Minimally Invasive Medical Devices (Shanghai) Co., Ltd. Management System

Biodegradable stents project feasibility tune	File Number	060,001	
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A purpose

Biodegradable stents project feasibility study.

2 Scope

Preparation by biodegradable polymers biodegradable stent products.

3 Responsibilities

3.1 Research Leader

Research Leader	Department	Responsibilities
Juan Meng	R & D	Organized and led the research project team, the project proposal to conduct a feasibility research activities, compiled System "product development project feasibility research report," and to transfer decision-review team reports Research reports.

3.2 Research Project Team

Project team members	Department	Responsibilities
Liang Hua	Market	Market research analysis completed
Lu Xuelian	Finance	Complete analysis of the economic feasibility study
Shan Chang	Sign up	Feasibility research and analysis completed registration
Qu g Yu	Clinical	Complete analysis of clinical feasibility study
Chen Chunyuan / Wuyi Dan	Legal Intellectual Property	Feasibility study completed patent analysis
Li Penghui	Produce	Complete analysis of the production feasibility study
Juan Meng	R & D	Complete analysis of the technical feasibility study

3.3 functional departments

Departments responsible for human research work to provide resources and knowledge support functions associated with the department responsible for auditing Correctness.

4 definitions

No

5 content

5.1 New Product Development Project Background

Coronary intervention for medical device experience from balloon dilatation catheter to permanently bare-metal stents, and then drug Permanent metal stents eluting two major breakthroughs. Drug-eluting stents implanted permanent metal not only effectively avoid the urgent Occlusive vascular complications, but also significantly reduce percutaneous coronary intervention (PCI) the incidence of restenosis. However, drug Stent was released locally in the lesion site of anti-proliferative effect of the drug in order to play the role of a temporary after 36 months after the junction efficacy Beam, after vasodilation need to restore healing presence of permanent metal stents becomes redundant. In addition, part of the permanent gold Belong there weaken coronary stent MRI or CT imaging, surgical revascularization interference, hindering the formation of collateral circulation, Inhibition of vascular positive remodeling, easy to form late thrombosis occurs late to catch up, and the need for dual antiplatelet therapy and other defects, So completely biodegradable absorbable stents become an important direction of future development of the stent.

Studies major domestic and international medical device company for biodegradable stents has become a hot spot. Early 2011 Abbott The company developed biodegradable polylactic acid scaffold Bioresorbable Vascular Scaffold (BVS) received CE certification, becoming the first Certified biodegradable stent products. Medtronic, Boston Scientific and other companies have launched a biodegradable support Research frame. Dunlop domestic company, Shenzhen LIFETECH science and technology has also begun research biodegradable stent.

5.2 Market research and analysis

5.2.1 The basic situation

5.2.1.1 Product Description main indications;

With Firebird2 bracket.

5.2.1.2 The existing primary treatment indications introduction;

PCI Overview

Percutaneous coronary intervention therapy (Percutaneous Coronary Intervention, PCI) refers to the use of percutaneous balloon catheter technology into other related equipment, lift crown Artery stenosis or obstruction, coronary flow reconstruction technique.

Commonly used methods include percutaneous coronary intervention:

• percutaneous transluminal coronary angioplasty (Percutaneous transluminal coronary angioplasty, PTCA): refers to coronary balloon angioplasty in the narrow sense;

• The coronary stent implantation; bare metal stents (BMS), drug-eluting stents (DES), biological Biodegradable stents;

• plaque ablation technique (atherectomy, rotational atherectomy, laser angioplasty) and so on.

5.2.1.3 The research product introductions, including the main use of the product for the crowd, function and breakdown.

The main purpose and function of the product, see the technical feasibility of research and analysis 5.4.5.

5.2.2 Market Analysis

5.2.2.1 Target Market:

China and both CE.

5.2.2.2 Target market:

Different consulting firms for Chinese coronary stent market forecast sales CAGR of 14-24% given.

U.S. consulting firm Frost & Sullivan's total Chinese coronary stent market revenues (based on hospital terminal sales price) from 2007-2014 compound annual growth rate estimated at 24% (Figure 1). U.S. JPMorgan Chase's December 13, 2011, "branch Aircraft sales: Chinese long-term opportunities, "the report expected 2011-2015 compound annual growth rate of 17% (Figure 2). And According to some estimates the growth rate and integrated market conditions gives the 2020 China sales of coronary stent market capacity

26,476,000,000 (Figure 3). The American Business insights consulting company sales data on the Chinese DES market from 2007

2016 estimated CAGR of approximately 14% (Figure 4)

Taking these various data, and due to the sales data Business insights consulting firm failed to indicate the source is given,

We therefore adopted consulting firm Frost & Sullivan in 2009 5.7 billion yuan terminal sales price as a predictor of the base,

CAGR of 19% to 14% and 24% of the average to be calculated, resulting in approximately 2020 -2022 market capacity forecast

Table 1 below.

By the end of 2010 consolidated the various consulting firms forecast data, we have predicted in 2011 the number of cases PCI surgery about 400,000 cases, suppo

Rack total market of about 650,000 implanted, the average number of stents implanted per patient 1.6 / cases.
But the combination of market conditions by the end of 2011
The combined effect of the factors to be reviewed and judged, in 2011 growth between 15-20% PCI surgery, so based on the average growth rate

Predictive value of 17.5%, and in 2010 280,004 thousand nine one hundred cases of PCI Ministry of Health, the number of cases calculated on the basis of official stat

Sales potential of the results in Table 1 below.

Table 1, the market capacity is estimated

Project	2020	2021	2022
Market capacity (million)	386.27	459.66	547.00
Stent sales (million units)	229	269	316

Figure 1, the coronary stent market total revenue (hospital-based terminal sales price)

Figure 2, the coronary stent market capacity

Figure 3, Chinese coronary stent market

Figure 4, the Chinese stent market

5.2.2.3 The main target market competitors

In recent years, the development of a bioabsorbable scaffold mainly include two categories: brackets and more absorbent polymers can absorb the metal alloy stent. Currently there are a variety of stents available, each bracket due to material
Different choices and production processes, with different physical and chemical properties and degradation time.
Up to now, although there is not a bioabsorbable stent obtain FDA marketing approval in the United States, but some clinical
Before the test, even in clinical trials have been carried out.

Table 2, the status quo biodegradable stent

Bracket	Stent platform	Stent wire Thickness (Mm)	Coating case	Through the outer diameter Tension shot (May)	Maximum Completion Time	Complete absorption time	The current situation
Igaki-Tamai	PLLA	170	No	≥8F	June	Twenty four	In clinical trials in Europe is approved for the tr
BVS							**ABSORB cohort A**
Revision 1.0	PLLA	156	Everolimus	1.4	A few weeks	Twenty four	**ABSORB cohort B**
Revision 1.1	PLLA	156	Everolimus	1.4	March	Twenty four	2011.1 CE
Orbusneich	3 * Lactide polymers		There is	1.1	June	-	There is no pre-clinical research d
REVA	Tyrosine-derived polycarbonates						
Generation I	Fiber	100	No	1.7	March to June	36	**RESORB FIM**
ReZolve	Tyrosine-derived polycarbonates Fiber	114-228	Siroliums	1.5	March to June	36	**2010FIM** start
IDEAL							
Generation I	Coating plus salicylate	200	O-hydroxy aldehyde	2.0	March	6	**WhisperFIM**

Generation II	Coating plus salicylate	175	Siroliums	1.5	-	-	Preclinical research program 2010 st
AMS					Number of days to		
AMS-1	Magnesium alloy	165	No	1.2	A few weeks	<4	**PROGRESS AMS FIM**
AMS-2	Magnesium alloy	120	No	-	A few weeks	> 4	Pre-clinical stage
AMS-3	Magnesium alloy	120	There is	-	A few weeks	> 4	Pre-clinical stage

Reference: J Am Coll Cardiol, 2010; 56: 43-78

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Figure 5 clinical studies biodegradable stents (Circulation 2011, 123: 779-797)

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5.2.2.4 Market trends: key drivers of future growth, the growth rate is expected; race is about to enter the field

Rival, the competitive landscape project development products to market, the need to pay special attention the industry leader in pipeline products.

