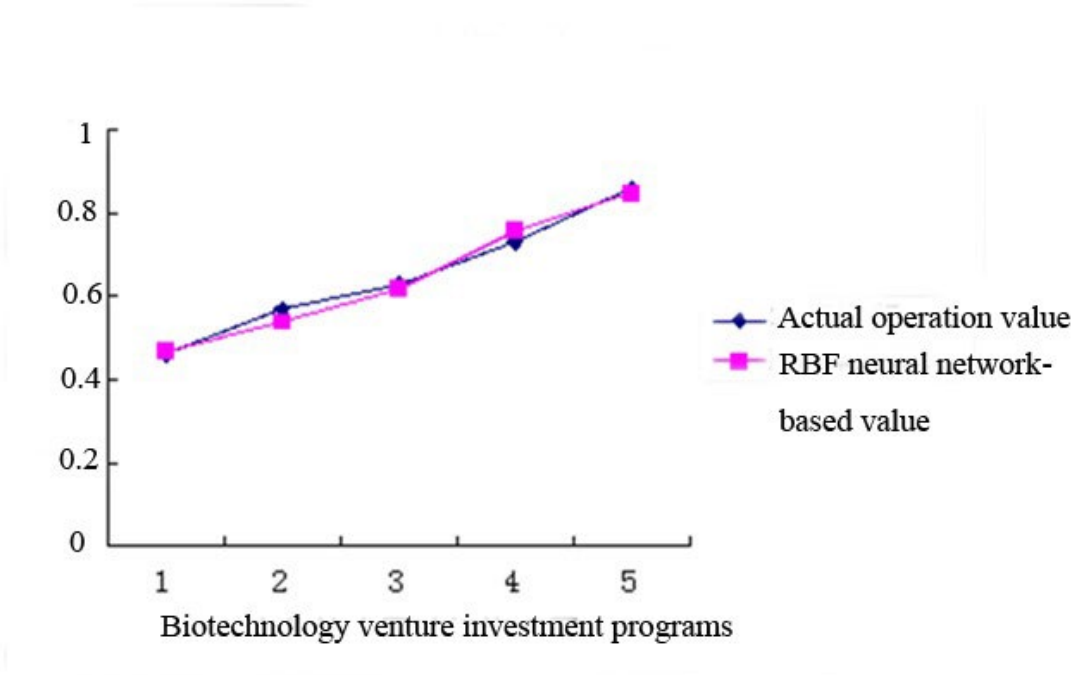

Figure 1: Comparison of comprehensive evaluation values and actual operation values

of products, replaceability of products, barrier entrance, market scale, competition level, market acceptance of products, development stage, investment scale, expected yield rate of investment, investment recovery period, discount rate, employment rate promotion, industrial adjustment promotion, influence on natural environment and social environment, manager ability, organizational structure, management scientificity, technical level, technology life cycle, intellectual property, marketing group, sales policy, capital operation ability, capital structure, industrial policy and local policy support.

Acquisition of sample data

Five most representative biotechnology venture investment programs in Xiamen, Fujian were selected as samples. The scores for different biotechnology industry venture investment evaluation indicators given by experts from the field were collected. The scores with large differences were removed, and the other expert comments were kept, in order to ensure the unity of data. Finally, 12 important indicators were obtained. In table 1, 0.1 stands for unimportant, 0.2 stands for not very important, 0.4 stands for moderately important, 0.6 stands for important, 0.8 stands for very important, and 1 stands for the most important.

The data demonstrated in table 1 were from the venture investment programs developed by multiple venture investment institutes in Xiamen, Fujian. The demonstration of the model was realized by MatLab2008 statistical software. The analysis results are shown in figure 1.

Comparison of cluster-RBF neural network based comprehensive evaluation value and actual operation value

It could be seen from figure 1 that, the simulation results of the cluster-RBF neural network training set agreed well with the actual operation results. The fitting coefficient was 0.912, and the testing error of the comprehensive evaluation model was 0.052. The results suggested that, the evaluation and prediction efficacy of the model was good, and the results were reliable, suggesting high practical values.

The relationship between biotechnology output value and venture investment

It could be seen from figure 2 that, the venture investment volume and the biotechnology production value tended to increase overall, and the fluctuation amplitude of venture investment volume was larger than the biotechnology production value, suggesting there was a relationship between them but the influence was not obvious. The total investment amount which was input into the biotechnology industry was regarded as the

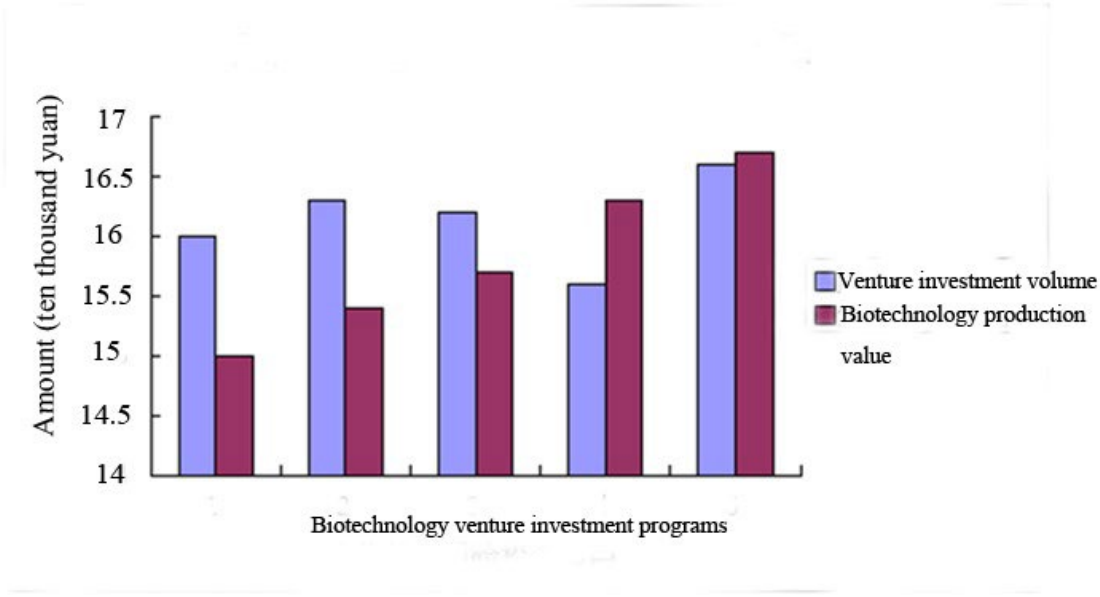

Figure 2: Relationship between biotechnology production value and venture investment

explanatory variable, and the venture investment volume and biotechnology production value in figure 2 were substituted into the relational expression. Regression analysis was performed using SPSS; the regression coefficient was 0.727. Therefore, it could be concluded that, every 1% of increase in the logarithmic value of biotechnology industry venture investment could result in 0.727% of increase in the industry program production value. The results suggested that, venture investment did not achieve the best the best effect in the biotechnology industry. It could be concluded that, China has not fully realized the mutual promotion effect between venture investment and the biotechnology industry, and the fluctuation amplitude of venture investment volume in the biotechnology industry was large, which was mainly attributable to national policies.

CONCLUSION

In conclusion, the biotechnology venture investment comprehensive evaluation model proposed in this study aims at improving evaluation accuracy, which is beneficial to the pre-judgment of venture investors and can provide referable theories and practical operation for venture investors and help them effectively evade investment risks, reduce the loss induced by wrong investment and improve investment return rate. This work is valuable for governmental departments timely controlling the market of biotechnology industry venture investment, establishing scientific and reasonable biotechnology industry venture investment evaluation systems, formulating relevant laws and policies that accord with national conditions to support and guide the reasonable development of biotechnology industry venture investment, optimizing industrial structure, and enhancing talent cultivation in the biotechnology industry and venture investment.

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Article

Discussion on Marketing Strategies for Medical Facilities under the New Environment

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ABSTRACT

After entering the 21st century, the economic and scientific and technological levels of China show a tendency of rapid rise. On account of it, medical level is also developing, and the requirements for medical institutes and equipments have become stricter. In recent years, the medical facility market in China is facing a complicated environment, and many traditional medical facilities have been gradually replaced. Medical marketing plays a crucial role in improving the position of Chinese medical facilities in the industry. In the perspective of the current new environment, this study investigated the marketing strategies of Chinese medical facilities, aiming to provide a reference for their positive development in the new environment.

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Keywords: New environment; medical facilities; marketing strategy; market; status

INTRODUCTION

With the expansion of demands on medical treatment and health in recent years, demands on medical facilities have also increased, and the development space for medical facilities has become larger.[1] To positively develop medical facilities, the implementation of marketing strategies should be emphasized. The number of medical facility producers in China is increasing, and the categories of medical facilities become diversified, presenting a good development trend.[2,3] Huge challenges also exist though there are favorable development opportunities. Foreign medical facilities constantly swarm into China, with the purpose of taking a share of the spoils in Chinese medical facility market, which intensifies the competition in the medical facility market.[4] Therefore, Chinese medical facility producers pay attention to the formulation of marketing strategies for medical facilities when improving their own technical competition. Through studying journal articles, Kriza C. held that, the supervision and guidance for medical facilities are lack of in China in the new environment, and a good connection should be kept between supervision institutions, health policy decision makers, national and international health technology evaluation network and medical facility producers.[5] Based on the connotation and essence of experience marketing, Huang T. Y. et al. put forward the strategy for experience marketing of health care facilities.[6] Taking medical facility company A as an example, Shi N. X. proposed solutions for some marketing management problems and final marketing strategies.[7] This study explored the marketing strategies of medical facilities under the new environment, aiming to assist the health development of Chinese medical facilities.

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THE NEW ENVIRONMENT FACED BY CHINESE MEDICAL FACILITIES

To satisfy the constantly improved requirements, various medical facilities are being development constantly. As a result, the market competition of medical facilities becomes more and more fierce. To gain a firm foothold in the medical facility market and highlight the advantages in the industry, the formulation of new marketing strategies is needed. The current new environment can be summarized as follows. With the further development of global economic globalization, market environment

has changed, and medical market has become international, leading to the intensive competition between medical facility products and the changed marketing level.[8] Though the new environment may be beneficial to the development of medical facility marketing, there are also new situations and challenges. The competitive level of medical facility products has changed gradually. The superhigh requirements on the medical level also promote the updating of medical facilities; hence, the sale of medical facilities has presented a new development direction. Moreover, governmental supervision reduces the burden of people and improves people's welfare, which makes the medical facility marketing more scientific and rational and plays an important role in the purchasing of medical facilities. Therefore, we should grasp the opportunities in the new environment and positively cope with difficulties and competition to promote the sale of medical facilities.[9,10]

FORMULATION OF MARKETING STRATEGY IN THE NEW ENVIRONMENT

Cultivation of Marketing Staff Ability

A sales team in which everyone gets a good knowledge of medical facilities and marketing should be established. Firstly, the sales staffs should be informed with the knowledge about medical facilities and sales.[11] Secondly, the sales staffs can communicate with medical staffs frequently to ask for the requirements of hospitals on medical facilities, thus to perfect products. While marketing products to customers face to face, the sales staffs should emphatically introduce the advantages of facilities and also consider the demands of customers; sincere attitude is also important to the sale of medical facilities. The self accomplishment of the sales staffs is the second point after they have acquired the professional knowledge. Good manner of dealing with people and elegant appearance are beneficial to the improvement of self accomplishment. During the enhancement of competition ability of medical facility producers and the expansion of medical facility sales, the overall accomplishment and working ability of the enterprise staffs should be improved, and moreover the cohesiveness of the enterprise staffs should be strengthened, which are helpful to strategic marketing in the new environment.

Establishment of Cooperative Relationships

To increase the sales amount of medical facilities in the new environment, the satisfaction of customers should be improved firstly. Many customers are involved as the purchasing decision makers and users are not the same. Decision makers are cautious in purchasing large-scale medical facilities as they will consider whether doctors will use medical facilities in the treatment of patients or not. To eliminate the worries of decision makers about the future, it is not enough to assist the clinical examination and treatment of patients through medical facilities relying on favorable price only. Correct marketing modes should be established based on the customer-oriented concept. Moreover, the loyalty of customers should also be paid attention to. The defects of medical facilities should be proposed immediately once being discovered. The sellers should treat customers with sincere attitude and build good service awareness for the purpose of long-term cooperation. They should contact with customers from time to time to ask for the problems encountered during use and positively work based on the concept of cooperation. In the situation of win-win cooperation, the products can be recognized by customers through their clinical use and development prospect in addition to technologies. But the customers who buy large-scale medical facilities usually cooperate with large-scale medical facility institutions. Therefore, the sales channels are narrow, and the customers are limited. To increase the sales amount of large-scale medical facilities, the sellers should establish a good cooperative relationship with customers to acquire their trust and improve loyalty.

Establishing Network Marketing Mode

The marketing strategies of medical facilities in China focus on marketing staffs. But with the constant development of social economy, network marketing has gradually been one of the main marketing channels. The convenience and diversification of network not only make customers convenient, but also bring lots of benefits for producers. Producers can display the medical facilities they produced and related information about medical facility institutions on webpage and establish consultation areas for the intentional customers to understand facilities deeply to build a comfortable relationship and promote the sale of medical facility products. It can be concluded from the above views that, network marketing is beneficial to the sale of medical facilities. Hence, the establishment of networking marketing mode is quite necessary.

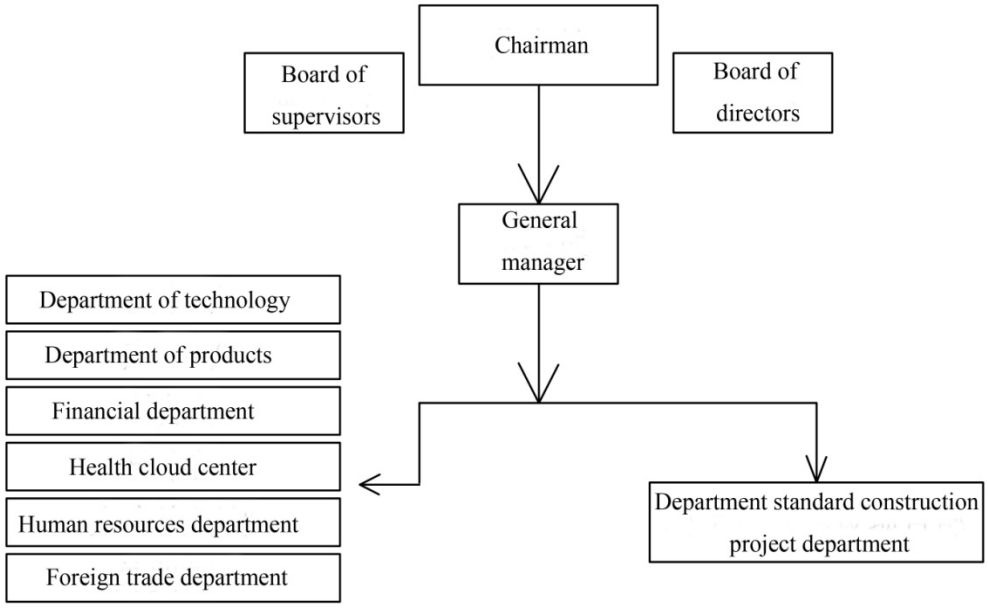

Figure 1: A schematic diagram of organizational structure of an institution

Investment of Medical Facility Advertisement

Besides sales staffs and network marketing, advertisement also has a huge effect on marketing. Advertising medical facilities in mass media and other professional media can improve brand effect and is also beneficial to the improvement of institutional images. Generally, advertisement can be achieved via television, newspapers and magazines; public service advertising is also feasible.

THE IMPLEMENTATION AND MASTERING OF STRATEGIC MARKETING

Implementation of Marketing

Organizational structure can ensure the normal operation of enterprise process, which is an effective basis for department set and function planning. Organizational structure can be designed according to marketing business based on relationship between superior and subordinate. As shown in Figure 1, the foreign trade development is no need to be established when medical facilities will not be exported to foreign countries.

Application of template user development mode

As mentioned above, sale is mainly achieved by salesman. The following client development mode was established for that kind of sales mode.

In the figure, clients are divided into five sections, i.e., new client screening, key client follow up, target client sample plate visit, field investigation and contract signing.[12] The procedures are repeated in order. As to the screening of new clients, carpet-style checking is adopted at first, i.e., all clients are informed with information about products; then the key clients are followed up, and the target clients are determined after specific communication and investigation; the target clients are invited to visit samples, and the intentional clients are determined; the intentional clients are arranged to investigate enterprise; contract is signed after details are implemented.

The formulation and perfection of marketing motivation mechanism

The formulation of marketing motivation mechanism is beneficial to the working efficiency and cohesive force of staffs. Moreover, the formulation of relevant examination and reward and punishment system can promote the initiative of sales and the competition of enterprises.

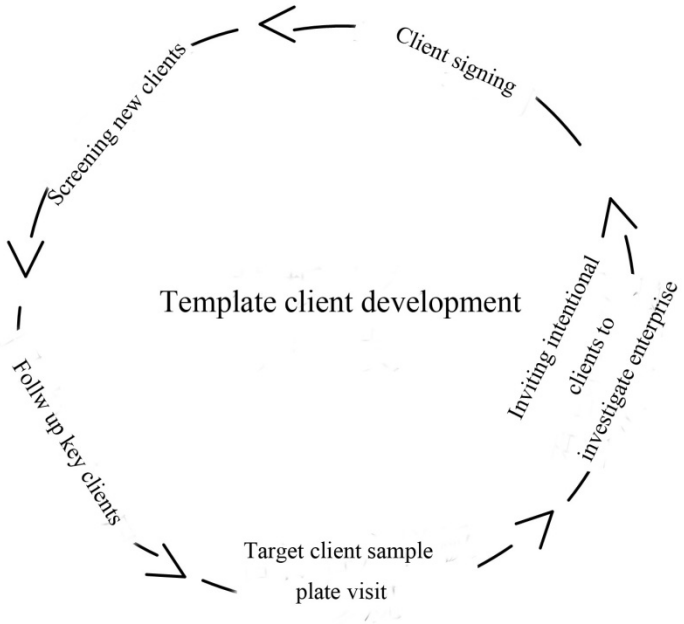

Figure 2: A schematic diagram of template client development.