Currently bioabsorbable stents problems: Technically speaking, the ideal time would be the future of biological degradation

One of the important issues to be solved absorbable stents. AMS-1 and BVS (1.0 version) stents showed high

The late lumen loss rate. IVUS and OCT confirmed after stent absorb small梁发生shrunken relevant, it also reflects

Stent defects in the production process and materials. There is evidence that positive remodeling of vascular stents appear

Within a month after, and negative remodeling continued six months. Therefore, the need for at least six months stent has a good

Supporting force. Secondly, and AMS-1 REVA display stand, without anti-proliferative drug bioabsorbable branched

Rack TLR rate was significantly higher than DES. Especially AMS-1 trial, 45% lumen restenosis due to neointimal

Caused by excessive proliferation. Therefore, the combination of the application of the anti-proliferative drug bioabsorbable stent is not necessary

May be less. Finally, due to the characteristics of multi-polymer material itself, making it prone during stent expansion

Stent fracture, particularly when the stent overexpansion. In the ABSORB cohort A trial, OCT found 3.0mm

Trabecular stent fracture stent expansion to produce 3.5mm. Although this result was only one case and only the card OCT

Real, but it should pay attention to.

China market status quo biodegradable stents: Abbott Absorb stent and DES-controlled multi-center clinical trial

China Clinical Research Center in 2012 is about to start ABSORB EXTEND trial; domestic Dunlop company, prone, etc.

The company also ongoing research and development of biodegradable stents and has entered the animal testing stage; independent domestic hospitals

R & D can be absorbed iron metal stents in progress (Fu Wai Hospital).

5.2.2.5 market position and share:

Given the high risk of death within the stent thrombosis, reduce the incidence of stent thrombosis should be bioabsorbable stents

One important goal of future research and development. Undoubtedly, the damaged blood vessels after percutaneous coronary intervention needs support

Frame, but nobody knows how long need to put brackets. DES while providing permanent support vascular restenosis and prevents

Narrow happen, but its long-term safety has been questioned. Bioabsorbable stent provides us with new thinking

Road, disappeared after stent play a role in avoiding long-term dual antiplatelet therapy, and no secondary stent

The risk of thrombosis. Furthermore, bioabsorbable stent does not interfere with non-invasive imaging such as MRI and CT diagnostic evaluation.

Equally important is the ability of blood vessels to remove the load of the so-called vascular stent is completely metallized. Bioabsorbable

Despite the development of stents has just started, but we have reason to believe that this technology will bring Interventional Cardiology Another revolution.

At present, most of the products bioabsorbable stent is still in development state, only Abbott's Absorb branch Frame based on its small number of cases of cohort A and B clinical findings in January 2011 and obtained CE approval Plans to enter the European market by the end of 2012. Its next expected enrolled 1,000 patients, mostly with DES control Center clinical trial ABSORB EXTEND trial is currently underway. According to current test results, the expert Conclusion given is: "not sure bioabsorbable stent is better than some currently used in clinical DES ". But also for the future of bioabsorbable stents to be expected:" the development of bio-absorbable stent Although only just started, but we have reason to believe that this technology will bring interventional cardiology leather again Life. "

Therefore, based on large-scale clinical studies currently unknown exactly how progress and results, whether there are new technologies The emergence of innovative improvements, we do not predict the future state of bioabsorbable stents market acceptance and accounted for There are rate case.

At present we can only be speculated based on existing domestic coronary stent market conditions: Abbott Laboratories has announced Its biodegradable stent Absorb for the European market is expected to 5% (price and operational factors), 2020 if

Biodegradable stents have not yet achieved a breakthrough clinical and technological advances, and taking into account possible technical proficiency and fitne Ying, a certain degree of acceptance of increased market share could reach 10%. The Chinese market Absorb Stents may be earlier than the other companies listed (Absorb stent formerly formerly known as BVS, expected in 2015 America State FDA approved), coupled with competitive biodegradable stents Dunlop company may launch the same period, if our products Performance, price and these two products can compete, and marketing strategy properly, in accordance with the 70% national product Species, 30% the proportion of imported varieties, and only the three varieties occupy 10% of the large share of the premise, we predict 2020 -2022 years our market share may be increased gradually from the beginning of the 3% to 5%.

Table 3, the market share

Project	2020	2021	2022
The company's market share (%)	3%	4%	5%

5.2.2.6 Pricing: Since there is no similar product price parameters, temporarily not accurate pricing. Price is the market

One important means of marketing and strategy tool, the same product in different markets pricing is based on comprehensive local market

Conditions and competitive strategy comes together, so although we saw Business insights consulting firm issued

Content Coronary Stent Market Outlook 2016 report shows Abbott biodegradable stent pricing is expected to 3000

Dollars, and may be five years from 8% increase on price (Figure 6), and January 11, 2011华

Wall Street Journal content John Capek, executive vice president of Abbott Laboratories medical equipment, said the company sought to

The product is priced at the current price multiples of drug-eluting stents. But China can not draw its pre-market price

Period.

Domestic prices are relatively fixed stent Since 2008 the Ministry of Health tender, and domestic production

The price of goods and imported goods ratio of 1: 1.6 (Figure 7). And in January 2010 the Ministry of Health in turn adopt a unified tender

Share work distributed to the local autonomous and Reform Commission policy advice given severe price cuts, currently consists of

Beijing suspended bidding work we do not judge the result makes the final price. But based

Morgan's 2020 report predicted domestic price 7960 yuan, 12,369 yuan price of imported products

(Domestic and imported goods price ratio of 1: 1.55) (Figure 8), biodegradable stent products domestically and abroad

Product prices will nearly 1: 1.6. Medical Affairs biodegradable stents forecast price range

10348-11633 yuan (terminal value), in this report averaged 10,990 yuan.

Figure 6, the global coronary stent prices

Figure 7, domestic and imported stent drug price comparison stent

Figure 8, Morgan forecast report

5.2.3 Related Products

This product complements the company's existing product markets.

5.2.4 experts recommend the product development

Balloon catheter total of 57 people involved in the questionnaire additional questions biodegradable stent supernumerary total of 20 people answered

The following three questions (FAQ doctor has not reached the level of well-known experts in related fields):

A, your ideal is completely biodegradable stents should have what performance?

B, you think it is totally biodegradable scaffold supporting force required to maintain long?

1 1 3

2

6 7

≤1 months

1-3 Months

3-6 months

6-9 months

1-2 years

30 years

C, you think it is totally biodegradable scaffold degradation completely acceptable time is?

2		1-3 Months
3	9	3-6 months
		6-12 months
3		About 1 year
		1-2 years
3		

5.3 Registration of clinical feasibility study

5.3.1 Product Category

According to "medical device classification rules" (Board Order No. 15), the product of Class III medical devices.

According to the classification principles MDD guidelines, in the European market, the product is Class III medical devices

5.3.2 Clinical Requirements

DES stent from the current SFDA's "drug-eluting coronary stent clinical trial guidelines' point of view,

Since the BVS stent in the treatment of the basic principles is that the great majority of DES stents overlap, so this parameter

Test principle is very instructive for the BVS stent. The company is doing clinical trials

Firehawk bracket is conducted in accordance with this principle. According to this principle, in addition to FIM test should be at least

Do more than 200 pairs of randomized controlled clinical trials, stents less than 1000 cases, specific details may refer to

Guidelines. But in the clinical follow-up time, BVS stent is much longer than the DES stents, because from Abbott

The company's situation, BVS stent completely degraded need at least two years, meaning that the stent degradation assessment

Situation and the condition of the patient, with at least 2 years before meaningful conclusions. According to Gao Yun Fu Wai Hospital Academician Lin comments, such holder at least three years of follow-up in order to effectively evaluate. Therefore, we should to clinical Less in accordance with the three-stage phase (FIM, randomized, controlled, single-group registration) to consider more than 1000 cases, follow-up period Should be estimated in three years.

5.3.2.1 product-related standards and regulations

Due to the positioning of the target market for the product to China, taking into account the European CE mark can be registered in this register feasible Of research, is listed first in China with applicable regulations, standards, guidelines, reference is made to the product. Stereotypes from product design to market in the process, including the design validation, in vitro / preclinical evaluation, animals Time span research experiments and clinical research costly process. 2019 current product set is obtained SFDA certificate of registration. In this process, as we update national legislation requires further improvement, Requirements applicable to drug-eluting stents on will certainly increasing. On the current situation, the ISO25539-1 has been transformed into GB, which applies to products in the coming years will ISO25539-2 Transformation. Biological evaluation of series GB / T16886 are gradually updated to maintain and ISO10993 series soon Consistent. In addition, the Medical Device Evaluation Center has also been launched against the drug-eluting stent guidance document Such clinical trials is updated guidance requirements and is suitable for the shelf life of the implant guide requirements, etc. So in the next 7-10 years, China's regulations and standards updates will greatly increase our capacity Commodities also put forward higher requirements. Thus, in the second part of the EU regulatory standards also apply to the analysis Registered within the country, especially for us this time span of the project, it is recommended to put the product in the beginning Positioned on high standards, refer to the CE standards and guidelines on product standards, design evaluation study, Preclinical studies Referring now EU registration requirements in order to reduce future differences, reduce unnecessary rework And re-evaluation, reduce the time cost.

Meanwhile, in the interventional treatment, all biodegradable stent is now a hot research coronary stent products, with When because of the use of absorbable / biodegradable materials and increases the difficulty of registration review. The product consists of drugs (Ray Rapamycin), a polymer coating (as a drug carrier), came together to form a polymer stent implantation main coronary Bracket parts. Because absorbable / biodegradable polymer, the current lack of relevant technical standards, so we evaluated

The relevant properties of the polymer, including degradation time, the degradation process, the molecular weight changes over time, the intermediate

Produce, etc., need to establish their own evaluation methods and indicators. Some performance-related projects may require bracket

Set up in a plurality of time points during the degradation is observed, for example, support force, strength, anti-extrusion performance to

Evaluation of the functional integrity of the stent (integrity). Evaluation process is best in a dynamic environment, with the greatest possible

Simulate the real situation in vivo. In the course of animal experiments, due to the interaction of the stent and the vessel wall, on the

To evaluate the performance of certain stent project may bring technical difficulties. And by histopathological studies

Evaluate the safety and effectiveness of products (including inflammation, fibrin deposition, coating process, remodeling) also

Is necessary. And the final healing and observation points may be based on the stability of the tissue to develop. And because

For the product is a high-risk project, regulators are likely to require companies to do than it is now doing a longer time-eluting stent coronary

Between studies to prove the safety of products (such as 2-3 years). Drug product containing the stent, the use of rapamycin.

Should take into account for the evaluation of drugs, such as drug identification, drug release and the like. Product design should take into account the drug

Drug loading (dosage) formulation of standards and basis. In animal studies should also consider the pharmacokinetics study,

Including research implant, local and drug content analysis part of the system as well as histopathology. In Shen

Reported during Firehawk CE after successful registration can also be used as a reference historical data Firehawk. Fully

Said, in previous work need to be fully prepared to literature, through a comprehensive body / animal experiments

Product performance and risk evaluation. With the SFDA, the EU notified body, the competent authorities shall consult as soon as possible

Related issues.

1) the product should follow Chinese laws and regulations:

State Council Order No. 276 - "Supervision and Regulation of Medical Devices"

State Food and Drug Administration Order No. 16 - "Medical Device Registration"

State Food and Drug Administration Order No. 15 - "Medical Device Distribution Enterprise License Management Measures"

State Food and Drug Administration Order No. 10 - "Medical Device brochures, labels and packaging identity management Provisions "

State Food and Drug Administration Order No. 5 - "Medical Device Clinical Trials regulations"

State Food and Drug Administration Order No. 31 - "Medical Device Standards Management Measures" (Trial)

2) SFDA technical review center guiding principles:

"Passive implantable medical device product registration dossier guiding principles"

"Passive implantable medical device product registration dossier written guidelines."

"Containing medical device product registration dossier written guidelines"

"The third category within the medical device registration application data outside the admissibility criteria."

"Passive implantable medical devices shelf life guidelines."

"Biological Evaluation of Medical Devices and review guide"

"Drug-eluting coronary stent clinical trials guiding principles" (issued)

2) technical standards should be consistent with the (national registration)

According to the current product characteristics listed below refer to the technical standards applicable to the specific product standards should be based on pro

Design features one by one analysis.

GB / T 191-2008 Packaging Pictorial signs

GB / T 6543-2008 transport packaging corrugated boxes with a single and double corrugated boxes

PART 2 GB / T 1962.2-2001 syringes, needles and other medical equipment 6% (Luer) taper

Sub: Lock fittings

GB / T 2829-2002 cycle inspection Sampling procedures and sample forms

GB / T 14233.1-2008 medical infusion, transfusion, injection equipment test methods Part I: chemical analysis

France

GB / T 14233.2-2005 medical infusion, transfusion, injection equipment test methods Part II: Biological test

Methods

GB / T 16886.1 -2011 Biological evaluation of medical devices Part 1: Evaluation and testing

GB / T 16886.3-2008 Biological evaluation of medical devices Part 3: Tests for genotoxicity, carcinogenicity and

Reproductive toxicity test

GB / T 16886.4-2003 Biological evaluation of medical devices Part 4: interactions with blood tests

Select

GB / T 16886.5-2003 Biological evaluation of medical devices Part 5: In vitro cytotoxicity tests

GB / T 16886.6-1997 Biological Evaluation of Medical Devices Part 6: Tests for local effects after implantation

GB / T 16886.10-2005 Biological evaluation of medical devices Part 10: irritation and delayed super-sensitized Reaction test

GB / T 16886.11-1997 Biological Evaluation of Medical Devices Part 11: Tests for systemic toxicity

YY 0285.1-2004 disposable sterile intravascular catheters Part 1: General requirements

YY 0285.4-2004 disposable sterile intravascular catheters Part 4: Balloon dilatation catheters

Symbol YY 0466.1-2009 medical equipment used with medical device labels, tags, and the first to provide information Part I: General requirements

YY / T 0313-1998 Medical Polymer Co., packaging, labeling, transportation and storage

YY / T 0695-2008 mini implants corrosion susceptibility of circulating potentiodynamic polarization Standard Test Method

YY / T 0640-2008 General requirements for passive surgical implants

Special requirements **YY / T 0663-2008** passive cardiac and vascular surgical implants arterial stent implants Special Requirements

3) the product should follow the EU regulations :(EU registration)

Medical Devices Act **(Directives):**

DIRECTIVE 93/42 / EEC, 2007/47 / EC relating to medical devices

DIRECTIVE 2001/83 / EC relating to medicinal products for human use

Medical devices suitable guides:

MEDDEV series:

MEDDEV 2.1 / 1 Definitions of "medical devices", "accessory" and "manufacturer"

MEDDEV 2.1 / 3 rev.3 Borderline products, drug-delivery products and medical devices incorporating, as integral part, an ancillary medicinal substance or an ancillary human blood derivative