Marketing Control

Control of marketing efficiency

Efficiency control includes control of salesman efficiency and control of sales promotion efficiency. Control of salesman efficiency includes daily number of visiting client, average visit time and key clients each month. According to the performance of salesman, targeted guidelines are formulated to improve sales work. Sales promotion efficiency can be improved by inviting intentional clients to attend activities such as charity party and recording and analyzing the parameters such as number of participants and regions.

Control of marketing strategy

Implementation of strategic control aims at keeping marketing works and plans consistent, timely feeding back information evaluation and modifying according to market changes.

CONCLUSION

The marketing of medical facilities is different from that of other products. Medical facilities are the fixed assets and the material basis for the survival and development of modern hospitals.[13] Under the support of hospital leaders, the steps such as equipment purchasing and regular maintenance and repair can produce huge economic benefits. In the new marketing environment, sticking to convention is infeasible; sales mode should changes according to environment.[14] This study firstly introduced the new environment and then formulated the marketing strategies for medical facilities based on the new environment. To ensure the effective proceeding of marketing strategy, the perfection of marketing organization, control of marketing strategy and control of marketing efficiency were proposed. This work aims to provide certain assistance for the marketing of medical facilities in China.

ACKNOWLEDGEMENT

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Article

Discussion on Strengthening Financial Supervision of Pharmaceutical Industry under the Background of New Medical Reform

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ABSTRACT

with the continuous development of the economy and the improvement of the medical technological level, China's pharmaceutical industry is also undergoing sustainable development while the market competition among pharmaceutical companies is being intensified. Leading the operation of pharmaceutical companies and promoting the progress of the pharmaceutical industry, financial regulation is the most important part of many management projects. Hence, strengthening the financial supervision of pharmaceutical companies has become the key to the development of the pharmaceutical industry. However, the financial supervision of domestic pharmaceutical companies under the new medical reform shows many problems, such as poor concept of financial supervision, weak basic supervision, weak budget management and control as well as poor cost control capacity, which make the financial supervision of pharmaceutical enterprises can not proceed smoothly. Therefore, corresponding countermeasures need to be developed. By analyzing the changes of the living environment of domestic pharmaceutical enterprises and the development of financial supervision under the new medical reform, this paper discusses the existing problems in the financial supervision of pharmaceutical enterprises, and puts forward corresponding measures to promote the development of the pharmaceutical industry.

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Keywords: new medical reform; pharmaceutical industry; pharmaceutical enterprise; financial supervision

INTRODUCTION

Though the intensification of the international economic integration situation has brought a strong impact to China's pharmaceutical industry, it also brought a broader development space for it. Faced with strong market competition and international pressure, China's pharmaceutical companies should seize the opportunity to rise to the challenge. As a very important part of many management projects in the pharmaceutical industry, the improvement and strengthening of financial supervision will have a significant impact on this. There are some researches on this regard. Wang Peng [1] believed that the new medical reform made important progress in drug prices and pharmaceutical companies should carry out reasonable economic activities and financial management work under the premise of following national laws and regulations to achieve the

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purpose of reducing business costs and increasing profits since financial management played an important role in the enterprise market competition. H Zhu [2] analyzed the objectives of the essential drug system, elaborated the reasons for government regulation, discussed the application and innovation of government regulation from the perspective of economics and proposed some countermeasures to establish incentive management to ensure the implementation of the essential drug system. This paper aims to analyze the changes of the living environment of the domestic pharmaceutical enterprises and the development of the financial supervision under the background of the new medical reform, put forward some problems in the financial supervision of the pharmaceutical enterprises, and give the corresponding solutions to strengthen the medicine industry's financial supervision, and promote the healthy and orderly rapid development of China's medical industry.

ENVIRONMENTAL CHANGES OF PHARMACEUTICAL ENTERPRISES UNDER THE NEW MEDICAL REFORM

Financial supervision is the prerequisite for the orderly conduct of production and sales activities of pharmaceutical enterprises [3-4], occupying the primary position in the economic management activities of pharmaceutical enterprises [5]. Hence, its specific implementation means is flexible according to the actual situation, keeping up with the real situation of the market economy. After the new medical reform, the market economy has experienced high-speed changes and a lot of problems appear in the financial supervision of pharmaceutical companies due to environmental changes [6], including changes in the external environment and changes in the internal environment. External environmental change refers to the change in the development trend from drug management system to creative system in order to meet the real needs of the development of pharmaceutical companies. However, the protection of intellectual property in the pharmaceutical industry is still inadequate, so the innovation of the pharmaceutical industry is still constrained even if the system has changed. Changes in the internal environment are reflected in the increasing financing difficulty which limits the development of pharmaceutical companies. For example, it has been more and more difficult for many pharmaceutical companies to turn to bank loans to avoid funding problems, and the cash flow efficiency is inefficient. And whether it is state-owned enterprises or private enterprises, a fixed financial regulatory model has been formed in the development process, to which certain impact will be brought by the new health care reform.

DEVELOPMENT STATUS OF FINANCIAL SUPERVISION UNDER NEW MEDICAL REFORM

With the economic development and social progress, China's social security system and pharmaceutical industry are also undergoing synchronized development. According to statistics, the national pharmaceutical industry's total output value in 2015 reached 25537.1 billion yuan. As of September 2016, the output value of enterprises above designated size has reached 1995.89 billion yuan, an increase of about 10% over the same period last year, and the growth rate has also increased. Therefore, China's pharmaceutical industry's output value showed a good growth trend [7], with a high growth rate. In view of this, the pharmaceutical industry has long been a very important part of China's national economy, and pharmaceutical companies have become a very important type of business in China. Nevertheless, there are still restrictions on the development of pharmaceutical companies, including not only industry vicious competition and superior policy constraints but also the chaotic situation in financial supervision. Therefore, China introduced a health care reform policy. In order to promote the construction of basic medical security system and improve the financial supervision ability of pharmaceutical enterprises and enhance the internal competitiveness of enterprises, the government has also carried out relevant guidance. Failing to coming up to expectations, the health care reform policy did not achieve significant results and there are still many problems to be solved in the financial supervision of pharmaceutical companies.

With the progress of the medical reform policy, China initially established a basic drug and health insurance directory, zero rate sales and other policies. Before the reform, pharmaceutical companies follow a relatively free and rugged financial regulatory concept, which aims to invest a lot of money in marketing to expand the market share, with no extra effort to carry out medical research and development. With the medical reform policy, pharmaceutical companies can have access to the basic drug and health insurance directory, which saves the funds on sales to carry out medical research and development and production so as to achieve the strategic purpose of sustainable development.

However, the drugs in the directory are priced by the National Development and Reform Commission, thus increasing the difficulty of enterprise cost control. The reform of the basic drug system in China in the new medical reform is a double-edged sword for pharmaceutical companies. On the one hand, the government

reformed the drug price formation mechanism, regulated the price management, and made the enterprise lose the freedom of pricing. On the other hand, the specification on drug production and circulation order made by the new medical reform also re-designated the development direction for enterprises and improved the competitiveness of enterprises. Yet, since foreign markets usually have high requirements on Western medicine in imported products, China's vast majority of drug exports are mainly based on raw materials. Besides, China's domestic market competition is fierce, leading to constraint on the development of the pharmaceutical industry, while the financial supervision of pharmaceutical companies is also facing new problems and challenges.

EXISTING PROBLEMS IN FINANCIAL SUPERVISION

Lagged Concept of Financial Supervision

As nearly half of the current pharmaceutical companies are transformed from the original state-owned enterprises, the concept of financial regulation is still the old type, which, though, can control and record the cost of corporate funds to a certain extent, is unable to deal with emergencies in an early and effective manner due to the lack of a sound financial early warning mechanism. Moreover, small groups formed in the traditional financial regulation mode due to personal interest can affect the progress of the new medical reform as well as the economic benefit of pharmaceutical enterprises, thus affecting the development of China's medical industry.

Imperfect Financial Supervision System

As the domestic pharmaceutical market is dominated by the buyer's market, the homogenization phenomenon is becoming more and more serious due to the imitation among different brands of drugs in the performance, appearance and sales aspects. In order to sell more products and produce more economic benefits, most of the pharmaceutical companies are more focused on the development of foreign sales and lay the emphasis of work on the management of economic efficiency, failing to realize the importance of financial regulation and its key position in the development of enterprises. As a result, basic management is ignored, many process systems are limited to the form, and position division is not clear. In addition, pharmaceutical companies also lack a clear financial supervision and assessment system to provide processing standards to deal with financial affairs as well as necessary process management and financial supervision to provide accurate and effective financial information, resulting in internal control problems.

Weak Cost Budget Control Ability

As the domestic pharmaceutical companies lack a clear and reasonable business strategy as well as a detailed market analysis, with unclear budget and poor executive force, their cost budget control ability is weak [8]. Because there is no occasional assessment and inspection of the financial situation, the capital and budget of enterprises are seriously deviated. Furthermore, a lack of financial plan adjustment corresponding to actual budget changes leads to the failure of timely controlling the budget of enterprises, which lowers the anti - risk ability of pharmaceutical enterprises.

Poor Cost Control Ability

The backlog of goods resulting from an unclear sales plan can cause the occupation of the enterprise's working capital while accumulation of goods in the warehouse will result in a waste of storage management costs and the lack of production equipment will increase the cost of business [9] and the lack of warehousing system and process will cause the cost accounting error. Besides, a lack of scientific financial regulation in raw material procurement can cause an increase in raw material costs, resulting in the cost control failure, which not only cannot meet the production needs, but also reduces the market competitiveness of enterprises, as shown in figure 1.

As shown in the figure, whether the raw material inventory in the warehouse is sufficient is determined after the formulation of the production plan based on the sales order, which will cause the failure in timely supplementing raw materials, slow down the production plan and delay sales orders. Moreover, temporary purchase of raw materials for production plans is likely to cause high raw material purchase costs and a waste of funds due to the failure in estimating drug raw material prices because of the constant fluctuations in raw material prices in the market.

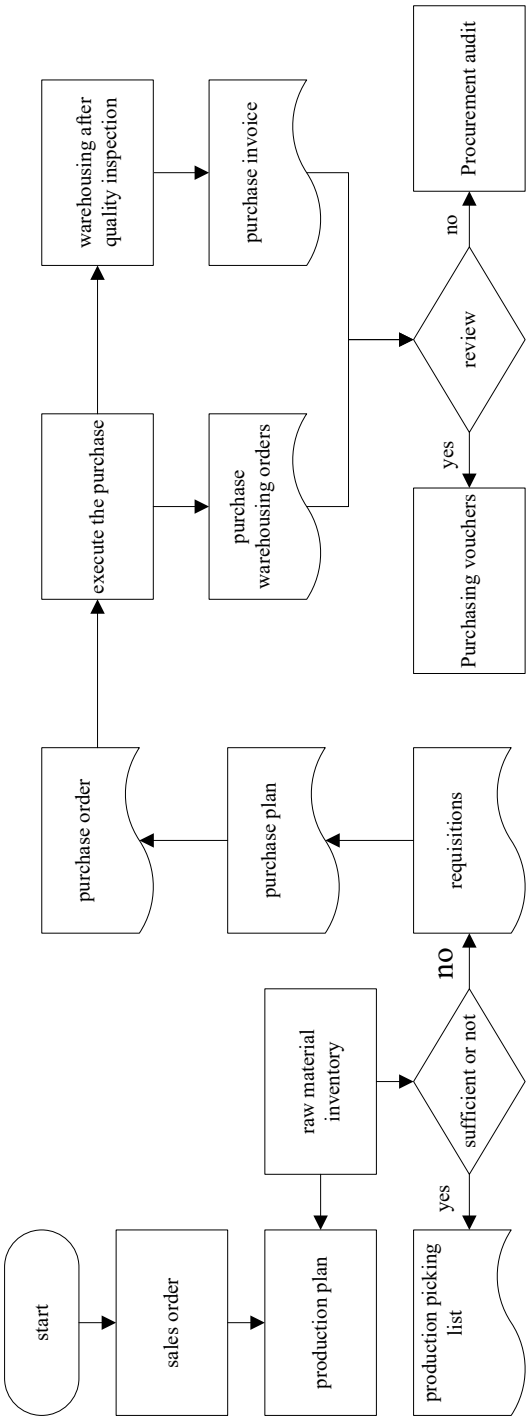

Figure 1: The raw material procurement flow chart of pharmaceutical companies

SPECIFIC MEASURES OF STRENGTHENING FINANCIAL SUPERVISION

Conversion of Concept of Financial Supervision

On the basis of changing the concept of financial supervision, pharmaceutical enterprises should establish a reasonable and feasible financial supervision and training system [10] to realize rigorous training and assessment of the financial supervision staffs in order to improve their ability of financial supervision as well as their ability to solve problems in a systematic way to adapt to the new environment. A scientific and viable financial regulatory strategy should be formulated based on the analysis of the new medical reform policy and the latest market trend, combining domestic policies with foreign regulation modes.

Improvement of Financial Supervision System

Pharmaceutical enterprises should improve the existing regulatory system combining with their own characteristics, strictly regulate the financial and audit work, and regularly review the work of the two, so as to fundamentally reduce risks. Besides, they should strictly divide the responsibilities and authority of the relevant financial staffs, optimize the organizational structure, explain all the nodes they control, improve the work supervision process, strengthen the advantages of financial supervision function, and promote the improvement of enterprise economic efficiency, as shown in figure 2.

With the development of pharmaceutical companies and the strengthening of capital control, the importance of financial data accounting has become increasingly prominent. By splitting the original cashier account position into cashier and accounting and including the accounting position into cost sales accountant to carry out second accounting on cost sales funds, cashier employees can better complete their jobs and accounting staffs can be more targeted to more detailed work to complete the accounting.

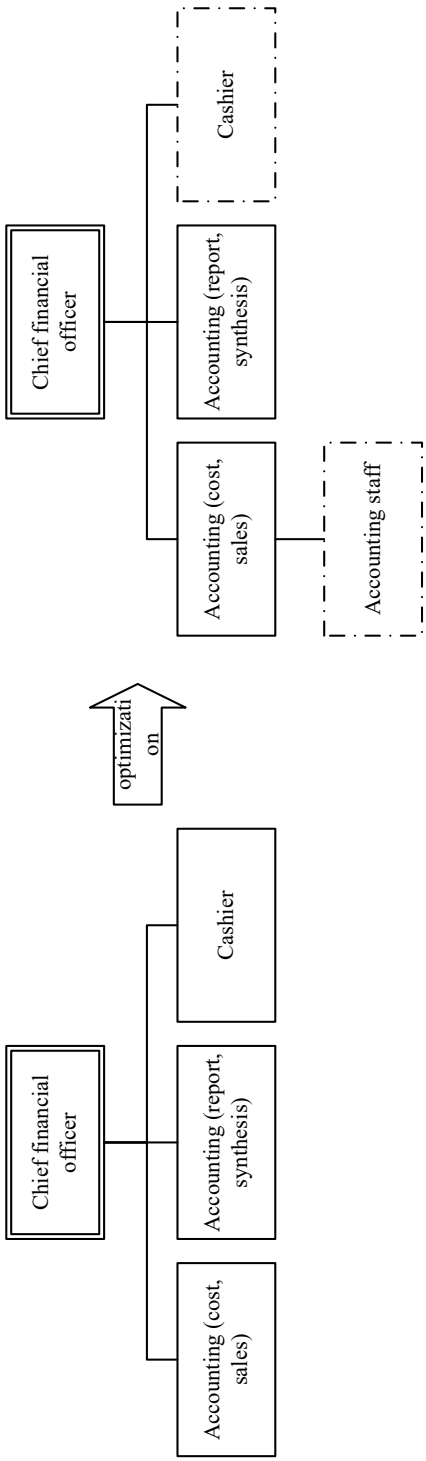

Figure 2: Optimization of the organizational structure of the financial sector of pharmaceutical companies.

Strengthening of Cost Budget Control

In order to make the cost management more standardized, enterprises can strengthen the management of budget funds, improve the relevant funds approval process and improve the normative review of tickets auditing [11]. In addition, enterprises can also create new sales models, increase the market's brand investment, or improve the performance appraisal tools. Meanwhile, financial regulators should also be familiar with health care reform policies as well as the price of medicine and strengthen communication with business people to ensure the speed of financial business processing. In this way, operational feasibility and manageability of budget costs can be achieved and risks of failing to control tax and internal costs can be avoided under the premise of ensuring the smooth flow of operations.

Reasonable Lowering of Costs

In order to control the cost, pharmaceutical enterprises should strictly follow the relevant management systems to establish a series of management processes including drug storage and return management, inventory early warning and reporting loss management so that that the contact between production and sales is more complete and precise to ensure the timeliness of inventory management and reduce capital occupation and waste. In the procurement, the enterprise must do a unified procurement and a unified distribution to realize the optimization of procurement costs under the premise of ensuring the number of procurement. At the same time, the price of raw materials should be timely grasped to closely link procurement plans and production plans so as to strengthen the grasp of the market situation.

Introduction of Relevant Economic Policies

In addition to the efforts of the enterprise itself, the Chinese government can introduce relevant economic policies. For example, through the introduction of funding guidelines, the financing methods of pharmaceutical companies can be more standardized so as to promote the optimization of corporate capital structure; through the introduction of credit standards, the credit rating of pharmaceutical companies can be more reasonable, so as to strengthen the enterprise credit management construction, thereby reducing financial risks; through the introduction of financial policies, credit standards can be regulated to reduce the cost, thereby reducing the occupation and waste of corporate liquidity; through the

introduction of tax policies, the pharmaceutical business tax behavior can be more standardized, thereby reducing the tax risk, in order to allow financial regulation of pharmaceutical companies to run in a more reasonable environment.

CONCLUSION

In the context of fierce competition in the world market economy, China's pharmaceutical companies are facing more and more challenges. As financial regulation is an indispensable economic management work for pharmaceutical companies to organize financial activities and deal with financial-related processes, it is an indispensable step for the pharmaceutical industry to strengthen financial regulation so as to improve the competitiveness of pharmaceutical companies themselves. A good job of financial supervision can not only coordinate the combination of various factors of production, but also well guarantee the orderly operation of the entire pharmaceutical business, to ensure the invincible position of pharmaceutical companies in the market competition as well as the healthy and orderly and rapid development of the entire medicine industry. As the financial supervision of China's pharmaceutical enterprises shows many problems in the new medical reform environment, pharmaceutical companies need to change the concept of financial supervision, improve the financial regulatory system, strengthen the cost budget management, reasonably reduce costs and improve information management investment in order to better conduct financial supervision so that China's pharmaceutical industry can develop in a better environment.

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Intellectual Property Management

Patenting Bioinformatics Innovations: Emerging Trends and Challenges in the United States

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ABSTRACT

Bioinformatics tools and techniques are useful not only to manage and analyze vast amount of raw biological data generated from various genomics research but also to understand the phenomena of biological system at the macromolecular level. The development of bioinformatics has come a long way from DNA sequencing tools of the Human Genome Project (HGP) era to DNA circuits and programmable synthetic biological devices in the twenty first century. The present article attempts to analyze and reveal the emerging trends in bioinformatics and computational biology research and innovation and challenges in patenting them under the current US patent regime.

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Keywords: Bioinformatics, Computational biology, *In Silico* screening, Patent, Structural genomics, USPTO

INTRODUCTION

Rapid development of high-throughput techniques in molecular biology and computational methods transformed biology into a data-rich science (Beck 2010). Genome projects are not only changing the understanding of biology but also generating mountains of *omics* (Barh, Zambare, and Azevedo 2013) data. For example, the Human Genome Project alone has generated vast amount of nucleotide data containing 3 billion base pairs (bp) residing in the 23 pairs of human chromosomes ("Human Genome Project Completion: Frequently Asked Questions" 2010). Analyzing, storing, organizing and retrieving raw biological data significantly propelled biological research. Bioinformatics and computational biology techniques manage the data interpretation and analytical tasks in a very efficient manner and offer useful information about how biological systems work and evolve over time. The nucleotide and amino acid sequence information are frequently used in conventional biological research. Besides that, sequencing new genes and assigning their functions, discovering single nucleotide polymorphisms (SNP), modelling three-dimensional (3D) structures of proteins etc. added a whole new dimension to modern biological research and development.

Although many bioinformatics tools and databases are publicly available in the internet, e.g. BLAST (Altschul et al. 1990), GenBank, EMBL, DDBJ, PIR, SWISS-PROT etc. (Kanehisa and Bork 2003), however, protecting bioinformatics tools and services as platform technology has been increased worldwide. Intellectual property (IP) protection of bioinformatics is inherently difficult. One of the main reasons is that it is multidisciplinary in nature. There are several ways in which bioinformatics IP can be protected (Harrison 2003) and patent is the most effective form of IP protection among them in which most of the components of bioinformatics innovations can be covered.

MATERIAL AND METHOD

The main source of the present study is patent literatures collected from the United States Patent and Trademark Office (USPTO). Patent literatures and its analysis serve an important role in assessment of technology, its development and forecasting (Narin 1998, Oppenheim 2000). Bibliometric data can be used to assess and forecast progress in the technological field (Martin 1995, Watts 1997, Daim 2006). Further, within the available bibliometric

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data sources, patent data have been extensively used to gauge innovative activity in a particular area (Pavitt 1985, Narin 1996). Moreover, changes in patenting activity are commonly used to assess the development stage of various technological fields (Andersen 1999).

The patent search and evaluation framework of the present study integrates IPC classification (Table 2), bibliographic, citation (Garfield 1955), network (Albert 2002) and statistical analysis. The title-abstract or title-claim keyword search is widely used to collect relevant patent data (Yan 2009). The principle motivating factor of using IPC classification in the present patent search framework is that the accuracy of patent categorization technique adopted by the World Intellectual Property Organisation (Fall 2003) to classify a large variety of bioinformatics innovations (Table 2).

The IPC guided framework has been applied to bioinformatics and computational biology patent publications in the US Patent and Trademark Office (USPTO). The present study has considered all patent applicants and assignees i.e., private companies and R&Ds, public R&Ds, academic institutions and individual applicants focusing on the patenting activity during the year 2012-2016.

THE GROWTH OF BIOINFORMATICS AND COMPUTATIONAL BIOLOGY RESEARCH AND INNOVATION

Bioinformatics tools and other advanced computational biology applications manipulate biological data in a variety of meaningful ways. Bioinformatics algorithms and software tools are generally involved in analyzing molecular biological data, particularly, DNA and protein sequences. However, its more advanced applications perform various complex tasks, e.g. mapping DNA and protein sequences, gene prediction (Wong 2016), modeling three-dimensional structure of proteins (Joyce et al. 2015) and drug discovery, modeling evolution (Liò and Goldman 1998) and cell division, simulating biomolecular interactions (Spiga, Degiacomi, and Dal Peraro 2014) etc.

Current Trends in Bioinformatics Patenting

The patenting trend in bioinformatics area is not as aggressive as seen in other fields of molecular biology or genomics innovations. However, a steady growth has been noticed in 2012-2016 time-frame. A sharp increase in patent-filing has been observed in last couple of years besides a noticeable increase in the number of issued patents since early 2013 (Figure 1).

Most of the patenting activities in last five years were mainly concentrated on three areas of bioinformatics and computational biology innovations. Machine learning and data mining secured the 1st position as the most successful area of technology with regard to number of patents granted during 2012-2016, followed by functional genomics or proteomics and sequence comparison involving nucleotides or amino acids (Figure 2). Although most of the patent-filing activities have been seen in the field of nucleotide or amino acid sequence comparison, one of the oldest areas of computational biology (Kanehisa and Bork 2003), however, this area has emerged as the third most successful area of technology in the list with regard to issued patents. Phylogeny or evolution has appeared as the least developed area with regard to bioinformatics innovation.

On the other hand, patenting activity in the field of programming tools or database system was average in last five years. Also, no major patenting activity has been seen in the data visualization area and placed at the 2nd last position in the list (Figure 2). However, the success rate in this area is highest in comparison to other areas. More than 55% out of the total patent applications filed in the data visualization area were finally granted by the USPTO.

Contribution of Academic Institutions and Private Companies Towards the Growth of Bioinformatics Research and Innovation

The present patent search & analysis observed that privately owned companies played a key role to the development of bioinformatics and computational biology innovations (Figure 3). The analysis of patent documents revealed that a large pool of different patent applicants/

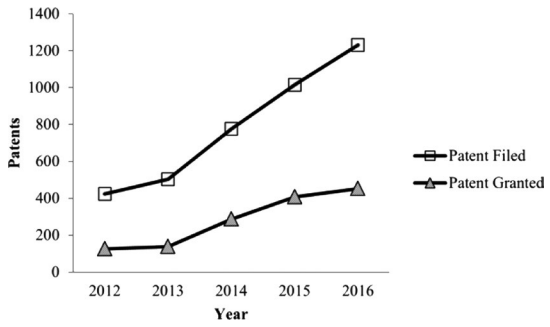

Figure 1: Annual distribution of patents in the area of bioinformatics and computational biology invention

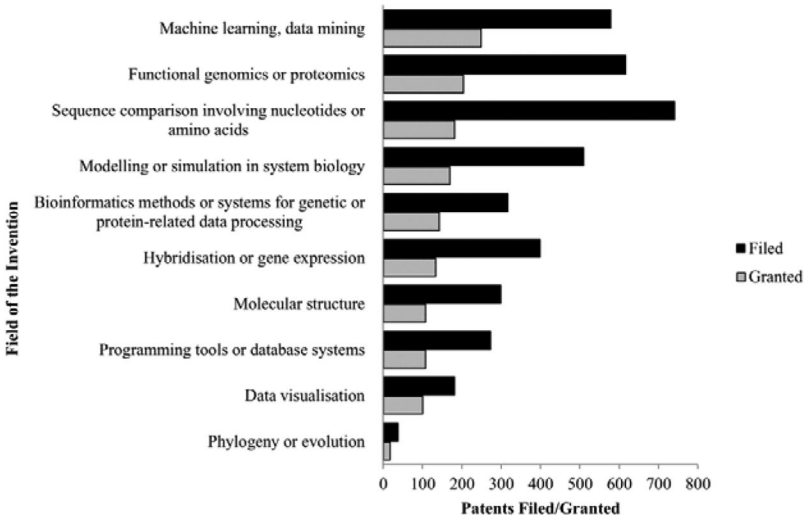

Figure 2: The Growth of research and innovation in different areas of bioinformatics and computational biology. The patent search was conducted for ten IPC subclasses relating to bioinformatics and computational biology patent applications as categorized in International Patent Classification version v7.0e - 15.12.2016. To showcase the most successful areas of bioinformatics research and innovation in 2012–2016, each IPC subclasses (representing each technological areas) have been arranged according to their counts of issued patents

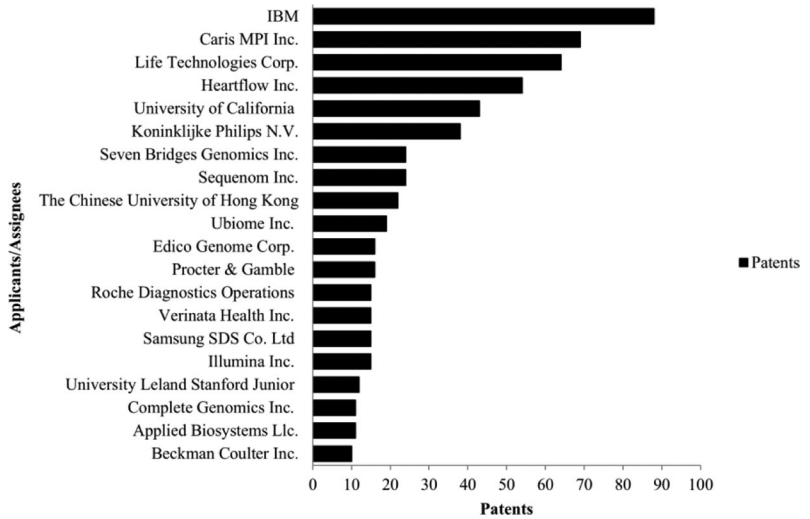

Figure 3: List of top twenty bioinformatics patent applicants/assignees. Twenty patent applicants/assignees have been arranged according to their patenting activities in the field of bioinformatics and computational biology research and innovation in 2012–2016

assignees have been involved in the innovation activity. However, in the present study, only top twenty patent applicants/assignees have been listed (Figure 3) according to their patenting performance during 2012-2016. The International Business Machines Corporation (IBM) has significantly contributed to the growth of bioinformatics and computational biology and placed at the top position of the list. The most active area of its bioinformatics research and innovation was sequence comparison involving nucleotides and amino acids followed by machine learning and functional genomics.

On the other hand, academic institutions have also played some active entrepreneurial roles (Etzkowitz, Webster, and Healey 1998) to the development of bioinformatics and computational biology. Present analysis noted that only three academic institutions were majorly involved in the patenting activity (Figure 3). The University of California has emerged as the major player followed by the Chinese University of Hong Kong and

the University Leland Stanford Junior. Patenting activity of the present study revealed that the University of California has put most of its inventive effort in system biology followed by functional genomics and machine learning. The present analysis also observes that the research and inventive effort in the area of functional genomics and proteomics is common to all three academic institutions and top three privately owned companies. Whereas, both the top private company and the academic institution, i.e. IBM and the University of California, were extensively involved in machine learning and data mining innovations.

PATENTING BIOINFORMATICS AND COMPUTATIONAL BIOLOGY INNOVATIONS

According to the American patent system, "any new and useful art, machine, manufacture, or composition of matter, or any new or useful improvement thereof" –are patentable. However, in relation to biotechnology innovations, the US patent regime has been witnessed several refinements in its patent-eligible subject matter jurisprudence starting from "anything under the sun made by man" (U.S. Supreme Court 1980) doctrine to *natural product/phenomena* exceptions applicable for genes or DNA sequences (SUPREME COURT OF THE UNITED STATES 2013).

Bioinformatics and computational biology are relatively new fields in the technology domain. It combines molecular biology, mathematics, statistics and computer technology as main components (Hagen 2000), (Luscombe, Greenbaum, and Gerstein 2001). Patenting bioinformatics inventions is relatively difficult not only because it is interdisciplinary in nature but also for its prophetic applications.

According to general practice of the United States Patent and Trademark Office (USPTO), innovations related to data *per se* are not patent-eligible (United States Court of Appeals 2014). The examination guidelines (United States Patent and Trademark Office 1996) for computer-implemented inventions made a clear distinction between "functional descriptive materials", e.g. data structures and computer programs which impart functionality when encoded on a computer-readable medium, and "non-functional descriptive material", e.g. music, literary works and a composition or mere arrangement of data which is not structurally and functionally interpreted to the medium but is merely carried by the medium. According to a report on the comparative study (Trilateral Patent Office 2002) conducted by trilateral patent offices[1], inventions that claim protein three-dimensional structural coordinates fall under the category of "information contents" and innovations related to these subject areas are not patent-eligible under §101 since they are nothing more than "mere presentations of information or abstract ideas".

Claiming Strategies in Bioinformatics and Computational Biology Patents

Patent claims are considered as the most vital part of patent specification (Daniel Richards 2016), written description of invention, for which protection is sought before the patent granting authority. Claiming patterns of promising technological areas, e.g. gene expression, functional genomics or proteomics, modeling in system biology etc., have become highly complex with the increase in understanding of these subject areas.

The major claiming strategies in the field of bioinformatics and computational biology inventions are given in Table 1 to present a clear view about what innovators intend to claim at the strategy level and the breadth of protections those hypothetical claims encompass when translated into actual patent claims.

There are eight major categories of claiming patterns (Table 1) abundantly found in ten different fields (Group 2010) of bioinformatics patents (Table 2). Inventions directed to type I, II and III as described in Table-1, are rarely considered as patent-eligible under §101 since they either claim an array of data or computer model or database encoded with data comprising names and structure.

Structural Genomics and Drug Designing Innovations

Computer assisted methods are extremely important in structural genomics (Goldsmith-Fischman and Honig 2003) and they are frequently used for Structure-Based-Drug-Design (SBDD). Newly evolving areas of biotechnology heavily rely on computer modeling and screening algorithms to data that describe a protein by its three-dimensional structure in order to design potential biopharmaceuticals. Protein three-dimensional structures represented by spatial arrangements of atoms or structural coordinate data are considered to have technical effect as long as they are used in an *in silico* or bioinformatics screening method to search for compounds.

There are three categories of inventions generally found in structural genomics patents. Inventions based on *information contents*, inventions directed to *in silico screening methods* that use structural information of

Table 1: Major bioinformatics claim types, hypothetical claiming patterns and their corresponding actual claims found in patent applications

Claim Type	Hypothetical	Actual Patent	
		Publication No.	Claims
Type-I Computer model and data array claims	Example-1: A computer model of protein P generated with the atomic coordinates listed in Fig.1.	US5453937	Claim-1: A method in a computer system for modeling a three-dimensional structure of a model protein the method comprising the computer-implemented steps of the template protein has an amino acid aligned with the amino acid of the model protein, establishing the position of each backbone atom of the amino acid
	Example-2: A data array comprising the atomic coordinates of protein P as set forth in Fig.1 which, when acted upon by protein modeling algorithm, yields a representation of the 3-D structure of protein P.	US20060141600	Claim-6: A data array comprising the atomic coordinates of an Argonaute protein as set forth in Table 3. Claim-7: An electronic representation of a crystal structure of an Argonaute protein or a portion thereof.
Type-II Claims directed to database with coordinate data	Example-1: A database encoded with data comprising names and structures of compounds identified by a method of identifying compounds which can bind protein P by comparing the 3-D structure of candidate compounds with the 3-D molecular model shown in Fig.1 which comprises the steps of…….(1), (2), (3), (n).	US20060141600	Claim-26: A computer-readable storage medium encoded with the Argonaute atomic coordinates of claim 6.
Type-III Pharmacophore claims	Example-1: A pharmacophore having a spatial arrangement of atoms within a molecule defined by the following formula: Formula-1 wherein (A) represents an electron donor atom and (C) represents a carbon atom.	US20080305041	Claim-2: A compound that modulates PF4 activity comprising functional groups I, II, III, IV, VII, IX and X wherein the distance between the functional groups in three-dimensions is about: 2.25±0.05Å between group I and II; 6.03±1.37Å between groups I and III; 6.92±1.60 Å between groups I and IV; Wherein functional group I corresponds to the OD1 atom of the amino acid side chain Asp7, functional group II corresponds to the OD2 atom of the amino acid side chain Asp7, in the PF4 sequence set forth in FIG. 1C (SEQ ID NO.1).
Type-IV 3D structure of protein	Example-1: An isolated and purified protein having the structure defined by the structural coordinates as shown in Fig.1.	US20070048853	Claim-1: An isolated protein having the structure defined by the structural coordinates as set forth in FIG. 4

Table 1: Continued

Claim Type	Hypothetical	Actual Patent	
		Publication No.	Claims
Type-V Protein Crystal	Example-1: A crystalline form of protein P having unit cell dimensions of a = 4.0nm, b = 7.8nm, and c = 11.0nm.	US6403330	Claim-1: A crystalline form of mammalian TRAP (tartrate-resistant and purple acid phosphate), and wherein the crystalline form of the mammalian TRAP has a crystal structure with atomic structural coordinates as given in Table 2, or with coordinates having a root mean square deviation therefrom, with respect to conserved backbone atoms of the listed amino acid sequence, of not more than 1.5 Å.
Type-VI Protein domain	Example-1: An isolated and purified molecule comprising a binding pocket of protein P defined by structural coordinates of amino acids residues 223, 224,295,343,366,370,378 and 384 according to Fig.1. Example-2: An isolated and purified polypeptide consisting of a portion of protein P starting at one of amino acids 214 to 218 and ending at one of amino acids 394 to 401 of protein P as set forth in SEQ ID NO:1.	US7700340	Claim-1: A crystal comprising an unphosphorylated Polo-Like Kinase 3 (PLK3) catalytic kinase domain polypeptide in complex with adenosine, wherein said PLK3 catalytic kinase domain polypeptide consists of amino acids 48-332 of SEQ ID NO: 1, and wherein said crystal is in space group C2 and has unit cell dimensions of a=145.95 , b=58.82 , c=47.10 , α=γ=90° and β=94.9°.
Type-VII In silico screening methods directed to a specific protein	Example-1: A method of identifying compounds that can bind to protein P, comprising the steps of: applying a 3-D molecular modeling algorithm to the atomic coordinates of protein P to determine the spatial coordinates of the binding pocket of protein P; and electronically screening to identify compounds that can bind to protein P. Example-2: A method of identifying compounds that bind to protein P by using the atomic coordinates of protein P shown in Fig.1 in a method of rational drug design.	US19995856116	Claim-1: A method for identifying a potential inhibitor for an interleukin-1β converting enzyme, comprising the steps of: (a) Using a three-dimensional structure of said enzyme as defined by atomic coordinates of interleukin-1β converting enzyme according to FIG.5; (b) Employing said three-dimensional structure to design or select said potential inhibitor; (c); (d) Contacting said potential inhibitor with said enzyme in the presence of a substrate to determine the ability of said potential inhibitor to inhibit said enzyme.