MEDDEV 2.4 / 1 rev.9 Classification of medical devices

MEDDEV 2.7 / 1 rev.3 Clinical evaluation: Guide for manufacturers and notified bodies

Appendix 1: Clinical evaluation on coronary stents

MEDDEV 2.7 / 2 Guide for Competent Authorities in making an assessment of clinical

investigation; notification

MEDDEV 2.7 / 3 Clinical investigations: serious adverse event reporting

MEDDEV 2.7 / 4 Guidelines on Clinical investigations: a guide for manufacturers and

notified bodies

EMEA Series:

EMEA / CHMP / EWP / 110540/2007 Guideline on the clinical and non-clinical

evaluation during the consultation procedure on medicinal substances contained in

drug-eluting coronary stents

EMEA / CHMP / 401993/2005 EMEA recommendation on the procedural aspects and

dossier requirements for the consultation to the EMEA by a notified body on an

ancillary medicinal substance or an ancillary human blood derivative incorporated in

a medical device

Another reference to foreign laws and regulations guide includes:

FDA Guidance for Industry: Coronary Drug-Eluting Stents- Nonclinical and clinical

studies (Draft)

FDA Guidance for Industry: Non-Clinical Engineering Tests and Recommended

Labeling for Intravascular Stents and Associated Delivery Systems

4) technical standards should be consistent with the :(EU / international standards)

According to the current product characteristics listed below refer to the technical standards applicable to the specific product standards should be based on pro

Meter characteristics analyzed one by one.

The main reference standard:

EN ISO 25539-2: 2009 Cardiovascular implants - Endovascular devices - Part 2:

Vascular stents

EN ISO 14971: 2009 Medical devices - Application of risk management to medical

devices

Biological **Standards:** Biocompatibility: **ISO10993 Series: Biological** evaluation **of medical**

devices:

EN ISO 10993-1: 2009 Part 1: Evaluation and testing within a risk management

process

EN ISO 10993-3: 2009 Part 3: Tests for genotoxicity, carcinogenicity and reproductive

toxicity

EN ISO 10993-4: 2009 Part 4: Selection of tests for interactions with blood

EN ISO 10993-5: 2009 Part 5: Tests for in vitro cytotoxicity

EN ISO 10993-6: 2009 Part 6: Tests for local effects after implantation

EN ISO 10993-7: 2008 Part 7: Ethylene oxide sterilization residuals

EN ISO 10993-9: 2009 Part 9: Framework for identification and quantification of

potential degradation products

EN ISO 10993-10: 2009 Part 10: Tests for irritation and delayed-type hypersensitivity

EN ISO 10993-11: 2009 Part 11: Tests for systemic toxicity

EN ISO 10993-12: 2009 Part 12: Sample preparation and reference materials

EN ISO 10993-13: 2010 Part 13: Identification and quantification of degradation products from polymeric medical devices

EN ISO 10993-16: 2010 Part 16: Toxicokinetic study design for degradation products and leachables

EN ISO 10993-17: 2009 Part 17: Establishment of allowable limits for leachable substances

EN ISO 10993-18: 2009 Part 18: Chemical characterization of materials

Other technical standards:

EN ISO 14630: 2009 Non-active surgical implants - General requirements

EN 20594-1: 1993 Conical fittings with a 6% (Luer) taper for syringes, needles and certain other medical equipment - Part 1: General requirements

ISO594-2: 1998 Conical fittings with a 6% (Luer) taper for syringes, needles and certain other medical equipment - Part2: Lock fitting

ISO 14644-1: 1999 Cleanrooms and associated controlled environments - Part 1: Classification of air cleanliness

ISO 14644-2: 2000 Cleanrooms and associated controlled environments - Part 2: Specifications for testing and monitoring to prove continued compliance with ISO 14644-1

ISO 14644-3: 2005 Cleanrooms and associated controlled environments - Part 3: Test methods

EN ISO 11135-1: 2007 Sterilization of health care products - Ethylene oxide - Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices

EN ISO 11138-2: 2009 Sterilization of health care products - Biological indicators - Part 2: Biological indicators for ethylene oxide sterilization processes

EN ISO 14937: 2009 Sterilization of health care products - General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices

EN 556-1: 2001 / AC: 2006 Sterilization of medical devices - Requirements for medical devices to be designated "STERILE" - Part 1: Requirements for terminally sterilized medical devices

EN ISO 11737-1: 2006 Sterilization of medical devices - Microbiological methods - Part 1: Determination of a population of microorganisms on products

EN ISO 11607-1: 2009 Packaging for terminally sterilized medical devices - Part 1: Requirements for materials, sterile barrier systems and packaging systems

EN ISO 11607-2: 2006 Packaging for terminally sterilized medical devices - Part 2: Validation requirements for forming, sealing and assembly processes

EN 980: 2008 Symbols for use in the labeling of medical devices

ISO 15223-1 2007 Medical devices - Symbols to be used with medical device

EN 1041: 2008 Information supplied by the manufacturer of medical devices

Clinical research criteria:

EN ISO 14155: 2011 Clinical investigation of medical devices for human subjects --Good Clinical practice

5.3.3 Clinical registration time, cost projections

Considering that patients and physicians on this new product acceptance, clinical trials estimated time of implantation Longer than the Firehawk, estimated at about 3.5-4 years of clinical follow-up of 3 years. Clinical trials cost component reference Firehawk stand trial, as well as enhance the price index, the estimated domestic clinical costs about 80 million yuan.

Sales and earnings estimates at this stage is more difficult for overseas markets quantitative analysis, clinical registration requirements if overseas, the Currently 80 million clinical budget may not be enough.

1) The basic flow

2) the time and expense

Content	Time	Costs
Type test	1 year to 2 years, depending on the Different project time	200,000
Clinical start	3 years 6 months	80000000
Over Ethics		
Clinical implants		
Clinical follow-up	3 years	
Authenticity verification	3 months	
System assessment	6 months	
Registration Information Summary	2 weeks	
Registration information submitted and reviewed	1.5 years	
To obtain a registration certificate		

Each time point above the expected progress in accordance with the ideal of the earliest completion time, the specific situation to the actual operation As circumstances prevail.

5.4 Technical Feasibility Study and Analysis

5.4.1, the purpose

Biodegradable stents for products before the technical feasibility of the project research.

5.4.2, the scope of

Biodegradable polymer scaffolds

5.4.3, the meaning of the terms or acronyms

No

5.4.4 Reference documents

MP / AS7.3-15 (Version: A) "key technical feasibility of regulations"

5.4.5, the basic functions of product realization, principles and applications of indications.

5.4.5.1, the basic functions

And the conveyor is completely biodegradable polymer scaffold composition, the stent surface may carry the drug, the balloon expansion Zhang style. Has the following characteristics:

a) within the 6 months and a similar expansion FB2 retraction rate after implantation, the supporting force and the drug release ability, prevent Restenosis;

b) After the completion of the role of the gradual degradation, and finally completely disappeared from the body.

5.4.5.2, the principle

Similar to traditional drug-eluting stents, stent delivery from the delivery system to the site of vascular stenosis, then By way of the expansion of the balloon to expand the stent to open. Withdrawing after the balloon, the stent remained in the lesion location, there Effectively play a supporting blood vessels. Meanwhile coated stent surface antiproliferative drugs that can inhibit neointimal Hyperproliferative prevent restenosis. Due to degradation bracket, the gradual loss of the mechanical properties of the stent, the most After the stent is absorbed completely degraded. Since then, there remain no longer intravascular stent, making long-term stent blood Reduce the incidence of bolt antiplatelet therapy to reduce the time for postoperative CT and MRI are no longer produced shadow Rang.