Table 1: Continued

Claim Type	Hypothetical	Actual Patent	
		Publication No.	Claims
Type-VIII Compounds/leads generated by in silico method	Example-1: A compound which can bind to protein P generated by a process of comparing the 3-D structure of candidate compounds with the 3-D molecular model shown in Fig.1 which comprise the following steps: (1), (2), (3) (n).	US20026490588	Claim-5: A ligand compound for a biopolymer which is retrieved by a method according to claim 1. [Claim-1: A method of selecting one or more ligand compound to target biopolymer from a three-dimensional structure database, which comprises the step of: (i) the first step; (ii) the second step; (iii) the third step of estimating the most stable docking structure through structural optimization, wherein; (iv) The fourth step; (v) The fifth step of repeating the step (iii) and the step (iv) for all of the trial compounds.]

Source: The Trilateral Co-operation, URL: www.trilateral.net/projects/biotechnology/WM4.pdf (last visited on 20th October, 2016), USPTO Patent Application Full-Text and Image Database (AppFt), URL: http://appft.uspto.gov/netahtml/PTO/search-adv.html, USPTO Patent Full-Text and Image Database (PatFT). URL: http://patft.uspto.gov/netahtml/PTO/search-bool.html (last visited on 21st October, 2016).

proteins and inventions based on the end products resulting from *in silico* or bioinformatics predictive methods, e.g. compounds and pharmacophores (Langer and Hoffmann 2006).

Inventions directed to pharmacophore[3], as exemplified in type-III, are considered as *mere* presentation of information or abstract ideas. Because, pharmacophores can neither be considered as a compound nor article of manufacture and they lack any immediate application to practical problems. Thus, such inventions are not patent-eligible (United States Patent and Trademark Office 1996) within the meaning of §101 of title 35 U.S.C.

A clear picture regarding the scope of protection of non-issued patent applications has been presented in Table-3.

The "isolated" and "purified" protein molecules (Type-IV, Table-1) having practical applicability but defined by their tertiary structural information are considered as patentable subject matter (United States Patent and Trademark Office 1996) under the US patents law.[4] In summary, the isolated and purified proteins represented either in the form of standard amino acid sequence or in the form of their three-dimensional structures or combination thereof, are patentable as long as they have credible utility, even if that utility is computationally asserted (Trilateral Patent Office 2002).

On the other hand, the crystalline form of protein (Type-V, Table-1) is considered as "composition of matter". Inventions directed to similar subject area are patent-eligible on the condition that it meets other vital criteria of the US patents law, e.g. credible utility, novelty etc (United States Patent and Trademark Office 1996).

The specific region or domain of protein molecules, e.g. active sites or binding pockets etc., plays an important role in receptor-ligand interaction. Inventions directed to such type of protein domains (Type-VI, Table-1) represented either in the form of standard amino acid sequence information or three-dimensional coordinate data are considered as "composition of matter". According to USPTO's general patent practice, inventions relating to similar subject area are patent-eligible within the meaning of §101 of U.S.C.35. Table 4 shows the scope of protection of issued patent related to various fields of structural genomics innovations.

Bioinformatics Tools and Database Related Innovations

Although computer programs are patentable[5] (United States Patent and Trademark Office 1996) with appropriate limitations (USPTO 2007), however, data array and computer-readable storage medium encoded with atomic

Table 2: Different fields of bioinformatics inventions as classified in International Patent Classification (IPC), version v7.0e - 15.12.2016.2

Sl. No.	Field of the Invention	IPC
1	Bioinformatics methods or systems for genetic or protein-related data processing in computational molecular biology including bioinformatics methods or systems where digital data processing is inherent or implicit, but not explicitly mentioned.	G06F 19/10
2	Modelling or simulation in system biology, e.g. probabilistic or dynamic models, gene-regulatory networks, protein interaction networks or metabolic networks.	G06F 19/12
3	Phylogeny or evolution, e.g. evolutionarily conserved regions determination or phylogenetic tree construction.	G06F 19/14
4	Molecular structure, e.g. structure alignment, structural or functional relations, protein folding, domain topologies, drug targeting using structure data, involving two-dimensional or three-dimensional structures.	G06F 19/16
5	Functional genomics or proteomics, e.g. genotype-phenotype associations, linkage disequilibrium, population genetics, binding site identification, mutagenesis, genotyping or genome annotation, protein-protein interactions or protein-nucleic acid interactions.	G06F 19/18
6	Hybridisation or gene expression, e.g. microarrays, sequencing by hybridisation, normalisation, profiling, noise correction models, expression ratio estimation, probe design or probe optimization.	G06F 19/20
7	Sequence comparison involving nucleotides or amino acids, e.g. homology search, motif or Single-Nucleotide Polymorphism [SNP] discovery or sequence alignment.	G06F 19/22
8	Machine learning, data mining or biostatistics, e.g. pattern finding, knowledge discovery, rule extraction, correlation, clustering or classification.	G06F 19/24
9	Data visualisation, e.g. graphics generation, display of maps or networks or other visual representations.	G06F 19/26
10	Programming tools or database systems, e.g. ontologies, heterogeneous data integration, data warehousing or computing architectures.	G06F 19/28

coordinates of protein are not patent-eligible under the present US patent regime. Moreover, the data array or the information storage medium encoded with protein three-dimensional structural coordinate data (*see* Type-I and II, Table 1) do not take part in the functional interaction with computer hardware or computing process. Because of these reasons, inventions related to those subject areas do not qualify as patent-eligible subject matter under §101.

Bioinformatics Method and System Related Innovations

The *in silico* or bioinformatics screening methods and systems that search for compounds using three-dimensional structural information of proteins are patent-eligible under §101 as they generate useful, concrete and tangible results (U.S. Court of Appeals Federal Circuit 1998). The novelty, obviousness and utility assessment for inventions relating to those technological areas are comparatively rigorous. The utility of an *in silico* screening method depends on the utility of the candidate compound it generates (*see* step (d) of claim-1, patent no. US5856116, Type-VII, Table-1) (United States Patent and Trademark Office 1996). Moreover, the 'useful-result' criteria for such bioinformatics screening methods are distinct from that of the criteria of usual utility test. It is a further inquiry of the compound and its practical application is required to be significantly functional in character (U.S. Court of Appeals Federal Circuit 1992). For example, a screening method is considered to be patent-eligible if its resulting compound is able to activate or inhibit certain key protein molecules to reduce blood pressure (United States Patent and Trademark Office 1996). (Abrupt ending of paragraph, require some more information). The current patent analysis observes that reach-through claiming patterns are common in majority of the computational biology patent applications. However, it is likely that the USPTO is also aware about this fact and dealing effectively under the current US patent regime.

CONCLUSION

With the advent of various genomic projects, a range of high-throughput techniques have been developed in last

Table 3: Representative list of non-issued US patent applications related to computer model and 3D structural coordinate information of protein, database of protein 3D structures and co-ordiante data and pharmacophores.

Invention	Publication Number	Scope of Protection
Three-dimensional Structure Of DNA Recombination/repair Protein And Use Thereof.	US20070031849	DNA recombination/repair protein complex having a three-dimensional structure substantially defined by the atomic coordinates.
Electronic Database Of Enzyme Substrate And Enzyme Inhibitor Structures	US20020161599	An electronic database comprising a plurality of enzyme substrate structures
Three Dimensional Coordinates Of Melanocortin-4 Receptors	US20050171000	A G-protein-coupled receptor having three-dimensional structure obtained by computer-processing of atomic coordinates and a method
Tripartitle Raftophilic Strutures And Their Use	US20080317767	A compound comprising a tripartite structure of C-B-A or C′-B′-A′
Drug Discovery Methods	US20110269732	Methods for assaying compounds for activity as Aurora kinase inhibitors and compounds having the features of the pharmacophore.
Pf4 Pharmacophores And Their Uses	US20080305041	A novel PF4 pharmacophore that is useful, inter alia, for identifying peptidomimetics and other compounds capable of modulating PF4 activity

Source: USPTO Patent Application Full-Text and Image Database (AppFt), URL: http://appft.uspto.gov/netahtml/PTO/search-adv.html (last visited on 23 October, 2016)

couple of decades. These molecular biological techniques have been instrumental not only to understand the biological phenomena with greater details but also generated vast amount of raw data. Various bioinformatics tools and computational biology applications have been played significant roles since the Human Genome Project (HGP) era, and now they have become an integral part of almost every fields of biological research. The diversity of molecular biological data has also been increased significantly in past decades alongside the increase in volume of raw biological data. Advanced mechanisms have been evolved to handle this highly diversified data which further proved to be extremely useful in understanding the underlying complex mechanisms of biological system. Machine learning applications and bioinformatics data mining have emerged as the fastest growing fields of computational biology. Importance of data visualization tools and techniques in biological data analysis cannot be ignored, though patent filing activity in this area was not impressive in last five years. Patenting activity in the area of functional genomics and macromolecular data analysis still remained as the most focused areas for academic institutions and private companies. The present analysis shows that the patenting activity in the field of bioinformatics and computational biology encompasses a wide variety of subject areas which include modelling or simulation in system biology, sequence comparison and discovery of single nucleotide polymorphisms (SNP), phylogeny, hybridization or gene expression, programming tools and database systems etc.

The challenges in patenting innovations have also been seen besides the success of these promising fields of computational biology. Although computer programs are patentable, however, data array or bioinformatics database systems, e.g. database containing atomic coordinate data of protein molecules, are not allowable subject matter under the current US patent regime. The overall patentability scenario in the field of structural genomics

Table 4: Representative list of granted US patents directed to protein 3D structures involved in computational methods and crystalline form of proteins represented by 3D structural coordinate data

Invention	Patent Number	Scope of Protection
Ligand Identification And Matching Software Tools	US 8468001	Screening method for generating leads/ligand for treatment of a disease
Three-dimensional Structure Of Complement Receptor Type 2 And Uses Thereof	US 6820011	Method of structure-based identification of candidate compounds
Annotating Descriptions Of Chemical Compounds	US 8468002	A computer-implemented method for screening a chemical compound to identify a lead for treating a disease
Three Dimensional Structures And Models Of Fc Receptors And Uses Thereof	US 6675105	A model of a Fc receptor (FcR) protein represents a three-dimensional structure.
Quantitative, High-throughput Screening Method For Protein Stability	US 7148071	A method of detecting a binding event involving a protein with a ligand
Rat Cathespin Dipeptidyl Peptidase I (dppi) Crystal Structure And Its Uses	US 7736875	An isolated crystalline form of a dipeptidyl peptidase I-like protein
Three Dimensional Structure Of A Zap Tyrosine Protein Kinase Fragment And Modeling Methods	US 6251620	A method for determining three-dimensional structure of protein-ligand complex
Human Il-18 Crystal Structure	US 7253260	Human IL-18 protein in a crystalline form represented three-dimensional structural co-ordinates
Three Dimensional Coordinates Of Hptp beta	US 7769575	A computer-implemented method of identifying a drug candidate compound
Crystallized N-terminal Domain Of Influenza Virus Matrix Protein M1 And Method Of Determining And Using Same	US 6090609	A crystallized N-terminal domain of the M1 protein of influenza virus
Structure-based Identification Of Candidate Compounds Using Three Dimensional Structures And Models Of Fc Receptors	US 6675105	A method of structure-based identification of candidate compounds for binding to Fc receptor (FcR) proteins
Three-dimensional Structure Of Complement Receptor Type 2 And Uses Thereof	US 6820011	A method of structure-based identification of candidate compounds for binding to complement receptor type 2 (CR2) proteins or to a complex of CR2 and its ligand

Source: USPTO Patent Full-Text and Image Database (PatFT). URL: http://patft.uspto.gov/netahtml/PTO/search-bool.html (last visited on 28 October, 2016)

and drug discovery is encouraging. Pharmacophores are not acceptable at the USPTO since they do not qualify the doctrine of article of manufacture. However, chemical compounds generated with the aid of computational methods are allowable on the condition that the compounds have credible utility with regard to their technical abilities.

In summary, it can be said that the research and innovation scenario in the emerging fields of bioinformatics and computational biology was encouraging in last five years. Some of the vital reasons behind this success include logical and less cumbersome patent examination strategies of the USPTO. Hence, a persistent growth in these fields is expected in days to come till any new patentability norms are introduced in contrary to current patent practice.

COMPETING INTEREST

The author declares that he is the sole author and no other author has any kind of interest in the manuscript.

ENDNOTES

1 Trilateral Co-operation between EPO, JPO and USPTO was set up in 1983 with the objectives including improvement of the quality of patent examination process, improving quality of incoming applications, solving common problems related to IPR protection, harmonization in practice between three patent office etc.

*See www.*trilateral.*net/projects/biotechnology/WM4.pdf* (last accessed 20th October 2016)

2 International Patent Classification, International Patent Classification, *See* http://web2.wipo.int/classifications/ipc/ipcpub7?notion=scheme&version=20170101&symbol=G06F0019100000&menulang=en&lang=en&viewmode=p&fipcpc=no&showdeleted=yes&indexes=no&headings=yes¬es=yes&direction=o2n&initial=A&cwid=none&tree=no (last accessed Jan 1, 2017).

3 According to the first definition offered by Paul Ehrlich in the early 1900, pharmacophore is "a molecular framework that carries (*phoros*) the essential features responsible for a drug's (*pharmacon*) biological activity". According to another well accepted definition, pharmacophore is "a set of structural features in a molecule that is recognized at a receptor site and is responsible for that molecule's biological activity". – *See* PHARMACOPHORE PERCEPTION, DEVELOPMENT AND USE IN DRUG DESIGN, edited by Osman F. Guner. However, IUPAC offered more specific definition in 1998: *"A pharmacophore is the ensemble of steric and electronic features that is necessary to ensure the optimal supramolecular interactions with a specific biological target structure and to trigger (or block) its biological response*". (*See* Langer and Hoffmann 2006).

4 *See* Comments of USPTO on trilateral comparative study of *"Protein 3D Structure Related Claims"; paragraph A-2 at page 65. URL: www.*trilateral.*net/projects/biotechnology/annex3w.pdf* (last visited on 22 October 2016)

5 According to USPTO's examination guidelines on Computer related inventions, 1996, computer programs alongwith or having functional relationship with computer processing means are patent eligible. For example: functional data structure that is capable of increasing efficiency of computer processing is patent eligible. However, mere data arrangements recorded onto a computer storage medium (e.g. a CD) is considered as *mere* "information content" which does not have any functional corelation with computer processing means and thus are not patentable. – *See* Examination Guidelines for Computer-Related Inventions (1996), https://www.uspto.gov/web/offices/com/sol/og/con/files/cons093.htm. (last accessed 20th December 2016).

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Article

Safety Management and Risk Communication of Genetically Modified Organisms

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ABSTRACT

With the rapid development of transgenic biotechnology, social economic benefits generated from it becomes more and more; however, the doubt on its safety never fades away. Whether transgenic technology is safe or not is always disputed. Different countries have released and established relevant genetically modified organisms safety management schemes and biotechnology risk communication mechanisms to ensure the long-acting, stable and healthy development of transgenic biotechnology. This study analyzed and compared the genetically modified organisms safety management schemes of United States and European Union and the biotechnology risk communication mechanisms of counties such as United States and Japan and then proposed some suggestions to perfect genetically modified organisms management regulations and risk communication long-acting mechanisms such as establishing sound laws and regulations, strengthening transgenic technology support, establishing information open monitoring platform and perfecting the risk communication function of relevant institutions, with the intention of ensuring the health and continuous development of transgenic organism industry.

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Keywords: transgenic organisms; safety management; risk communication; long-acting mechanism

INTRODUCTION

Transgenic organism is developed by transferring exogenous genes to organisms. With the rapid development of transgenic biotechnology, it brings many benefits, but also induced many safety problems. Therefore, it is urgent to do transgenic organism safety management and risk communication to promote the long-acting and stable development of transgenic technology. Many trails and studies have been done on the transgenic safety management and technology risk communication in China and abroad. He Xiaoyun et al.[1] compared the safety management of transgenic organisms in China and Brazil and found China could strengthen relevant management regulations by formulating relevant laws and regulations, enhancing governmental information transparency and strengthening law enforcement efforts. Through comparing risk assessment for environmental toxins with genetically modified organisms in environment, Rajan SR et al.[2] found the inherent uncertainty and inevitability beyond expectation of risk assessment in complex system, emphasized the values of carrying out decision support research, tolerating uncertainty, improving transparency and establishing interdisciplinary institutions that could solve the complex interaction between eco-system and society. This study aims to provide a theoretical basis for perfecting relevant policies in China and proposed some improvement suggestions and advices through comparing the genetically modified organisms safety management and risk communication system in China, United States and European Union, with the intention of promoting the smooth and healthy development of biotechnology safety.

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HAZARDS OF GENETICALLY MODIFIED ORGANISMS

Genetically modified organisms are developed by adding genetic fragments with special function to organisms by genetic technology to make the created organisms carry the functions of the genetic fragments such as parasitie disease resistance and high nutrition. Generally, genetically modified organisms are in no difference with natural organisms in the aspect of appearance; however, its safety has been always doubted. Whether genetically modified organisms are safe or not has not been confirmed. But genetically modified organisms can cause harms to agriculture, environment, biodiversity and human health.

Harms of Genetically Modified Organisms

Genetically modified organisms can strengthen the resistibility of injurious insects. It has been found that cotton bollworm can produce resistance to genetically modified cotton.[3] If genetically modified organisms are planted in large area, ordinary injurious insects can produce antibodies and evolved to more injurious insects which is more difficult to be eliminated, which can cause huge harms to agriculture and biological environment.

Besides improving the resistibility of injurious insects, genetically modified organisms can also cause harms to non-target organisms and even result in death of beneficial insects. A study[4] found that BT transgenic corn pollen could result in the death of more than 40% of monarch butterflies, but ordinary corn pollen had no such condition. Though the experts who were called together by United States Environment Protection Agency have declared corn pollen will not be so concentrated in the wild, the event still raises the doubts of the public on the safety of genetically modified organisms.

Genetically modified organisms can exert an effect on other related species by means of field pollination. For example, transgenic rice developed by Bayer Corporation causes genetic pollution to long-shaped rice and thereby induces dispute.[5] But usually there is lack of isolation measures for genetically modified organisms; as a result, genetically modified crops are mixed with non-genetically modified crops, causing severe consequences.

Harms of Genetically Modified Organisms to Environment and Biodiversity

Most of genetically modified crops are endowed with new properties such as insect resistance, high temperature resistance and salinization resistance. Those crops can be planted in large area in areas which are not suitable for them to survive because of those properties. As a result, they forcibly occupy the living environment in which original organisms in the ecosystem live, leading to the reduction or even extinction in the ecosystem and causing damages to biological environment and biodiversity.

Harms of Genetically Modified Organisms to Human Health

Genetically modified organisms may produce the following effects on human health. The first one is that organisms are toxic. Secondly, the effectiveness of antibiotics might be reduced if people took genetically modified food containing genes which are labeled by antibiotics. The third effect is allergic reaction. Genetically modified food may express some kind of protein through inserting specified genetic fragment. But allergic reaction may be induced if the protein is allergen. Some researchers transferred allergic protein genes into soybean to improve the content of sulfur-containing amino acid in 1996; however, that kind of soybean was forbidden for commercial production as some people produce allergic reactions after taking the soybeans.[6,7]

Many countries have released relevant safety management measures to solve the safety problems of genetically modified organisms.

SAFETY MANAGEMENT AND RISK COMMUNICATION OF GENETICALLY MODIFIED ORGANISMS IN CHINA AND ABROAD

Safety management of genetically modified organisms refers to carrying out activities such as decision, planning, organization and control to realize safe application of transgenic biotechnology and adopting effective means in aspects of technology, organizational management, risk evaluation and communication to eliminate hidden dangers and prevent accidents. Risk communication as an important component plays an important role in the process of safety management.

Safety Management System in China

China implements hierarchical and phase management assessment system and has set up State Committee for the Safety of Agricultural Transgenic Living Things for technical assessment of application at different stages. As to identification, qualitative identification system is implemented; transgenic agricultural products without obvious identification will be forbidden. Agricultural administrative department of the State Council is responsible for supervision and monitoring works. Agricultural genetically modified organism safety management interdepartmental joint conference system established by the State Council is responsible for negotiating and making decisions when management works have problems.

Relevant management regulations have been issued for different steps of genetically modified organisms such as research and development, testing, putting into production and sales in China, and certain achievements have been obtained. But through comparing with some developed countries, it is not difficult to found that there are still some problems in the safety management in China, including imperfect risk communication mechanism, imperfect management team construction system, weak management service function, bull management, deficiency of special legislation, low law enforcement strength and deficiency of fund investment. Moreover, the public with little understanding of genetically modified organisms becomes panic and even resistant about genetically modified organisms because of science popularization deficiency of relevant knowledge and media's exaggeration of its safety.

Safety Management System Abroad

There are three management modes, i.e., United States mode, European Union mode and the mode between United States mode and European Union mode. United States mode refers to specialization and cooperation, coordinated management, loose management and risk analysis following substantial equivalence principle on the basis of genetically modified products. European Union mode refers to unified management, independent legislation, strict management and risk analysis following precautionary principle on the basis of process. Mode between United States and European Union refers to risk analysis based on equivalence principle and (or) precautionary principle and emphasis on both process and products. Table 1 is the comparison of United States mode, European Union mode and mode between United States mode and European Union mode which follows by Japan and Korean.

Biotechnology Risk Communication System in China and Abroad

Risk communication in United States is carried out by the United States Federal Government and public research institutes. The United States Federal Government encourages the public to participate in government decision-making such as public review, public conference, expert conference and information release. Means adopted by public research institutes include positively listen to the public, answer questions in a scientific way and scientifically carrying out researches according to social requirements and regulations.

Denmark takes a cautious and precaution attitude towards genetically modified organisms and moreover set up special funds and charge policy taking laws as a guarantee to ensure the risk assessment and management of genetically modified organisms. The public in Denmark involved in risk communication and assessment in the form of consensus committee[8] at first and institutionalized consensus committee in 1987.

Japan supervises and monitors multi-agent cooperation. Science and Technology Agency is responsible for managing and controlling laboratory studies; Ministry of Agriculture, Forestry and Fisheries is responsible for managing restricted field trails and environmental safety; Ministry of Health and Welfare is responsible for food safety and feed safety.[9] Japan promotes accurate scientific understanding of the public and improves their confidence through multi-level and multi-angle interaction using consensus conference mode.[10]

Coordination framework and platform for agricultural genetic modification risk communication have not been established in China. Management departments at different levels can only characterize risk communication as emergency or temporary works. Moreover, failing to effectively integrate the research and development power that scatters in universities and institutes severely affects the scientific research of agricultural genetically modified organisms, which weakens the auxiliary function of research and development institutes on the decision-making of managers. For the public, the available effective information only includes relevant legal system, evaluation guidance and technical standards. The public has misunderstanding on genetically modified organisms due to the low disclosure scope and degree of genetically modified organisms.

Table 1: Comparison of foreign safety management system

Country	Management mode	Legal system	Supervision institutes	Supervision means
United Sates	A loose mode following reliable scientific principle; controlling biotechnological products rather than technology	No independent legislation; institutions such as United States Environment Protection Agency and Food and Drug Administration formulate laws for different genetically modified food, for example, Policy for Food Derived from Genetically Modified Plants and Research Guide for Recombinant DNA Molecule.	Specialization and cooperation; coordinated management	Establishing perfect supervision system, strictly examining law enforcement; setting up channels to supervise illegal behaviors; voluntary labeling.
European Union	A strict node; adopting precautionary principle	Independent legislation; hierarchical legislation for genetically modified organisms and foods; formulating tracking and labeling system for genetically modified foods	Unified management	Implementing tracking system and compulsory labeling to know the source and destination of genetically modified organisms in steps of research and development, production and sales.
Japan	Supporting the development of transgenic technology and moreover raising doubts on its safety; between United States mode and European Union mode	Independent legislation; two levels for legal management regulations, such as Japan Cartagena Law and Food Sanitation Law; formulating relevant management regulations based on the above laws according to the utilization mode and usage of genetically modified organisms.	Management by six departments	Coexistence of voluntary labeling and compulsory labeling
Korea	Between United States mode and European Union mode; not encourage or discourage	Definite safety management framework; different departments formulate different laws according to their functions, for example, Ministry of Agriculture and Forestry formulated Testing and processing management methods for agricultural research related genetically modified organisms and Department of Health and Welfare formulated Standards for Genetically Modified Food Identification.	Coordinated management by different departments	Compulsory labeling for genetically modified agricultural products and foods

SUGGESTIONS AND COUNTERMEASURES FOR PERFECTING GENETICALLY MODIFIED ORGANISM SAFETY MANAGEMENT SYSTEM

The following countermeasures are proposed based on the actual conditions of China, in order to solve the current problems of genetically modified organism safety and refer to foreign experience.

Establishing Diversified Safety Management System

It is suggested to perfect safety supervision system[11] by clarifying responsibility subjects and department responsibilities, strengthening management service function and increasing team construction input to create a professional and high-efficient supervision team.[12] Moreover, it is necessary to establish and prefect safety assessment technical standards and perfect biosafety prevention and control systems such as safety permission system, safety reporting system, on-site safety inspection system and inspection and quarantine system.

Supervising and Managing Genetically Modified Products

Genetically modified organism identification standards should be formulated, and enterprises should identify products strictly following standards. Genetically modified products sell separately, and the steps of research and development, testing, putting into production and sales are strictly monitored. As a result, the source of the products can be traced in every step, which can help solve problems and ensure consumers' rights and interests.[13]

Perfecting the Establishment of Laws and Regulations System of Genetically Modified Organisms

It is suggested to improve biosafety management related legislation grade, strengthen the establishment of laws and regulations system for biological risk communication, formulate special genetically modified organism safety management laws, improve law enforcement efforts and punishment intensity and establish prevention and emergency response mechanism[14] to avoid possible risks and hazards.

Popularizing Knowledge of Genetically Modified Organism

It is suggested to popularizing relevant theoretical knowledge of application of genetically modified organisms in production and life by means of newspaper, network and television to make the public accurately know and rationally deal with genetically modified products and eliminate blind panic.

Perfecting Genetically Modified Biotechnology Risk Communication Mechanism

Through making a general survey of risk communication experience of United States, Japan and Denmark, it is found that, they emphasize on multi-angle communication with the public, encouraging the public to involve in decision-making and solving public's doubts. Therefore, it is suggested to establish similar consensus conference system to strengthen confidence of the public and accurate understanding of genetically modified products, communicate with the public with flexible and targeted communication mechanism,[15] encourage the public to positively involve in relevant genetically modification risk communication activities, and increase decision-making transparency. By doing that, the public can correctly understand the feasibility and risks of genetically modified products.[16]

Referring to the experience of Japan, risk communication can be taken as definite job function, and special risk communication institutes can be set to responsible for monitoring safety of genetically modified organisms and providing comprehensive risk evaluation and communication.

Basic research on genetically modified organisms risk communication should be strengthened, and talent teams should be established to cultivate professional work team with high scientific literacy and proficient risk communication skills which can effectively cope with emergencies.

CONCLUSION

Transgenic biotechnology is still in the initial stage in China. The imperfect safety management system and deficiency of risk communication make most people worry about the safety of transgenic technology and genetically modified food and doubt about the induced social ethical problems. Referring to foreign successful experience and considering the actual condition of China, the government formulates reasonable safety management schemes, implements feasible risk communication countermeasures, deepens the understanding of the public on transgenic technology, relieves the negative emotion of the public, guides reasonable perception on risks, and increases their confidence on governmental department. As a result, the management subjects become diversified, and a new pattern of common governance of market, society and government forms. We should also realize that the advancement of science and technology level is not only an edged tool for promoting social advancement, but also the undertaker shouldering social responsibilities. Transgenic technology should be developed to guide human life, improve human life quality, and enrich life style. Under such correct guidance, transgenetic technology will make uncountable contributions.

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Article

Intellectual Property Problems of Biodiversity in Multi-dimensional Perspective

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ABSTRACT

The characteristic of biodiversity is the country or national ownership of biodiversity resources, while intellectual property protects private interest and emphasizes privatization. The conflict between them directly results in the weak protection of biodiversity; as a result, many economic benefit disputes generates between the developed countries and the developing countries. Therefore, coordinating the correlation between biodiversity and intellectual property becomes especially important. Though the Convention on Biological Diversity (CBD), Trade Related Aspects Intellectual Property Rights (TRIPS) and International Union for the Protection of New Varieties of Plants (UPOV) convention have made stipulations, the complete coordination is still difficult to be realized due to the limitations. Biodiversity is impossible to be the object of intellectual property, but biotechnological products or traditional knowledge produced because of the application of biodiversity can be the direction of intellectual property protection. China which is a great power in aspects of biodiversity resources and biotech cutting-edge technology not only has to keep the biodiversity of China away from infringement, but also needs to positively involve in intellectual property laws formulation and international corporation, maintaining the common interests of the developing countries, and make contributions to the intellectual property protection of biodiversity.

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INTRODUCTION

Biodiversity refers to the generic term of all living species in the earth including plants, animals, microorganism and their heritable variation as well as the ecological complexity, and it includes three different layers, i.e., genetic diversity, species diversity and ecosystem diversity. Currently, biodiversity resources are facing with the problems of excessive development induced exhaustion and the plagiarism of local resources by non-local governments and enterprises. Protection based on intellectual property is the most effective method though it is not the only one method. Laws concerning biodiversity resources and intellectual property include the Convention on Biological Diversity (CBD), Trade Related Aspects Intellectual Property Rights (TRIPS)[1] and International Union for the Protection of New Varieties of Plants (UPOV) convention. Though relevant laws have made stipulations, resource utilization and protection are still facing many problems. On account of that, many foreign scholars carried out studies. Foreign scholars Chang YM and Ross K[2] found that, many enterprises gained benefits from genetic engineering experiments based on the traditional knowledge of local farmers and biological resources in other countries without payment, which thereby caused conflicts; moreover, the behavior also induced the reduction of plant species around the world. They proposed that, the government should protect the rights of farmers to realize the maximum biodiversity and social best welfare. Taking the developing countries and the developed countries as the research subjects, Gao Qian,[3] a Chinese scholar, compared the protection regulations for transgenosis intellectual property between those countries, discussed the serious problems such as the

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commercial monopolistic behaviors and genetic plagiarism behaviors of transnational corporations, and put forward that protecting domestic biological genetic resources and farmers' benefits was the key in the construction of intellectual property laws. This study aims at analyzing the limitations and necessity of solving the problems existing in relevant laws about the utilization and development protection of biodiversity intellectual property by interpreting them and proposing relevant solutions and suggestions taking China as the subject of discussion.

UTILIZATION OF BIODIVERSITY INTELLECTUAL PROPERTY

Before 1980, biological resources were regarded as the public property of all human beings, and any country and individual could not monopolize biodiversity resources but could use arbitrarily. Because of the viewpoint, the developed countries violently collected and pillaged genetic resources information of the developing countries which own more biological resources.[4] With the development of the society and the advancement of science and technology, damages of human activities to biological environment become more and more fierce. Moreover, the rapid development of biotechnology requires for larger demands on biodiversity resources, but biodiversity resources have been extremely scarce due to excessive pillage by human beings and the neglected protection. There is conflict between the publicity characteristic of biodiversity resources and the privacy characteristic of intellectual property.

Intangible Genetic Utilization of Biodiversity – Taking Monsanto Beans Event as an Example

As mentioned before, the uneven global scientific and technological development and biological resource distribution induces the conflict between few developing countries and developed countries. Though the developed countries have no rich resources, they keep the common biodiversity resources for their own, i.e., extracting and purifying excellent genes from the rich diversity resources of the developing countries, producing better products, and applying for patents using the cutting-edge biological science and technology. But the resource owners not only cannot get any economic benefits not all, but also have to pay high patent fee when they use the products. Genetic resources center is considered as the source of all new species; more genetic resources indicate more usable genetic genes.[5] As the recognition of China on genetic resources started late, the event of Monsanto beans stroke us heavily.

China with vast territory and abundant resources possesses 9.6 million square kilometers of territory. China which has more than 90% of bean species over the world is a country which really controlled bean species. Till 2000, Monsanto Company discovered high output and disease-resistant genes from a wild bean which was given by China using cutting-edge technology and then produced anti-disease transgenic bean seeds with high output and oil pump capacity. After that, Monsanto Company applied for international patents about high-yield beans and its cultivation and detection to 101 countries including China, and put forward 64 patent protection requests. Since that, every country including the origin of the wild bean - China has to pay patent fee before using the transgenic bean.

Tangible Carrier Utilization of Biodiversity –Taking Traditional Chinese Medicine as an Example

Most of the developing countries own much more species resources than the developed countries. The developing countries and the local citizens own better conditions and solutions for the protection and sustainable use of local biodiversity according to the valuable experience which was spread by predecessors over hundreds of years. But the violent pillage of the developing countries to local biodiversity resources directly accelerates resource exhaustion and ecosystem collapse.

Traditional Chinese drugs mainly originated from China,[6] and only few came from foreign countries. Since ancient times, Chinese people have accumulated rich knowledge about traditional Chinese medicine through countless practical experiences and compiled them into relevant works. They are indispensable in Chinese historic culture. Shennong tasted hundreds of herbs in ancient time, which is a model of drug testing by oneself and medical expansion.

Biodiversity resource is the basis of traditional Chinese medicine, and the prescription of traditional Chinese medicine is directly prepared by creatures, which is significantly different with western medicine. Chinese laws have specific regulations for the species, patent and commercial protection of traditional Chinese medicine, but have not stipulated the exclusive rights of herbs. The right of preparing herbs using traditional methods will be threatened seriously if someone prepares traditional

Chinese medicine using Chinese herbs and applies for patents.

For example, Bothrocaryum controversum and Erigeron breviscapus which are the effective prescriptions that were spread from the ancestors of South Yunnan were made into drugs that could be used for treating cardiovascular and cerebrovascular diseases and relieving cough by some companies. But the local citizens got no benefits though their traditional knowledge was stolen.

BIODIVERSITY AND INTELLECTUAL PROPERTY RELATED LAWS

CBD emerges at the right moment because of the existence of the above problems. Besides CBD, there were many intellectual property laws which are related to biodiversity.

CBD

CBD which was passed in June 1992 is an international convention for protecting living resources on the earth.

The main purpose[7] of CBD is to protect biodiversity, realize the sustainable utilization of biodiversity components, and share commercial benefits and realize utilization in other forms in a fair and reasonable way.

CBD stipulates that, the developed countries should make up the developing countries for the cost they spend on protecting biological resources with new supplemental funds and transfer technologies to the developing countries in a more affordable way, thus to make the protection of biological resources on the earth more convenient; signatory countries should catalogue and compile the plants and wild animals in their frontiers and formulate plans for protecting endangered animals and plants; the developed countries should establish financial institutions to help the developing countries to exert plants for checking and protecting animals and plants; the countries which utilize the natural resources in another country should share research achievements, profits and technologies with that country.

Relevant Regulations of TRIPS

As one of the international conventions which have attracted much attention besides CBD, TRIPS set up an international standard which concerns the international protection of intellectual property and has been extensively accepted. Differing from the target of CBD, the purpose of TRIPS is to provide the minimum but powerful international protection for intellectual property.

Article 2, Section 27 of TRIPS[8] stipulates that, members may exclude from patentability inventions, the prevention within their territory of the commercial exploitation of which is necessary to protect ordre public or morality, including to protect human, animal or plant life or health or to avoid serious prejudice to the environment, provided that such exclusion is not made merely because the exploitation is prohibited by their law. But Article 3 (b)[9] further stipulates that, plants and animals other than micro-organisms, and essentially biological processes for the production of plants or animals other than non-biological and microbiological processes. However, members shall provide for the protection of plant varieties either by patents or by an effective sui generis system or by any combination thereof.