5.4.5.3, indications

Application of biodegradable stents indicated for:

Improvement of ischemic heart disease in patients with vascular stenosis symptoms, vascular lesion length less than the applicable 30mm, Reference vessel diameter 2.54.0mm;

Single-vessel disease;

Protected left main coronary artery disease;

PTCA patients in acute occlusion or on the verge of closing;

PTCA results are unsatisfactory, significant residual stenosis lesions;

Coronary restenosis after PTCA.

5.4.6, identify key technologies

5.4.6.1, the key to the development of techniques to identify

The product development in key development technologies are as follows:

The key technologies	Expectations indicators, performance	Bottleneck	Impact	Similar products in
1, Material selection	The elastic modulus of the material is high, Toughness, the yield strain is small.	More difficult to have both kinds of mechanical properties, Suitable material, or the material after processing, it Mechanical properties meet the requirements.	Various systems can not select the co- Easy to collapse, easy to break when Bracket big rebound.	Absorbable BVS: PLLA Supported, REVA expansion deriva Polycarbonates; BTI Polytyrosine acid Vascular synthetic ca And so on. Which tyrosine-derive
	The rate of degradation of materials suitable	Degradation experiments a longer period, a large impact on the development schedule. V		
	Biological materials require high security	Medical-grade biodegradable polymers are foreign suppliers, mining Purchase cycle is very long.	Slow degradation may occur late blood Bolt. Degradation after stent implantation Prone to inflammation or other adverse reactions Should.	试用中容 Salicylic carbonate and Anhydride ester are re
	Material may be at room temperature d Longer storage.	Biodegradable polymers easy to aging, it needs to have In order to achieve long-term storage.	Machining cycle determines the stent material Shelf life.	Laboratory synthetic m No market

2, Pipe extrusion	Uniform size pipe extrusion	Currently the company's existing extruders are not suitable for degradable material The extruded material, resulting in unevenness of the size of the extruded pipe. Uniform.	Pipe size caused by uneven material Inside and outside the pipe decreases.	Some foreign supplier Good for extrusion tub Timber, but the price i Long purchase cycle
3, the pipe Deal with	After treatment makes the pipe optimal Technology.	Process involving off a series of parameters between Department of complexity;	Pipe parameters Performance.	Abbott BVS stent so Workers using a specia PLLA L-Art treatment Polylactic acid-based r
4, Structural Design	Small stent coverage	The smaller the harder bracket coverage designed to support Structure.	Large increase in the coverage of several restenosis Rate, easily affect collateral blood supply.	BVS 24%
	Supporting force to achieve the level o	Support forces and coverage, profile difficult to juggle. Lack of supporting force can not be completely softened		BVS 117Kpa
			Changed.	

	By design, reducing stand back Bomb	Designed to reduce the resilience of local deformation of the stent, will lead to A large amount.	Poor adherence, resulting in thrombus generation.	BVS 6.5 ± 7.2%
5, Bracket Cutting	Cutting process does not affect material properties	Conventional laser cutting machine cause thermal degradation of the material, to Achieve biodegradable stent cutting method. New cutting technology Requires a lot of exploration work.	Appearance and performance of the stent does not conform With requirements.	Basically adopt similar Cut with a femtosecon Cut.
6, Stent crimping	After crimping the stent profile is sufficiently small, Anti-de-load power and similar metal stents.	The traditional technique leads to stent crimping the stent fracture, or Crimping rebound great, stand easy to slip. Need to develop The new crimping technology.	When crimping the stent fracture, or from the input Slip on the transmitter.	After crimping Profile BVS bracket: 1.4mm; REVA bracket: 1.7mm Magnesium stents AM
7, Bracket developing Technology	Display position and the stent may be X-degradable State.	Xdegradable material does not develop light.	If the bracket is completely developed, will Doctor's operation to bring a lot of inconvenience	Most competitors mini Used in developing th Way point.

8, Drug coating Technology	The outer surface of the drug-coated stents	If the outer surface of the stent drug filled trenching technology, the Grooving process is the greater challenges. If you do not use Trench Technology, then the point where the drug may be difficult to determine.	Inner and outer surfaces are sprayed using drugs Endometrial velocity mode, the stent will Slower	Currently in clinical st Biodegradable stents Still using the tradition

	The process of spraying or medicine n	Spraying impor	For the drug-eluting stents	The outer surface of th
	Frame body impact	Dissolution or swelling of the body effect.	School performance degradation	Methods. BVS stent ca
				Everolimus drug is
				Matter.
9,	Without affecting the performance of sterilization,	Conventional ethylene oxide sterilization can be reduced	Can not be effectively	Because
Product Sterilization	Reduce the effectiveness of sterilization	Affect the mechanical properties of the material the	Shorter time	Marketed products, it i
		Sterilization methods and parameters.		Cut aware of similar p
				The sterilization.

5.4.6.2, to identify key processes

Critical process	Key points
Pipe extrusion process	Uniform size.
	Molecular weight decline is not obvious.
After the pipe treatment process	Select the appropriate process parameters to obtain toughness and strength to meet the requirements of
	Timber.
Bracket cutting process	Set the appropriate cutting parameters without affecting the performance and apparent scaffold bar Pieces, the fast cutting.
Stent crimping process	After crimping the stent profile is small enough, the anti-off force, and the like contained in a metal br
Drug dispensing process	Coated on the outer surface of biodegradable drug-eluting stent
Bracket sterilization process	Without changing the performance conditions of the stent, to ensure the effectiveness of sterilization

5.4.6.3, supporting the identification of key equipment

Key equipment	Device Uses	Claim
Pipe Extrusion Machine	Biodegradable materials for the extrusion	Stent design requirements extrusion sizes meet the requirements, the extrusion process molecu
After the pipe handling equipment	Pipes for post processing of biodegradable	Requires precise control of processing parameters.
Femtosecond laser cutting machine	For stent cutting	Femtosecond laser light source can be programmed biodegradable stent accurate cutting, cutti
Stent crimping machine	Biodegradable stents for crimping	After crimping the stent Profile meet clinical requirements, stand high enough resistance to de
Drug dispensing machine	Drug-coated stents used to point	The outer surface of the stent contained in a suitable amount of the drug, the coating is firmly

5.4.7 Development Status domestic and related technologies

Research as a relatively new technology, biodegradable polymer scaffolds are major public at home and abroad Secretary attention. U.S. Abbott (Abbott Vascular, Santa Clara, CA) R & D BVS stent is the only CE certification (2011) of the product, but the listing is still some time away. Other products in the clinical research stage include: REVA Medical (Boston Scientific, Natick, MA) of REVA stent and Bioabsorbable Therapeutics Inc. (BTI) (Menlo Park, CA) The IDEAL bracket. Their development status are as follows:

Abbott production BVS everolimus-eluting stent body semi-crystalline PLLA material, Coating is a random copolymer L-and D-lactic acid from racemic polylactic acid material, drugs everolimus. Stents are coated with drugs inside and outside surfaces, drug loading was 100 μg/cm 2. Stents are ABSORB/Cohort A,

ABSORB Cohort B and ABSORB Extend clinical trials. Early clinical ABSORB Cohort A's

It was found that most of the stent in two years after the probe has disappeared, indicating that the stent has been degraded by the body to absorb.

Three years of clinical MACE event rate was 3.4%, but also demonstrate the effectiveness and safety of the stent. In structure and material

After two terms of improved materials, BVS stent were ABSORB Cohort B and ABSORB EXTEND groups

Clinical trials. ABSORB Cohort B of the study found that the improvement in the 6 months after the stent after BVS

Lumen area of only 4% lower, and metal DES stents level close, indicating improved BVS stent

Implanted in the late performance has been significantly improved.