The stipulation excludes animal and plant species and biotechnology methods out of available patents, grants the member countries with discretionary power on the right, and moreover affirms the rights of the cultivator of new plant varieties.

UPOV and UPOV Convention

UPOV is an inter-governmental organization whose head office was located in Geneva, Switzerland, and it is responsible for establishing an effective plant species protection system in the purposes of benefiting the society and encouraging the development of new plant varieties.

The principles of UPOV[10] are as follows. Contracting parties consider that, protecting new plant species is of great important in the development of national agriculture and the protection of breeders' rights. Contracting parties realize several special problems induced by the acknowledgement and protection of breeders' rights especially the limitation on the execution of the rights because of public benefits. Contracting parties hold that, the problems which are taken seriously by many countries should be solved respectively according to the united and clear principles.

Besides the above conventions related to the protection of biodiversity intellectual property, some non-governmental organization such as World Wildlife Fund (WWF), International Union for Conservation of Nature and Natural Resources (IUCN) and World Resources Institute (WRI) also involve relevant issues in different perspectives.

PROTECTION OF BIODIVERSITY INTELLECTUAL PROPERTY

Necessity

In some sense, biodiversity is in a close correlation to intellectual property. In the perspective of the current global situation, protecting biodiversity with intellectual property will satisfy the interest demand of multiple parties. Even in the perspective of China's national condition, the enhancement of the protection is imperative. The necessity reflects on:

1. Biodiversity provides enough resources for intellectual property

Since human was born, it has been a part in ecological chain, and human beings are linked with other creatures in the nature. The existing creatures have been occupied important roles in the whole ecological chain and maintained the balance of the whole ecological system. The extinction of a species may induce the fracture of ecological chain and the collapse of the whole ecosystem.[11] Human is a kind of creature with the highest intelligence. To obtain more comfortable life, human beings gain what they want from multiple creatures to satisfy their basic necessities of life. With the improvement of bioscience technology, people have attempted to use the part what they want such as genes through science and technology more than using biological resources directly.

Many backward areas can still utilize the local biodiversity resources according to the experience and knowledge which are spread by the ancestors, though there are no high-level technologies for developing those resources. However, many foreign institutes stole the resources and applied for patent for their own use. The plagiarism of agricultural and medical knowledge is the most serious, for example, the events of Bothrocaryum controversum and Erigeron breviscapus mentioned before.

Ecosystem is the treasure house of natural raw materials for bioscience. Human beings get so many research achievements because of the existence of biodiversity. Biodiversity resources will be wantonly developed and exhausted if there is no protection of intellectual property.

2. Reasonable intellectual property system will protect more extensive biodiversity targets

Intellectual property system is regarded as a motivation mechanism that can promote science and technology progress, economic development and culture prosperity. But currently, protecting original which is the original intention of intellectual property system is difficult to be realized, because the protection of biodiversity has many shortcomings.[12] Many research and development achievements of biodiversity especially the achievement of genetic resources are applied for patent after being improved based on local genetic resources and traditional knowledge. Intellectual property can protect the research achievement that is obtained by researchers, but is unable to protect local genetic resources and traditional knowledge. That is because research achievements are private and not owned by specific person.

Thus it is necessary to make intellectual property system more reasonable. Only reasonable intellectual property system is one of the effective approaches for promoting the development, protection and sustainable utilization of biodiversity resources[13] to avoid the irreversible damages of different countries to biodiversity because of interest dispute.

3. Standardizing relevant intellectual property system will brings benefits to all interested parties

Except a small part which has been protected by the current intellectual property, the majority of biodiversity resources are beyond the protection of intellectual property or other laws. Providing legal protection to the acquisition of all biodiversity resources and their achievements with intellectual property can not only bring huge profits to the institutions that involve in research and development, but also generate huge returns to resource owners and some economic and social benefits to the people in origin of resources. Moreover, the mutual corporation reduces the cost of resource acquisition and development and avoid more legal and trade disputes.

Intellectual property system is a double-edged sword. Though it can protect biodiversity resources to some extent, the conflicts between them determine the existence of limitations in such protection.

Limitations

1. The communality of biodiversity is in conflict with the exclusive privacy of intellectual property.
2. Biodiversity is tangible property which can only be discovered but cannot be invented, while intellectual property is intangible which emphasizes on individual invention.
3. Intellectual property is reproducible. Individuals in biodiversity may be copied by

bioscience; however, the whole ecological chain and ecological environment cannot be copied.

4. Intellectual property is not applicable to biodiversity because of regionalism.[14] Many habitats of animals and plants cover the borders of two countries, and some creatures even migrate between two remote counties every year.
5. Intellectual property is protected by intellectual property law within legal time and losses legal effect after the period, while biodiversity resources related knowledge is accumulated over thousands of years and will become public property after the period.
6. In the current international protection system for intellectual property, there is a huge gap between the positions of the developing countries and the developed countries, and the relevant international conference is intended to maintain the interests of the developed countries[15] rather than the developing countries.

Intellectual property is not the only way protecting biodiversity resources because of so many conflicts between them.

4. The countermeasures and suggestions which can be adopted by China

China has rich biodiversity resources and once experienced biodiversity resource pillage by the developed countries like other developing countries. But China owns cutting-edge science and technology which is comparable with that of the developed countries, and moreover Chinese researchers have applied for thousands of genetic patents.

Due to the special double identity, China should formulate relevant countermeasures for protecting biological resources or biodiversity as soon as possible.

1. Legal regulations of biodiversity resource knowledge intellectual property should be perfected to emphasize China's ownership of all biological resources within the border of China and establish the acquisition method and standards of biodiversity resources in China and relevant interest sharing principles.
2. Patent Law should be perfected. To maintain the rights of biodiversity resource own countries and regions, patent applicants should clarify the origin of resource when applying for biological resource related patent and demonstrate the certificates which can suggest the qualification for the development and utilization of local resources.
3. Remote areas and minority areas are encouraged to develop traditional knowledge, apply for patent, and bring local biodiversity resources into the category of intellectual property.
4. For the weak science and technology fields in China, it is suggested to actively propose resource share and joint development to the institute which masters a technology, which can protect the pillage of China's resources and improve the level of science and technology of China.
5. For the relatively strong science and technology fields in China, relevant development plants can be formulated to positively, rapidly and safely transform biodiversity development achievements into intellectual properties and protect them.
6. The scientific research institutes in China should go abroad and positively involve in the development, utilization and protection of global biodiversity enjoying intellectual property and share.
7. China should positively participate in international cooperation, discuss the schemes and technologies which are beneficial to creatures, and maintain the common interests of the developing countries while formulating and perfecting international intellectual property convention.

CONCLUSION

Whether biodiversity intellectual property protection associated legal regulations are feasible is actually related to the distribution of interests and resources. The developing countries hope to get biotechnology from the developed countries, while the developed countries are eager to obtain resources from the developing countries even though they have mastered cutting-edge technology. Excessive drawing of biological resources can not only damage the earth, but also bring about human's own destruction. Perfecting intellectual property system and developing biotechnology on the premise of resource protection can not only bring benefits to both parties, but also can make contributions to the protection of biodiversity on the earth on a long view.

Protecting biodiversity with intellectual property not only satisfy the desire of the developing countries for the technical support for the development and protection of biodiversity resources but also meet the demand

of the developed countries which own advanced technologies on biodiversity resources and economic benefits. Nevertheless, intellectual property system can only be one of the measures for the protection and sustainable utilization of biodiversity resources due to the conflicts between intellectual property and biodiversity, and the implementation of intellectual property protection system is bound to be constrained by other legal regulations to avoid abuse.

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Article

Wearable Large Volume Injectors Hold Promise for Success in Commercialization of Biologics

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ABSTRACT

With so many biologics in development and no patient-centric way to deliver them, it was inevitable that innovative delivery solutions would emerge that enable a new pharmaceutical product to meet two top criteria for successful commercialization: satisfy patient demands for easy drug administration without disruption to their everyday lives, and address health system demands for lower costs and more value. The solution lies in combining biologic drugs with the more advanced large volume wearable injectors to enable patients to self-inject even the most viscous formulations and volumes of up to 50 mL with ease and comfort in their homes or workplaces.

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Keywords: Large volume wearable injectors; combination products; biologics; drug delivery; cancer; autoimmune diseases; viscosity; formulation; rare diseases; self-administration; subcutaneous injections; patient-centricity

GROWTH MARKET FOR COMBINATION PRODUCTS: BIOLOGICS DELIVERED BY WEARABLE LVIS

The pipeline for the pharmaceutical industry will continue to be driven by the development of biologics and biosimilars. Since most biologic formulations are highly viscous due to their molecular composition, they are frequently administered in large volumes via intravenous (IV) infusion and, by necessity, in the healthcare facility setting.

In a 2016 Accenture survey of more than 200 executives at leading pharma companies in the United States and Europe, 85% of respondents said their companies plan to increase spending on patient-centric capabilities over the next 2 years.[1] For administration of biologics, easy-to-use wearable LVI's that are based on pain-free injection technology provide this patient-centricity—among other benefits.

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INCREASE IN PROMISING NEW BIOLOGICS AND BIOSIMILARS TO TREAT MULTIPLE DISEASE STATES

Biologics and biosimilars encompass an array of products such as vaccines, blood components, somatic cells, gene therapy, as well as recombinant therapeutic proteins. Over the past 20 years, several biologics have demonstrated proven efficacy and safety as evidenced by first-in-class therapies such as bevacizumab, rituximab, trastuzumab, and imatinib that are used to treat a wide variety of autoimmune diseases and certain types of cancer. While these previously approved products are projected to have continued high sales, hundreds of new experimental biologics have entered the pipeline and comprise more than 50% of products undergoing pharma development.[2] According to the National Institutes of Health clinical tests database, there are more than 900 biologics currently being studied in clinical trials in multiple therapeutic areas for numerous

disease states, with the largest growth occurring in the therapeutic areas of cancer (and cancer-related conditions), infectious disease, and autoimmune disorders. In addition, increasing emphasis has been placed on developing biologics to treat rare diseases.[3] All signs indicate that the trend for increased development, approval, and use of biologics will continue into the foreseeable future.

VISCOSITY AND VOLUME CHALLENGES WITH BIOLOGICS

From the perspective of treatment administration, the main challenge of biologics resides in their molecular complexity, in many cases their long-chain protein composition that results in a dense, highly viscous solution. Given the high viscosity of most biologics, and the fact that biologics are not suited for oral administration, these products have traditionally been administered intravenously (IV) as a 1- to 2-minute bolus injection or diluted and infused continuously or at specific intervals over longer periods of time, depending on the specific biologic product and therapeutic indication. Preparing an IV requires a high degree of technical skill and can be more challenging with elderly or cognitively challenged patients. Intravenous injections also carry a risk of systemic infection and require medical observation for side effects including infusion site reactions. For these reasons, IV administration of biologics must be performed by trained staff at the hospital or physician's office. The entire process for IV infusion of biologics is therefore inconvenient for the patient and represents a substantial time and resource burden to the healthcare facility.[4]

The subcutaneous route may be the optimal method of administering most biologics and has distinct advantages over other injection methods. While skilled personnel are required to administer IV and IM injections, subcutaneous injections are routinely self-administered by patients.[5,6] Subcutaneous injections use short, small bore needles that are more comfortable and have a comparatively lower risk of infection or other complications. For patients requiring multiple, daily doses, subcutaneous injections can be administered at several alternative sites.[6] When administered through the subcutaneous route, biologics are transported through the capillaries and lymphatic system, with the result being a sustained and slower systemic absorption that avoids the immediate, sharp peak concentrations.

SUBCUTANEOUS INJECTION OF BIOLOGICS: OVERCOMING THE VOLUME CHALLENGE

While the subcutaneous route may present advantages for administering many biologic therapies, subcutaneous injections are limited in the amount of drug product that can be delivered and tolerated by the patient in a single injection. In most cases, the volume of bolus subcutaneous injection is limited to 1-2 mL. One approach to circumvent these volume limitations includes increasing the concentration of the active ingredient in the formulation. However, one of the main constraints in biologic formulation development is the exponential relationship between the concentration and formulation viscosity. For large protein biologics such as monoclonal antibodies (mAbs), volume and bioavailability constraints must be addressed before subcutaneous injections can be used in place of intravenous dosing regimens. Monoclonal antibodies often have high dose requirements and as a consequence must be formulated at very high concentrations, which typically result in highly viscous drug products. These highly viscous formulations cannot be readily injected, particularly when smaller-gauge needles are used to reduce the patient's pain or discomfort.[7,8]

Achieving optimal therapeutic concentrations is often limited by manufacturing processes and other constraints such as pH and osmolality, along with the use of certain excipients.

Given that these formulation properties need to be kept within specified ranges to prevent patient discomfort and injection-site reaction, increasing the administered volume of drug product is left as the only practical option to deliver a larger dose. There are limitations, however, to how rapidly a volume of drug can be injected subcutaneously. While there is wide variation in the optimal injection time among individual drug products, and although information regarding the relationship between injection volume and speed is limited, it is understood that subcutaneous space cannot tolerate rapid injection of increasingly large dose volumes, as tissue disruption and site reaction occur. Furthermore, if the subcutaneous injection is rapid and the volume is too large, the product may leak outside the body through the injection site, thereby reducing the bioavailability relative to the total dose. Finally, patient self-administration using a manual subcutaneous injector is not practical due to the fact that the larger volume requires longer injection time and increases the difficulty for the patient to hold the device at the injection site.

WEARABLE LARGE VOLUME INJECTORS (LVIS): AN ELEGANT SOLUTION

With the continued increase in marketed biologic products, the new wearable LVI delivery systems are now able to improve the bioavailability of biologics and overcome their inherent concentration, viscosity, and volume challenges. These systems are patient-centric devices that simplify the self-administration of large volumes (> 1 – 2 mL) in a controlled manner. Understanding subcutaneous tissue pressure has been critical for designing injection devices that are acceptable to patients, especially during potentially lengthy administrations of biologic therapies. A recent study found that patient discomfort is related to increased pressure and mechanical strain in the subcutaneous space, which is more directly related to increasing flow rate than to volume.[9] These new systems overcome the large-volume injection challenges by allowing the patient to administer increased volumes into the subcutaneous space more slowly. By extending the subcutaneous injection time, LVIs increase patient comfort and expand the possibilities for large volume self-injection.[9,10] Due to the need for longer duration of injection, these devices are temporarily attached to the body at an appropriate injection site.

Current wearable LVIs range in size, dimension, complexity, and functionality. Some wearable LVI devices use computer-based systems integrated with electric or electrohydraulic motors that offer a variety of pre-programmed dose administration settings. The working parts of other simpler LVI devices are purely mechanical yet allow for a wide range of injection volumes and flow-rate settings, and provide injection pause features and patient data collection using wireless technology. Some LVI devices utilize prefilled syringes while the most advanced, from Enable Injections, use standard vials or syringes along with a platform technology for automated mixing, reconstitution, and warming of refrigerated drug product. It also delivers the largest doses, up to 50 mL. Most LVI devices are designed to adhere to the injection site skin using an adhesive and are small, unobtrusive, and disposable.

Since LVI devices are built to simplify the self-administration of a subcutaneous injection over relatively longer periods of time, numerous human factors considerations have been incorporated into their designs. Foremost among these include ease of use, patient comfort, and discretion. To simplify patient device operation, LVIs utilize clean ergonomic designs and can typically be operated using an intuitive 3-step process consisting of placement, activation, and injection initiation. Patient comfort is a top concern with wearable LVIs. These subcutaneous devices use small bore needles that are never visible to the patients, incorporate pause and flow-rate control features to allow for patient control and comfort. Another important safety feature includes automatic needle retraction to prevent accidental needle sticks to patients and caregivers. As patients prefer discretion during self-administration, most LVIs are designed with a low profile with smooth edges to that allow them to be easily and safely concealed beneath clothing over extended periods of time.

WIDER IMPLICATIONS OF WEARABLE LVIS: A HAND-IN-GLOVE FIT WITH THE NEW HEALTHCARE PARADIGM

The new model for healthcare is one that drives down costs by reducing the time and resource burden on healthcare facilities by promoting efficiencies including individual self-care under the right conditions. Wearable LVIs fit neatly into this new paradigm. A time-and-motion study undertaken in eight countries reported significant time savings for both healthcare professionals and patients through the use of subcutaneous versus the IV route of administration. These findings suggest a potential for reduced waiting times, greater appointment availability, and improved efficiency of oncology units with use of the subcutaneous formulation. Furthermore, compared with IV drugs, the majority of participants in the study considered subcutaneous drugs clinically safer and more cost-effective, resulting in higher patient satisfaction.[10]

In many cases biologics will continue to be administered by healthcare professions in a hospital or other point-of-care setting using the IV or subcutaneous route of administration as the situation dictates. However, the introduction of wearable LVIs will allow a large segment of patients to discretely self-administer their high volume biologic treatment subcutaneously in a safe and efficacious manner, and in the process reduce the time and resource burden on healthcare facilities.

CONSIDERATIONS IN CHOOSING A WEARABLE HIGH VOLUME SUBCUTANEOUS DELIVERY DEVICE

The process for determining the appropriate biologic product and patient population for use of a wearable LVI is multifaceted and will need to be carefully considered by healthcare professionals. Healthcare specialists will

need to select the right system and device to deliver the chosen biologic using the optimum treatment protocol for a particular patient. Treatment administration variables include injection frequency, dose volume, drug viscosity, delivery rate, and duration.[11] Human factor considerations include pain reduction, portability, and convenience, each of which influence treatment compliance and preference rates among the target patient populations. Physicians will of course need to assess individual patient factors to determine the appropriate candidates for self-administration of a biologic using LVIs.

Other external and device-related aspects that might impact the selection of an LVI system include the range of doses used to treat a specific patient population, the requirement for small or incremental dose adjustments, specific ergonomic or ease of use considerations, and the need for refrigeration. Prior to subcutaneous injection, many biologic products need to be warmed to room temperature, which represents an inconvenient 30-minute step. Consequently, there is a need for a delivery system capable of transferring the highly viscous product while rapidly warming the drug to room temperature.[12]

Today's more sophisticated drug delivery devices are differentiated from legacy injection systems in several important ways. Some novel systems currently make use of standard vials and syringes and in the process minimize the drug stability issues frequently observed in new container closer development. In conjunction with the use of vials and syringes, the new injection systems automatically warm the drug as the injector is filled, thus reducing the usual wait time required when using a refrigerated drug product. The newest systems also automate the mixing and reconstitution of lyophilized drugs, which removes patient variability and error from the mixing process. In terms of minimizing pain and improving patient comfort, the new injection systems use the smallest needle possible and allow the patient to pause the injection or make adjustments in flow rate. Although capable of injecting large volume biologics up to 50 mL, the injectors themselves are small and designed with a low profile that can be discreetly worn on the body beneath loose clothing, which allows freedom of mobility. The newer devices incorporate the latest in simple data-capture technology, which can be used to monitor the patient's adherence to therapy and promote compliance.