REVA stent using tyrosine-derived polycarbonates (PDTE) for the skeleton, paclitaxel coating and

Stent body material added to the iodine atom stent has developed properties under X-ray. The first generation of mining REVA stent

With a slide lock structure, beginning from June 2007, REVA stent called RESORB of clinical research

Study, 4-6 months of partial fracture after stent implantation, triggering cause revascularization rate is lower than the target location

Expectations. Therefore, REVA second generation uses spiral slide lock design, the use of sirolimus drug coating,

Renamed ReZolve stents, recently in a second clinical trial will begin.

IDEAL developed by BTI polyanhydride esters stent using a polymer material, this material is based

Polymerizing the monomer salicylic acid, sirolimus stent coating carrying drugs, so this bracket may

With anti-intimal hyperplasia and inflammatory dual role. From July 2009 IDEAL bracket beginning to enter clinical research

Study. Find stent intimal inhibition is not sufficient, and the stent may be less with a drug, the drug is released too soon

And other factors. IDEAL second generation stent design to increase drug loading, reducing the drug release rate based.

Wall thickness of the stent also declined. IDEAL recent second generation stent will enter clinical trials.

In addition to the above-described results of several clinical studies have been made of the stent, there are some products are in clinical or

Those who pre-clinical stage. Such as Elixir developed DEsolve bracket, choose PLLA stent body,

Carry Novolimus drug, drug loading was 5mcg / mm, has completed the stent body FIM experiment in 2011

Into the end of clinical research; Arterial Remodeling Technologies developed ART bracket, mining

Polylactic acid material as the stent body, has yet to carry the drug, the experiment will begin in early 2012 FIM.

Domestic companies for the study of biodegradable stents has made some progress. From some of the industry will

Conference information can be learned: Shandong Hua, Beijing Dunlop, Chengdu Institute of Organic Chemistry, Peking University, Southwest post

Polymer scaffold so conducting research through the University of biodegradable; LIFETECH Shenzhen, Beijing Dunlop also be born

Magnesium metal stents biodegradable material. However, there are no products to enter clinical studies, product technology

And there is little performance publicly reported.

5.4.8, inside and outside the company can use the technology and resource analysis

The key technologies	Technical reserves	Qualified personnel	Whether the need to borrow Help of external resources
Material selection	Evaluation and selection of the material side France already has some experience. And structure, renders the stent Supporting force to achieve metal stents water Level.	Has specialized technical personnel engaged Material selection; The company has specialized in biological Degradable materials development team.	No
Pipe extrusion	Have a certain biodegradable materials Extrusion experience.	There is someone in the extrusion Development Work, with deep scores Sub-material related theoretical knowledge Knowledge.	No
Support structure design	Has the structure and performance of the stent The relationship between the depth Analysis. And material combination makes A metal support bracket force reaches Stand level.	There is someone in the structural design, Have material relevant knowledge and Rich scaffold design Experience.	No
Bracket Cutting	Femtosecond lasers have been used to purchase In stent cutting.	Studies have someone stand Cutting Methods have been developed stent Inspection.	No
Drug coating technology	Can be partially applied Firehawk Drug dispensing technology.	There will be someone to stand drug research Coatings, with drug-eluting stents R & D experience.	No
Delivery system	Mature development platform conveyor system	There will be someone to study transport system Systems, with extensive transportation system System development experience.	No

5.4.9, the key technology assessment

The key technologies	Assessment results	Alternative
Material selection	Basically feasible.	Select the company independently open New biological hair can Degradable material (cross-linked Type).
Pipe extrusion	Basic feasible Need to improve the stability of the pipe size.	Outsourcing pipe
Pipe after treatment	Basically feasible.	
Support structure design	Feasible, supporting force and metal stents comparable level.	
Bracket Cutting	Feasible.	
Stent crimping	Feasible.	
Bracket developing technology	Basically feasible.	
Drug coating technology	Feasible	
Delivery system	Feasible	
Product Sterilization	Some preliminary attempts have been made, the basic feasible	

5.4.10, risk assessment and response measures

Species	Risk Name	Occurrence Chance	Measures the degree of harm	
Materials	Material suppliers instability or collapse	Low	Medium	1, the use of other suppliers; 2, the use of raw materials, development pl
	Long material supply cycle, affecting the production and development progress	High	Low	Procurement plan
	Policy changes led to the declaration of the material cannot be imported	Low	Serious	1, domestic suppliers; 2, raw material development platform within the c
	Storage properties of materials can not meet the requirements	Low	Serious	1, using a shorter lead times (a lot of pressure for sales and transportatio
	Degradation process hazards, such as degradation of debris, causing inflammation	Low	Serious	2, the use of raw materials development platform within the company to Biocompatibility of degradation products research
	Disease, thrombosis, destroy the patient's immune performance			
	Pipe Size uneven	Severe low		Outsourcing pipe (increased costs);
Bracket	Poor performance of the stent delivery system	Less severe		Lower profile
	Bracket developing technology development fails	Very low	Medium	Bracket does not develop (the doctor's operation affected).
	Changes in product performance in harsh transport conditions	Serious low		Product design is to consider the harsh environment of extreme transpor
Process	Failed sterilization methods developed	Severe low		

	Coating process development failure	Severe low		
	Crimping process optimization failure	Medium	Medium	
Test	Changes in national standards, making our R & D needs Additional data or additional work	Moderately higher		And SFDA closely tracking the latest developments in domestic and fore
	Environmental differences lead to performance changes in vivo scaffold	High	Medium	Experimental study on this issue through the pre-animal experiments an
Staff	Key employees leave, extended leave or promotion	Lower low		Through document control and reserve personnel training, technical loss
Various external factors, poor communication between departments, with the high, resulting in	R & D behind schedule.	Medium		Enhance communication between departments, to establish smooth com

As a new technology, biodegradable stents development process more uncertain factors, does not exclude the risk of failure in R & D on some technical difficulties

Technically has made great breakthroughs have been for most of the key technologies to determine its feasibility, the lower the probability of failure of key technol

5.4.11, it is recommended

After two years of research and development, some of the key properties of biodegradable stents, such as the support force, acute retraction, Profile has reached the

The technical feasibility higher. Recommendations for project approval, the product of a more comprehensive development of the system.

5.5 Production Feasibility research and analysis - depending on the project can be cut

Production is expected to make based on the following analysis table, estimated production costs for:

	2020	2021	2022	2023	2024
Production cost (yuan / pcs)	793.00	752.26	664.95	606.70	593.30

Production is expected to manufacture analysis table (in accordance with the annual listed separately)

Project Category		Pipe extrusion	Cutting	Surface treatment	Drug coating	Conveyor	Total annual Total
2020	Raw materials Cost	8.8 yuan / pcs	0.0	1.47 yuan / pcs (solvent)	Drugs: 1.5 yuan / pcs Coating: 0.38 yuan / pcs Solvent: 0.77 yuan / pcs	Referring FB2 (268 Yuan / pcs) Packaging costs increase: Aluminum foil bags (1.5 yuan / Pcs) + Deoxidizer (3 yuan / pcs) + dry Dry agent (2.7 yuan / Pcs) Labor costs increase: 50 yuan / pcs	12.92 / P
	Equipment	Extruder: 1 set * 400W = 400W Pipe surface treatment Machine: 3 sets * 100W = 300W	Cutting Machine: 13 Taiwan * 400W = 5200W	Cleaning Machine: 2 * 0.5W = 1W Microscope: 4 * 0.2W = 0.8W Size seized: a Taiwan * 55W = 55W Parse box: 4 * 0.5W = 2W	Spraying equipment: 18 sets * 45W = 810W Analytical equipment: 3 sets * 0.5W = 1.5W Balance: 5 * 10W = 50W Microscope: 5 * 0.2W = 1W Hood: 2 * 1W = 2W Cleaning Machine: 2 * 0.5W = 1W Blender: 4 * 0.2W = 0.8W		6825.1 Wan