PHARMA-DEVICE PARTNERSHIPS

Given the projected increase in development of biologics coupled with innovations in biologic delivery systems that may increase patient autonomy and reduce healthcare costs, a natural partnership is underway between drug and medical device companies. In the US, FDA regulations point toward a path to approval that includes biologics and their associated delivery systems as drug/device combination products, with both the biologic and device components requiring approval under biologic license application (BLA) process. Since the biologic regulatory pathway requires a rigorous clinical program, LVI devices can be leveraged to achieve success by providing flexible dose administration and data gathering capability during early phase pharmacokinetic studies. The BLA itself will need to contain extensive device design information and provide summaries of device-focused human factors studies. Synergistic drug and device company partnerships that effectively play to each other's strengths under a comprehensive strategy should lead to regulatory marketing approval, commercialization, and future improvements to lifecycle management of the combination products. Ultimately, the innovator pharmaceutical companies require an elegant solution for the delivery of their biologic product that medical device companies provide.

SUMMARY

Development, approval, and use of wearable large volume injectors (LVIs) for subcutaneous delivery of biologics facilitates self-administration, increases patient comfort and compliance, and reduces cost and resource burdens in harmony with the new healthcare paradigm that emphasizes outcomes. Current market forecasts predict robust growth for LVI device companies, with projections of up to $8.1 billion by 2025. Biologics, when combined with these patient-centric delivery devices, hold promise to provide greater success in commercialization.

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Article

Do VC Firms of Different Ownership Structures Exert Heterogeneous Impact on the SMEs' Profitability?

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ABSTRACT

This article is to investigate the heterogeneous effect of Venture Capital (VC, in abbreviated form) on the profitability performance of small and medium sized enterprises (SMEs, in abbreviated form) in China, from the perspective of VC firms' different ownership structures. Based on the panel data of the listed firms on the Chinese SME board, the regression results show that overall the VC backing is significantly correlated with the profitability of the SMEs in a positive way. After focusing on the VCs' characteristics in the ownership structures, it is proven that the foreign VC firms can have the strongest positive impact on the ventures' profitability performance; the Chinese private VC firms can have the positive impact on the SMEs' profitability, but the impact is weaker than that of foreign VCs and stronger than that of governmental VC in a positive way; the governmental VC firms exert the significantly negative effect on the ventures' profitability.

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Keywords: Venture capital, SMEs, Ownership Structures, Profitability

INTRODUCTION

There is a big wave of entrepreneurship in China with the big support of Chinese government, in the aim of triggering the technological innovation and industrial upgrading, hoping to increase the employment and ensure the healthy economic development[1]. The Chinese government is regarded to play the dual roles, one way as the policymakers and regulators, the other way as the active participants in the process of the VC investments, not only offering guidance funding as the limited partners, but also establishing the VC firms as the general partners directly operating the VC investments. In accordance with WIND (one of the biggest financial datasets in China), the Chinese government VC funding raised in the Capital market amounted to 1 trillion and 500 billion RMB, and the total of assets managed by central and local government amounts to 2 trillion and 200 billion RMB by 2015. The Figure 1 shows, the Venture Capital investments have risen to 366.468 trillion RMB by the end of 2015 with the average year on year increasing rate of 0.2334 since 2006. The VC investment cases amounted into 4926 cases by the end of 2015, with the average year on year increasing rate of 0.2807 during 2006 and 2015. While with the booming of VC market in China, whether the VC investments can improve the performance of entrepreneurial firms has triggered the great interest among the academic scholars and practitioners. The entrepreneurial firms with good quality and big growth potential will attract the entry of VC financing; on the other side the involvement of VC financing can also exert positive impact on the ventures' performance and technological innovation progress[2]. Is the performance superiority of entrepreneurial firms that comes first to attract the VC financing or is the participation of VC that comes first to improve the efficiency and performance of funded firms remains an unresolved question. It is also with little attention in the academic circle that whether different VC firms in different

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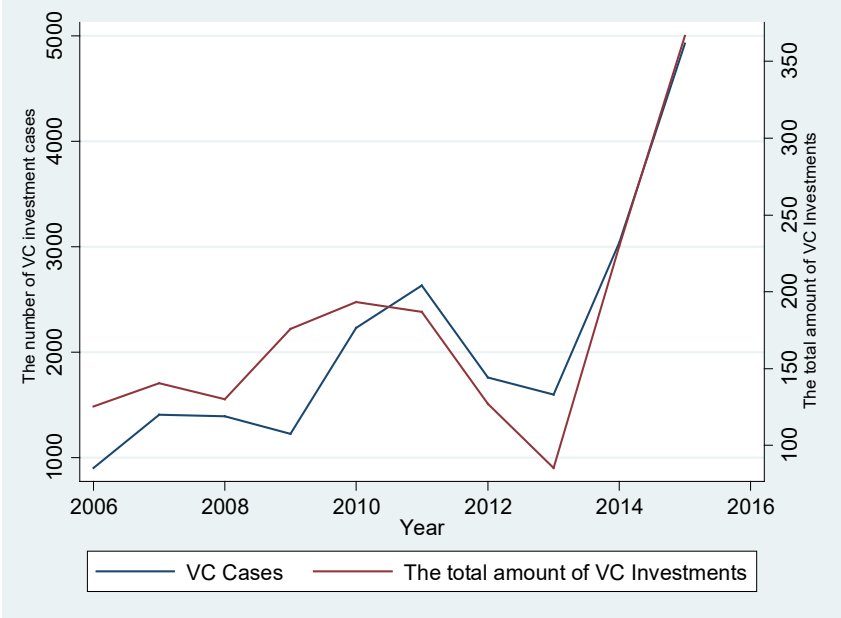

Figure 1: The growth of VC investments in China during 2006–2015
The source is form WIND financial database.

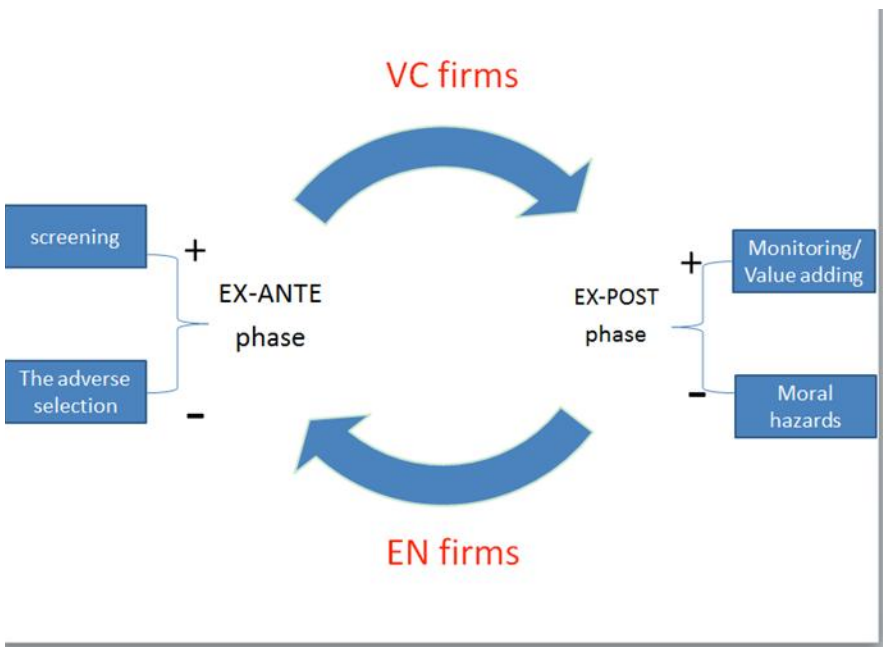

Figure 2: The analysis of VCs' effect during the ex-ante and ex-post phase

ownership structures can exert heterogeneous impact on the performance of the small and medium sized firms.

The Figure 2 exhibits the roles and mechanisms of VC financing during the different stages of VC investments. The whole processes of VC investments include the venture screening, the deal negotiating and the agreement signing in the ex-ante phase; the staged VC financing, the close monitoring and management of investments, as well as the exit of investments during the ex-post phase. Accordingly, the theoretical study and achievements on the mechanism of venture capital on the operational performance of entrepreneurial firms also mainly focused on VC firms' roles during these two phases. Scholars supporting the positive functions of

VC firms mainly focus on the positive roles of VC firms, namely the ex-ante scout and ex-post coach. The roles of scouts imply that compared with other kinds of traditional investors, VC firms can better handle the situation of extreme information asymmetry utilizing the advantage of their own special networking resources and the strict screening procedures and the due diligence[3]. As a result, the VCs can pick out the SMEs with better technology capability or superior performance. During the venture-screening stage, the VC firms usually implement the strict standards in the prudent evaluation and selection of target companies, aiming to select the most outstanding companies. While the functions of VC firms during the ex-post phase can be categorized into three kinds: the monitoring effect, the value-adding effect and financial support. After the entry of the Venture Capital the VC firms will function more like the mentor, and the Venture capitalists not only provide financial support to venture enterprises, but also actively participate into the ex-post ventures' development and offer value-added services to the management of venture enterprises, closely monitor the ventures' operation to better deal with the information asymmetry and lower the agency risks between the ENs (entrepreneurs) and VCs[4]. Moreover the VC firms also provide more of the important professional expertise, investment and financing channels and management experience for enterprises, in order to add the value of ventures. The expertise and experience of venture capitalists and the ability to resolve the crisis are often regarded as the increasingly more important and valuable contributions for the funded venture firms.

Contrarily, some scholars are also in the view of VCs' negative correlation with ventures' performance, arising from the adverse selection in the screening process and moral hazards in the ex-post monitoring process. During the ex-ante phase, for the big uncertainty of the external environment, and high information asymmetry between the principles and agents, VC firms have to face great difficulty and big costs in the stage of information gathering, filtering, analyzing, which will cause that "lemon effect" in the VC industry[5]. For the lemon effect of VC industry, the value of venture firms cannot be estimated efficiently, but are often valued by average level of entrepreneurial firms in the context of high information asymmetry, which cause that the value of better quality firms are often underestimated; only the firms with inferior quality are willing to accept the bidding price offered by the VC investors based on the average level of venture firms. The firms with superiority in the performance will self-select out the VC market, and finally the firms seeking and getting funded are not the best candidate in the industry[6]. In the ex-post phase the moral hazards might arise from the side of the SMEs financed and supported by VCs, such as the insufficient efforts from ENs in the operation, the abuse of capital and financial resources, the investee firm' cheating or window dressing activities in the financial situation for the sake of the private benefit of receiving the subsequent VC financing. The moral hazard could also be from the other side of VC firms, in which the VCs are also motivated to seek the private benefit on the cost of harming the development of the funded firms, such as the insufficient efforts of VCs in the support of ventures during ex-post monitoring process, the free-rider problem in between the VC firms the syndicated investment, the stealing of creative ideas and core technologies from the funded VC firms, VCs' blackmailing and threatening activities to stop the successive financing, VCs' investing in the other competitors while harming the future development of the funded firms etc. We can see that the theoretical and empirical analysis about VC firms' functions and roles in the performance of the funded firms is still inconsistent, and this paper aims to investigate the mechanisms and impact of VC firms as well as the heterogeneous effect of VCs on the profitability performance of the small and medium sized firms based on the panel data of Chinese SME board.

THEORETICAL ANALYSES AND BASIC HYPOTHESIS

Due to the under-developed construction and weak framework of credit reporting system in China and immaturity of governmental and legal supervision over the financial systems, the SMEs usually face the problems of severe external financial constraints in the context of the bank-oriented financial system. And also the Chinese SMEs face the difficulty of raising fund from the stock market, though the Nasdaq-liked boards—SME Board and the GEM board have been introduced since 2004 and 2009. These two boards has rather strict standards for the IPO application, with the SME Board requiring the issuing firms to make the net positive profit of more than 30 million RMB on average during the the last 3 fiscal years before IPO; with the GEM Board requiring the issuing firms to make the net positive profit of more than 10 million RMB on average during the last 2 fiscal years, as well as keep the historical record of making successively growing profit during the last 2 years before IPO. Such strict requirements on the profitability of the issuing firms set up big obstacles for the SMEs to achieve the necessary funding from the stock market. Especially for those start-ups with little tangible assets, big growth potentials and technological advantages, but still not profitable yet, will find it

more difficult to gain the financial capital from the traditional financial channels. The VC firms mainly invest in those unlisted firms with high-risks and but huge growth potentials, aiming to make huge economic returns at the exit of investments when the value of the funded firms are enhanced greatly afterwards. The VCs are considered to play important roles in financing the small and medium sized companies and monitoring the operational activities of the funded firms, offering value-adding services such as the expertise, the social connections and consulting services etc. beneficial to the enhancement of the corporate governance and performance of the funded venture firms[7]. Therefore we propose the hypothesis

H1: The venture backed SMEs show the superiority of the profitability, compared with the peers without the VC backing.

To study VC firms' heterogeneous impact based on VCs' different ownership structures, this paper categorized the listed firms into four kinds: firms with no venture backing, firms supported and financed by foreign VCs, firms backed by the Chinese private VCs, and the firms financed and supported by the governmental VCs. If the firms are backed by more than one VC firm in the syndicated VC investments, the ownership structure of the leading VC firm at the first round of VC financing will determine the capital background and ownership structure for this particular researched sample firm in this empirical analysis. For example if the listed firms are backed by different syndicated VC investors, with the leading VC being the foreign VC, then this firm will be regarded to be supported by the foreign VC firm.

China has attracted the venture capital investments around the world, since the China's government started the development of VC industry by initiating a set of supportive and favorable policies in 1980s. Because of the capital control regulations, the foreign VC often runs in the off-shore mode, to avoid the Chinese regulation supervisions. In the off-shore mode the foreign VCs will establish a holding company, with major shares hold by the foreign VCs and the entrepreneurs together. Through the acquisitions, this holding company will take total and real control of the entrepreneurial firm back in the mainland. Through the off-shore mode, the foreign VCs can raise fund form the overseas capital market, and can actually invest in the Chinese SMEs by investing into the overseas holding company literally. Such round trip mode can help foreign VCs to avoid the strict regulatory restrictions in the China and employ the flexible terms and capital operation modes similar as in the US market[8]. Thus the VCs can have bigger scales in the fund size since its investors are more diversified including the pension funds, insurance firms, universities, banks and larger cooperation as well as the wealthy individuals[9]. While the domestic VCs raise funds mainly from the governmental agents, universities and corporations, as for the strictness in the Chinese institutional restrictions for the investment channels of the insurance firms and banks (mostly state owned). The off-shore mode of VC investments can make the foreign VCs implement better mechanisms (such as the limited partnership), which can not only set up a better incentive to stimulate the efforts of GPs, but also help to attract more capable and efficient managers to join the VCs, by establishing a closer and more sensitive relationship between the payment of VC managers of the investment performance. Compared to the centralized personnel system with strong administrative color in the domestic VCs, the management of foreign VCs can show higher efficiency in the management. The Figure 3 mainly exhibits that, the foreign VCs in China may have the difficulties in the information gathering and processing for the unfavorable factors in the geological distance, the cultural barriers and weak social connections, the foreign VCs can also enjoy more of advantages in the expertise, experiences and fund scales as well as the flexibility in the international mode of Venture Capital operations. In the view of the analysis above we propose the hypothesis

H2-a: the foreign VCs can exert the significantly positive impact on the funded firms' profitability, compared with non-venture backed firms; and H2-b: such positive impact on the funded firm's performance in the profitability is significantly stronger than that of the domestic VCs in China.

With rapid growth of Chinese VC industry, the domestic VCs paly more and more important roles, since the total investment of domestic VCs have exceeded the foreign investments since 2010. The Chinese private VCs usually only have limited capital sources; with raising fund mainly form the institutional investors, large firms, university endowments. It is not until 2007, with the reform of company law, and then the limited partnership is just legalized in the VC market. The form of Chinese VC funding firms starts to change from the limited company mode to the limited partnership mode. Under the strict contractual relationship between the Chinese private VC firms (GPs) and the limited partnership investors (LP), it is demanded that the VC firms must pursuit as much of investment returns for the LP investors as possible, and also undertake the unlimited risks and liabilities in the investments[10]. The predetermined regulations on the funding size, term and the compensation mechanism of VC funding manager in the agreement, as well as the stress in the follow-up refunding and reputation

Figure 3: The advantages and disadvantages of foreign VCs in the operation of venture capital investments

establishing and maintaining in the VC market, motivate the VC firms not only to implement "prudent investigation" of the ventures in the stage of ventures screening, and but also to closely monitor the operation and development of investee firms to avoid the moral hazard problem caused by the extreme information asymmetry, and also pay attention to offering the value-adding services and support in the aspects of professional and technical and business knowledge, market channels, human resources to increase the probability of the future success in the VC investments[11, 12]. Therefore we propose

H3-a: the Chinese private VCs can exert the positive impact on the SMEs' profitability, compared with non-venture backed firms; H3-b: and such impact is significantly weaker than that of the foreign VCs; H3-c: but such impact is significantly stronger than that of the governmental VCs.