	Extrusion: 4 people	Cutting:		Spray: 2 * 5 * 12W = 120W	
Labor costs	* 12W = 48W	2 * 4	Cleaning: 2 * 2 * 12W = 48W	Spray Test: 5 * 12W = 60W	5160000
The	Inspection: 1 person	* 12W = 9	Inspection: 2 * 4 * 12W = 96W	Cleaning and inspection: 1 * 1 * 12W = 12W	
	* 12W = 12W	6W		Solution preparation: 2 * 12W = 24W	
	Extruder:				
	30m2 * 0.45W / m2 =	13 * 9 * 0			
Venue fees	13.5W	.04W = 4	0.0	Solution preparation: 20m2 * 0.45W / m2 = 9W	116.28
With	Surface processor:	.68W		Painting workshop: 18 * 6 * 0.45 = 48.6W	Wan
	3 * 30m2 * 0.45W / m				
	2 = 40.5W				
Equipment dimension					
Care and maintenance					
Costs					
Supplies and					
Utilities	Hydro: 14.4 yuan / pcs; supplies 38 yuan / pcs; Other 4 yuan / pcs, Subtotal: 56.4 yuan / pcs				
With					
Management and					
Sales Charge					
With					

Raw materials				Drugs: 1.5 yuan / pcs	
Cost	8.8 yuan / pcs	0.0 1.47 yuan / pcs (solvent)		Coating: 0.38 yuan / pcs	12.92 / P
				Solvent: 0.77 yuan / pcs	
				Spraying equipment: 33 sets * 45W = 1485W	
	Extruder: 1 set		Cleaning Machine: 2 * 0.5W = 1W	Analytical equipment: 5 * 0.5W = 2.5W	
	* 400W = 400W	Cutting Machine:	Microscope: 6 units	Balance: 7 units * 10W = 70W	Referring FB2 (268
Equipment	Pipe surface treatment	21 Taiwan	* 0.2W = 1.2W	Microscope: 7 units * 0.2W = 1.4W	Yuan / pcs) 11022.9
	Machine: 4	* 400W = 8	Size seized: a Taiwan * 55W = 55W	Hood: 2 * 1W = 2W	Packaging costs increase Wan
	* 100W = 600W	400W	Parse box: 6 units * 0.5W = 3W	Cleaning Machine: 2 * 0.5W = 1W	Plus: foil bag
2021				Blender: 4 * 0.2W = 0.8W	(1.5 yuan / pcs)
				Spray: 2 * 9 * 12W = 216W	+ Oxygen scavenger (3 yuan
	Extrusion: 4 people	Cutting:		Spray Test: 8 * 12W = 96W	/ Pcs) + desiccant
Labor costs	* 12W = 48W	2 * 7 people	Cleaning: 2 * 2 * 12W = 48W	Cleaning and inspection: 1 * 2 * 12W = 24W	(2.7 yuan / pcs) 7920000
The	Inspection: 2 people	* 12W = 16	Inspection: 2 * 6 * 12W = 144W	Solution preparation: 2 * 12W = 24W	Labor costs increase
	* 12W = 24W	8W			Plus: 50 yuan / pcs
	Extruder:				
	30m2 * 0.45W / m2 =	21 * 9 * 0.			
Venue fees	13.5W	04W = 7.5	0.0	Solution preparation: 20m2 * 0.45W / m2 = 9W	173.16
With	Surface processor:	6W		Painting workshop: 33 * 6 * 0.45 = 89.1W	Wan
	4 * 30m2 * 0.45W / m				

	2 = 54W						
Equipment dimension							
Care and maintenance Costs							
Supplies and Utilities	Hydro: 14.4 yuan / pcs; supplies 38 yuan / pcs; Other 4 yuan / pcs, Subtotal: 56.4 yuan / pcs						
With Management and Sales Charge							
With Raw materials Cost	8.8 yuan / pcs	0.0 1.47 yuan / pcs (solvent)			Drugs: 1.5 yuan / pcs Coating: 0.38 yuan / pcs Solvent: 0.77 yuan / pcs	Referring FB2 (268 Yuan / pcs)	12.92 / P
2022	Equipment	Extruder: 1 set * 400W = 400W Pipe surface treatment Machine: 5 * 100W = 600W	Cutting Machine: 31 units * 400W = 12400W	Washing machine: 3 sets * 0.5W = 1.5W Microscope: 10 * 0.2W = 2W Size seized: a Taiwan * 55W = 55W Parse box: 10: 0.5W = 5W	Spraying equipment: 48 * 45W = 2160W Analytical equipment: 8 * 0.5W = 4W Balance: 12 * 10W = 120W Microscope: 12 * 0.2W = 2.4W Hood: 2 * 1W = 2W	Packaging costs increase Plus: foil bag (1.5 yuan / pcs) + Oxygen scavenger (3 yuan / Pcs) + desiccant (2.7 yuan / pcs)	15753.7 Wan

					Cleaning Machine: 2 * 0.5W = 1W Blender: 4 * 0.2W = 0.8W	Labor costs increase Plus: 50 yuan / pcs	
Labor costs The	Extrusion: 6 people * 12W = 72W Inspection: 3 people * 12W = 36W Extruder:	Cutting: 2 * 9 people * 12W = 21 6W	Cleaning: 2 * 3 * 12W = 72W Inspection: 2 * 10 * 12W = 240W		Spray: 2 * 12 * 12W = 288W Spray test: 12 * 12W = 144W Cleaning and inspection: 2 * 2 * 12W = 48W Solution preparation: 2 * 12W = 24W		11400000

		30m2 * 0.45W / m2 =	31 * 9 * 0.			
	Venue fees	13.5W	04W = 11.	0.0	Solution preparation: 20m2 * 0.45W / m2 = 9W	192.96
	With	Surface processor:	16W		Painting workshop: 34 * 6 * 0.45 = 91.8W	Wan
		5 * 30m2 * 0.45W / m				
		2 = 67.5W				
	Equipment dimension					
	Care and maintenance					
	Costs					
	Supplies and	Hydro: 14.4 yuan / pcs; supplies 38 yuan / pcs; Other 4 yuan / pcs, Subtotal: 56.4 yuan / pcs				

	Utilities						
	With						
	Management and						
	Sales Charge						
	With						
	Raw materials Cost	8.8 yuan / pcs	0.0	1.47 yuan / pcs (solvent)	Drugs: 1.5 yuan / pcs Coating: 0.38 yuan / pcs Solvent: 0.77 yuan / pcs		12.92 / P
		Extruder: 1 set * 400W = 400W	Cutting Machine: 34 Taiwan * 400W = 13600W	Washing machines: 4 * 0.5W = 2W Microscope: 12 * 0.2W = 2.4W Size seized: a Taiwan * 55W = 55W Parse box: 12: 0.5W = 6W	Spraying equipment: 54 sets * 45W = 2430W Analytical equipment: 10 * 0.5W = 5W Balance: 14 units * 10W = 140W Microscope: 14 units * 0.2W = 2.8W Hood: 2 * 1W = 2W Cleaning Machine: 2 * 0.5W = 1W Blender: 4 * 0.2W = 0.8W	Referring FB2 (268 Yuan / pcs)	
2023	Equipment	Pipe surface treatment Machine: 6 units * 100W = 600W				Packaging costs increase Plus: foil bag (1.5 yuan / pcs) + Oxygen scavenger (3 yuan / Pcs) + desiccant (2.7 yuan / pcs)	172 470 000
	Labor costs	Extrusion: 8 people * 12W = 96W	Cutting: 2 * 10 * 12W = 24 0W	Cleaning: 2 * 4 * 12W = 96W Inspection: 2 * 12 * 12W = 288W	Spray: 2 * 14 * 12W = 336W Spray test: 13 * 12W = 156W Cleaning and inspection: 2 * 2 * 12W = 48W Solution preparation: 2 * 12W = 24W	Labor costs increase Plus: 50 yuan / pcs	13320000
	The	Inspection: 4 people * 12W = 48W					