In 1985, the first VC firm with the governmental capital background was set up with the approval of the Chinese State Council, in the aim to attract more of the participation of social capital into the VC industry. Generally in this paper, the governmental VC firms are referred as the Venture capital institutions directly set and owned by the government administrations or state-owned enterprises. The funding resource of government VCs mostly come from the state-owned enterprises, and the government financial allocation and the governmental guarantee loan[10]. The governmental VCs do not totally operate in the market-oriented mechanism, and the economic returns is not the sole goal of governmental VC financing, and the governmental VC funding also serve in other social responsibilities such as in the promotion of economic development, the new high technology invention and innovation, and employment increasing[13]. The governmental funding generally do not have the fixed duration term, thus the VC firms do not have the subsequent financing pressure as the private firms or the foreign firms. Moreover the governmental VC fund managers are not employed directly from the labor market, but assigned by the higher-level governmental departments, and they are often in lack of the managerial experience and expertise in the related areas and the performance of their investments do not closely correlate with the payment of their own. Due to the lack of effective incentive mechanism in stimulating the maximum of VC capitalists' efforts, the screening and monitoring functions of VC firms will be impeded to the certain extent[14, 15]. Therefore the governmental VCs will not respond quickly and timely to the market, and also cause the problem of the low efficiency and misallocation of resources, in the process of screening and nurturing of venture firms. Therefore we propose

H4: the Chinese governmental VCs exert the significantly negative impact on the SMEs' profitability performance.

DATA, VARIABLES AND MODELS

Data and The Constructions of Variables

The main ways for the VC firms to exit the investments are including IPO, M&A, buy-back and Liquidity etc. Since the IPO is considered to be the most successful way of exiting the investments and the SME board is one of the main channels for VC firms to exit the investments in the SMEs. Thus this paper selects the listed firms on the Chinese SME board, listed during 2004 and 2014, to be the data samples. By further checking WIND database, we set up the treatment group of 279 listed firms possessing the background of VC/PE financing and supporting. In order to build up the control group of non-venture backed firm, this paper employ the methodology of propensity scores matching by standards of industry, firm's age, the firm's provincial location, and get 279 SMEs with no background of venture financing as the control group of the research sample firms. For the explained variable of SMEs' profitability, we chose the return on net assets (*Roe*) of the firm to be the proxy of the financial performance of the SMEs. The explanatory variables include the dummy *Vbk* variable to indicate whether the firm has the background of VC backing; which is equal to 1, if the firm is invested in by VC/PE firms before being listed, 0 if the firm is not invested in by VC/PE firms before being listed. To estimate the influence of VC firms' features in ownership structures on VCs' value adding effect, we add the dummy *fback*, *pback*, *gback*, to represent whether the VCs have the foreign, Chinese private and governmental capital background respectively. We also introduce the interaction term *vc_g* (the iteration term between *Vbk* and *gback* dummy), *vc_f* (the interaction term of *Vbk*fback*), *vc_p* (the interaction term between *Vbk* and *pback* dummy) into the regression models to estimate whether VC firms in different ownership structures can exert heterogeneous impact on the profitability of the SMEs. To control the impact of other influential factors, the models also contain the dummies indicating the different industries of SMEs, locations of the SMEs, as well as the years of being listed. The control variables include the firm size and the turnover rate of total asset, the asset liability ratio. As show in the table 1 is the detailed illustration about the variables' definitions.

Models

The estimation model 1 shown in the equation (1) is to estimate the overall impact of VC backing. To testify *H1*, the relationship between VC backing the profitability of the funded firms, this paper introduces *Vbk* (the dummy to index whether the firm has the VC financing background before being listed). *Vbk' s* coefficient will imply that the influence of VC investments on the profitability of the SMEs; for example when *Vbk* is correlated with *Roe* significantly in the positive direction, it will imply the VC investments show the positive impact on the firm's profitability. The control group of variables contain *dtr* (the asset liability ratio), *ast* (the log of firm's total asset), *tor* (total asset turnover rate), and the dummies for different industries and years, to control the influences of these factors. The panel data regressions with the random effect including the firm and year fixed effects are employed to control for differences between firms and across time, respectively.

$$Roe_{it} = \alpha_i + \lambda_t + \beta_1 ast_{it} + \beta_2 tor_{it} + \beta_3 dtr_{it} + \delta_1 Vbk + \sum_{i=1}^{12} \chi_i I\_dummy_i + \sum_{j=1}^{13} \gamma_j Y\_dummy_j + \xi_{it} \quad (1)$$

To testify the *H2* whether the foreign VC firms have significant different impact on the funded firms' performance in the profitability, this paper then employs *Vc_f*, interaction term between the dummy *fback* (representing whether the firm is financed by the foreign VC firms) and *Vbk* to be the explanatory variable in the regression model 2 as explicated in equation (2). If the interaction term *Vc_f* is significantly correlated with *Roe* in the positive way, then it can be proven that the firms backed by foreign VCs perform significantly better than the firms financed and supported by domestic VCs. And the foreign VC firms can have stronger impact on the profitability performance of SMEs. The fixed time and firm effect combined with panel data regression with random effect is employed to control the influence of other observable and unobservable factors

$$Roe_{it} = \alpha_i + \lambda_t + \beta_1 ast_{it} + \beta_2 tor_{it} + \beta_3 dtr_{it} + \delta_1 Vbk + \delta_2 Vc\_f + \sum_{i=1}^{12} \chi_i I\_dummy_i + \sum_{j=1}^{13} \gamma_j Y\_dummy_j + \xi_{it} \quad (2)$$

The model 3 in the equation (3) is to estimate the impact of Chinese private VC firms, and estimate whether the Chinese private VC firms can have significantly different impact on the funded firms' profitability, in comparison

Table 1: The Definitions of Variables

Variables		Definition
Profitability	Roe	The net returns/the average net assets (excluding non-recurring profit and loss)
	Roa	The net returns/the average total assets (excluding non-recurring profit and loss)
Explanatory variables	Vbk	0/1, indexing if the sample firm is financed by VC firm before IPO
	gback	0/1, indexing if the sample firm is financed by the governmental VCs before IPO
	fback	0/1, indexing if the sample firm is financed by the foreign VCs before IPO
	pback	0/1, indexing whether the sample firm is financed by the Chinese private VCs before IPO
	Vc-f	The interaction term, defined to be *Vbk*fback*
	Vc-p	The interaction term, defined to be *Vbk*pback*
	Vc-g	The interaction term, defined to be *Vbk*gback*
Control variables	tor	The turnover rate of total asset
	dtr	The asset liability ratio
	ast	The logarithm of the firm's assets
	ΣSDY	year dummies to indicate the different years covered by the data samples
	ΣSIY	industry dummies to indicate the different industries covered by the data samples

Table 2: The Venture Capital Overall and heterogeneous Impact on the Roe of SMEs

	1	2	3	4
	Roe	Roe	Roe	Roe
Vbk	0.0087**	0.00463**	0.0036**	0.00399**
	(1.67)	(1.91)	(1.75)	(1.77)
tor	13.43***	13.42***	13.43***	13.44***
	(29.57)	(29.58)	(29.57)	(29.61)
ast	–0.0268***	–0.0271***	–0.0268***	–0.0266***
	(–10.43)	(–10.57)	(–10.40)	(–10.37)
dtr	0.146***	0.146***	0.147***	0.148***
	(15.33)	(15.35)	(15.33)	(15.47)
Vc-f		0.0402***		
		(3.31)		
Vc-p			0.00363	
			(1.14)	
Vc-g				–0.0316***
				(–3.20)
ΣSDY	yes	yes	yes	yes
ΣSIY	yes	yes	yes	yes
N	4019	4019	4019	4019
p	0	0	0	0

*Note: ** p < 0.1, *** p < 0.05*

with those VCs of different ownership structures. In the model 3 the interaction term between *Vbk* and *pback* (indicating if the firm is supported by the Chinese private VC firms) is our main concern and if *Vc-p's* coefficient is positive and significant, it will mean that the domestic VCs will exert stronger positive impact, compared to the VCs in different ownership structures and capital backgrounds. Otherwise the domestic VCs cannot function as efficiently as other VCs in promoting the profitability of the funded firms in the profitability.

$$\begin{aligned} Roe_{it} &= \alpha_i + \lambda_t + \beta_1 ast_{it} + \beta_2 tor_{it} + \beta_3 dtr_{it} \\ &+ \delta_1 Vbk + \delta_2 Vc\_p \\ &+ \sum_{i=1}^{12} \chi_i I\_dummy_i \\ &+ \sum_{j=1}^{13} \gamma_j Y\_dummy_j + \xi_{it} \end{aligned} \tag{3}$$

We include *Vc-g*, the interaction term between *Vbk* and *gback* (indicating if the firms are supported by the governmental VC firm) into the model 4, to further test whether the governmental VC firms can have significantly different impact on the funded firms' profitability. If *Vc-g* is in the significantly positive correlation with *Roe*, the stronger impact of governmental VC firms can be thus verified. It the correlation is estimated be negative and significant, and then it can be illustrated that the governmental VCs can only have weaker incremental impact of the funded firms' profitability, in the comparison with VCs of different ownership structures.

$$\begin{aligned} Roe_{it} &= \alpha_i + \lambda_t + \beta_1 ast_{it} + \beta_2 tor_{it} + \beta_3 dtr_{it} \\ &+ \delta_1 Vbk + \delta_2 Vc\_g \\ &+ \sum_{i=1}^{12} \chi_i I\_dummy_i \\ &+ \sum_{j=1}^{13} \gamma_j Y\_dummy_j + \xi_{it} \end{aligned} \tag{4}$$

THE ESTIMATION RESULTS

For all the regressions models 1-12 (* $p < 0.2$, ** $p < 0.1$, *** $p < 0.05$), the control variable *ast's* coefficient is estimated to be negative and significant by the 1% level and it is can be inferred that there exits the significantly negative correlation between the *roe* and the company's scale. It is also to say the smaller is the size of the listed companies on the SME board, the higher of roe the SMEs will perform with. And such results are contrary to the conclusion from some of the traditional empirical studies holding that the net assets yield is positively related to firm size. It might be for the reason that the listed firms on the SME board are mostly small and medium-sized enterprises, possessing different ways of management from those of large sized companies. The enterprise management level is more simplified in the small sized firms, the managerial staffs are mostly capable of dealing with multi-tasks and the decision-making should be faster and more efficient than in the large enterprises. The advantages of speedy reaction and efficient decision-making, more flexibility in the management and higher growth in the development, make the SMEs to show a better profitability performance. The asset liability ratio is found to be positively correlated with roe of the firm, for the coefficient on *dtr* being estimated positive, which is also to say that the higher is the debt ratio, the more profitability will the firm present. In fact for the SMEs, when they have higher leverage ratio, the leverage

Table 3: The Heterogeneous Impact of the Chinese private VCs on the Roe of SMEs, compared to that of foreign VCs and governmental VCs respectively

	5	6
	Roe	Roe
Vbk	0.0355***	–0.0267***
	(2.94)	(–2.76)
tor	13.70***	13.60***
	(29.13)	(29.29)
ast	–0.0263***	–0.0256***
	(–9.85)	(–9.71)
dtr	0.145***	0.141***
	(14.73)	(14.44)
Vc-p	–0.0352***	0.0273***
	(–2.88)	(2.75)
ΣSDY	yes	yes
ΣSIY	yes	yes
N	3732	3859
p	0	0

*For model 5 the sample firms only include non-venture backed SMEs, the SMEs supported by the foreign VCs and SMEs backed by the Chinese private VC firms. For model 6 the sample firms only include non-venture backed SMEs, the SMEs backed by the governmental VCs, and SMEs backed by the Chinese private VC firms. ** p < 0.1, *** p < 0.05*

Table 4: The Venture Capital' Overall and heterogeneous Impact on the Roa of SMEs

	7	8	9	10
	Roa	Roa	Roa	Roa
Vbk	0.00381**	0.00368**	0.00296**	0.0055**
	(1.75)	(1.73)	(1.85)	(1.67)
tor	8.892***	8.886***	8.890***	8.894***
	(32.28)	(32.29)	(32.28)	(32.31)
ast	–0.0121***	–0.0123***	–0.0121***	–0.0121***
	(–7.59)	(–7.69)	(–7.58)	(–7.55)
dtr	–0.0359***	–0.0359***	–0.0359***	–0.0354***
	(–6.23)	(–6.24)	(–6.23)	(–6.13)
Vc-f		0.0198***		
		(2.57)		
Vc-p			0.00153	
			(1.19)	
Vc-g				–0.0156***
				(–2.46)
ΣSDY	yes	yes	yes	yes
ΣSIY	yes	yes	yes	yes
N	3958	3958	3958	3958
p	0	0	0	0

*Note: ** p < 0.1, *** p < 0.05*

effect will be amplified and it then can be expected to make higher profitability in the further performance. The *tor*, the total asset turnover ratio is also proven to be positively correlated with the roe performance of the SMEs at the level of 0.01. The total asset turnover ratio is the ratio of net sales to average total assets during the certain period of time. The total assets turnover rate is an important index for the comprehensive evaluation of the operational quality and utilization efficiency of the whole assets. The higher is the turnover rate, the quicker can the SME implement the total asset turnover, also reflecting the firm's stronger ability in sales. Enterprise often can employ the puerile way of sales, accelerating the asset turnover; increase the absolute amount of profit. From the model 1 of table 2 we can see that *Vbk's* significant regression coefficient is 0.0087, which demonstrates that the venture backed SMEs show the superiority in the profitability over the non-venture backed SMEs. The VC backing generally has significantly positive effect on the firms' profitability. Thus, the hypothesis about VCs' positive impact as depicted in *H1* is proven.

In the model 2 of table 2 we can see that *Vbk*'s coefficient is 0.00463, positive and significant, which means that the SMEs supported and financed by the foreign VCs present superiority in profitability, to the extent of 0.04483 over the SMEs which not financed and supported by VCs, but to the extent of 0.0402 over the SMEs financed and supported by the domestic VC firms. In model 3 we can see that *Vc-f*'s coefficient is found to be both positive and significant, as implying that the impact exerted by the foreign VCs' on the SMEs' profitability is stronger than that of the domestic VC firms by 0.0402. Thus *H2-a, H2-b are both proven.*

In the model 3 of table 2 we can see the significant coefficient of *Vbk* is 0.0036 and *Vc-p's* coefficient is insignificant. Which implies the Chinese private VC firms exert the positive influence on the profitability of the investee SMEs, but to the insignificant extent compared with other VCs overall and the hypothesis *H3-a* is verified. In the model 5 of table 3 the samples firms exclude

the SMEs backed by the governmental VCs, and are left with firms without VC backing, and the SMEs backed by the foreign VCs and Chinese private VC firms. *Vc-p's* significant coefficient is –0.0352, which implies that the positive impact of domestic VCs is significantly weaker than that of foreign VCs and the hypothesis *H3-b* is verified. The samples firms in model 6 exclude the SMEs backed by the foreign VCs, and are left with SMEs without VC backing, and the SMEs financed and supported by Chinese private VCs and the governmental VCs. The *Vc-p's* significant coefficient is 0.0273, which implies that the positive impact of domestic VCs is significantly stronger than that of the governmental VCs. Thus, *H3-c* is verified.

In model 4 *Vc-g*'s significantly negative coefficient is –0.0316 and the *Vbk*'s significantly positive coefficient is 0.00399, which implies the governmental VC firms have the negative impact on the funded firms' performance in the profitability, since the SMEs backed by the governmental VC firms play more inferiorly than those non-venture backed firms in the roe by –0.02761. Moreover the SMEs backed by the governmental VC firms show the inferiority of profitability by –0.0316, over the firms financed and supported by VCs of other ownership structures. Thus *H4* is proven.

THE ROBUSTNESS OF ESTIMATION

In above estimation results as can be concluded that for the VCs of different ownership structures, their overall impacts on the profitability are different. To check the reliability the conclusions, the variable of *roa, the returns ratio of total assets* is used to index the financial performance in probability and we estimate the similar regression models again in table 4 & 5. As the results shown in the mode 7 of table 4, the VC investments present significantly positive effect on the funded firms' profitability in the index of *roa*, since *Vbk's* significant coefficient is 0.00381 and *H1* can be verified again. And the foreign VCs can not only exert the positive impact on the SMEs (since the foreign VC backed SMEs outperform the non-venture backed firm in *Roa*) but also show the strongest positive impact on the *roa* of the SMEs, compared to the SMEs financed by the domestic VC firms (for the estimated significant *coefficient of Vc-f* is 0.0198) and *H2a, H2b* can be testified again. And the Chinese private VCs can also exert the positive impact on the SMEs, since the significantly positive coefficients of *Vbk* in model 8 is 0.00296. At the same time *Vc-p's coefficient* in model 8 is 0.00153 but not significant. Thus it can be concluded that such impact of domestic VC firms is not significantly different from other types of VCs in a general way. But after distinguishing the foreign VCs firms and governmental firms, the domestic VCs can show weaker positive impact than the foreign VCs, but stronger positive impact than the governmental VCs, for that the significant coefficient of *Vc-p* in the model 11, 12 is – 0.0175, 0.0134 respectively.

Table 5: The Heterogeneous Impact of the Chinese private VCs on the Roa of SMEs, compared to that of foreign VCs and governmental VCs respectively

	11	12
	Roa	Roa
Vbk	0.0163***	–0.0147***
	(2.11)	(–2.36)
tor	9.133***	8.900***
	(31.52)	(31.7)
ast	–0.0119***	–0.0117***
	(–7.14)	(–7.16)
dtr	–0.0381***	–0.0377***
	(–6.35)	(–6.41)
Vc-p	–0.0175***	0.0134***
	(–2.23)	(2.1)
ΣSDY	yes	yes
ΣSIY	yes	yes
N	3683	3798
p	0	0

*For model 11 the sample firms only include non-venture backed SMEs, the SMEs supported by the foreign VCs and SMEs backed by the Chinese private VC firms. For model 12 the sample firms only include non-venture backed SMEs, the SMEs backed by the governmental VCs, and SMEs backed by the Chinese private VC firms.** p < 0.1, *** p < 0.05*

CONCLUSIONS

It can be concluded that the support of VC firms can impose the positive impact of the SMEs' probability in China, but the VC backing also show the heterogeneous impact on the profitability of the SMEs, for the VCs with different ownership structures. The foreign VCs show the strongest positive impact on the SMEs' profitability, which might because of that the foreign VCs are more prudent in the ventures screening process, and also more experienced in monitoring process of investments. The private VCs also have the positive impact of the profitability of the SMEs, but the impact is significantly weaker than that of foreign VCs and significantly

stronger than that of the governmental VCs. The governmental VCs can only influence on the SMEs' profitability in the negative way significantly. It might be because of that compared to the private VCs, the governmental VCs often run in the less market-oriented mechanism, which might lead to the problems of misallocation of resources and the low efficiency in the ventures screening and nurturing process. It is then suggested that the VC industry in China should be less of the direct government intervention or participation, and more of the VC investments should be encouraged implemented by the private sectors.

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