	Venue fees With	Extruder: 30m2 * 0.45W / m2 = 13.5W Surface processor: 6 * 30m2 * 0.45W / m2 = 81W	34 * 9 * 0.04W = 12.24W	0.0	Solution preparation: 20m2 * 0.45W / m2 = 9W Painting workshop: 34 * 6 * 0.45 = 91.8W	207.54 Wan
	Equipment depreciation Care and maintenance Costs	4.5 yuan / pcs (in accordance with FB2 of 3.5 yuan base Basis on estimates)				
	Supplies and Utilities With Management and Sales Charge With	Hydro: 14.4 yuan / pcs; supplies 38 yuan / pcs; Other 4 yuan / pcs, Subtotal: 56.4 yuan / pcs				
Unit Cost 2024	Raw materials Cost	8.8 yuan / pcs	0.0 1.47 yuan / pcs (solvent)		Drugs: 1.5 yuan / pcs Coating: 0.38 yuan / pcs	Referring FB2 (268 Yuan / pcs) 12.92 / P

				Solvent: 0.77 yuan / pcs		Packaging costs increase Plus: foil bag (1.5 yuan / pcs) + Oxygen scavenger (3 yuan / Pcs) + desiccant (2.7 yuan / pcs) Labor costs increase Plus: 50 yuan / pcs 172 470 000
	Equipment	Extruder: 1 set * 400W = 400W Pipe surface treatment Machine: 6 units * 100W = 600W	Cutting Machine: 34 Taiwan * 400W = 13600W	Washing machines: 4 * 0.5W = 2W Microscope: 12 * 0.2W = 2.4W Size seized: a Taiwan * 55W = 55W Parse box: 12 * .5W = 6W	Spraying equipment: 54 sets * 45W = 2430W Analytical equipment: 10 * 0.5W = 5W Balance: 14 units * 10W = 140W Microscope: 14 units * 0.2W = 2.8W Hood: 2 * 1W = 2W Cleaning Machine: 2 * 0.5W = 1W Blender: 4 * 0.2W = 0.8W	
	Labor costs The	Extrusion: 6 people * 12W = 72W Inspection: 3 people * 12W = 36W	Cutting: 2 * 9 people * 12W = 216W	Cleaning: 2 * 3 * 12W = 72W Inspection: 2 * 10 * 12W = 240W	Spray: 2 * 13 * 12W = 312W Spray test: 12 * 12W = 144W Cleaning and inspection: 2 * 2 * 12W = 48W Solution preparation: 2 * 12W = 24W	11640000
	Venue fees With	Extruder: 30m2 * 0.45W / m2 = 13.5W Surface processor: 6 * 30m2 * 0.45W / m2 = 81W	34 * 9 * 0.04W = 12.24W	0.0	Solution preparation: 20m2 * 0.45W / m2 = 9W Painting workshop: 34 * 6 * 0.45 = 91.8W	207.54 Wan

Equipment dimension	
Care and maintenance	
Costs	
Supplies and Utilities	Hydro: 14.4 yuan / pcs; supplies 38 yuan / pcs; Other 4 yuan / pcs, Subtotal: 56.4 yuan / pcs
With	
Management and	
Sales Charge	
With	

Note: FB2 data provided by the Treasury

In the budget the cost of production, but also give full consideration to the production process pass rate factors some processes, as follows:

Each semi-quantity production processes qualified table

Process	Pipe extrusion	Cutting	Surface treatment	Stent	Conveyor and packaging
Pass rate	80%	70%	90%	80%	95%
Daily output (Pcs)					
The flow	1958	1566	1096	986	790

Through qualified Rate calculation					
Equipment Open Fixed rate According to ERP estimates Count	8085%	8085%	8085%	8085%	8090%

Preparation cycle (production): Process Validation (design transfer 7 months) + pre-production (6 months) period = 13 months

Additional information: If Firehawk spraying equipment can not be transferred to the biodegradable stent products, you may need a new paint shop and purchase equip
Biodegradable scaffold outside cutting the need for new purchase special cutting machine, so cutting workshop also need to create, not existing equipment and worksh

Production is expected to manufacture specific detailed analysis table.

5.6 Feasibility patent research and analysis

5.6.1 Analysis of Key Patent Status target market technology

Related products, target market is currently set at China and Europe. Therefore, the first Chinese patent and international patent applications were Do a search, and then by the R & D engineers R & D project is technically part of the screening closest several patents, and then by the knowledge Property Room patent on these key patents, regional, legal status were analyzed in order to determine these patents for public Secretary biodegradable stents affect product strategy.

When searching for Chinese patents, R & D projects through discussions with the Ministry, using the "biodegradable", "blood" and "support Frame "search keyword combinations, retrieved a total of 115 Chinese patent R & D engineers after a preliminary screening, selected its The 30 more related patents, which also has a minimally invasive medical devices (Shanghai) Co., Ltd. application. In the further After comparison, the focus of China screened out two patents (see Table 4).

Overall, the impact of the degree of the retrieved Chinese patents and technologies developed by the company is not high, including the following two focus Patents. Many applicants for universities and other academic research institutions, mostly corresponding patents do not apply to industrial production or practical appli Use; applicant's patented technology for the enterprise has been mostly known for existing technology or have weak novelty and creativity. As such, From the retrieved patent term, does not my company's products may have a greater obstacle to patent in the Chinese market.

Table 4: China's key patents

Patent Application No.	Name	Applicants	Introduction	Legal Status
200410013749	In the preparation of poly-lactic acid as L- The shape memory material of the medical Uses	Harbin University	PLLA (poly-lactic acid L-) for Biodegradable shape for the medical-recalled	China - Authorization
200980150101	Bioabsorbable polymer composition Physical and medical equipment	奥巴斯尼茨 Medical Corporation	PLA or other homopolymer And PCL or PLA-TMC Mixture of crystalline nature Improve the mechanical properties	United States - open Europe - open China - open

When foreign patent search, due to foreign technology is relatively mature, and there are many medical device industry companies Industry in terms of biodegradable scaffold research and development work for a long time, so a very large number of patents. For this reason, we have chosen Choose to search for a company's existing and potential competitors of patent manner, the keyword "Biodegradable / bioabsorbable stent" and the patent applicant (ie, the main competitor) combination of retrieval. Select competitors include the following: Abbott Vascular, Boston Scientific, Medtronic, Biotronik, Arterial Remodeling Technologies (ART), Bioabsorbable Therapeutics, Inc. (BTI), Biosensors, OrbusNeich, Igaki-Tamai, Endovasc, Tepha, Sahajanand Medical Technologies, Amaranth Medical, Inc., retrieved a total of 127 patents (including some belonging to the same patent family). After R & D projects Engineer assisted screening (see Table 5) and then further analysis for the following Key patent.

Due to the patented regional characteristics, we are concerned that the focus of the patent in the target market, whether patent applications. From Table 5 Legal status of each patent can be seen, these key patents have been a period of international applications entering the national phase, That is in addition to the country has entered, and can not re-enter other countries. Since the target market for our company projects between China and Europe Chau, therefore, from the perspective of products on the market, we need only consider the application for a European patent technology and our products

Technology related to the similarity.

Therefore, Table 5 International Application No. WO2009155206, WO2007105067 and WO2007105068 patent,

Because it had no European patent application, if we only put the product in the European market, the possibility of infringement does not exist. And right

Table 5 in International Patent Application No. WO2008002469 and WO2009099958 of these two patents, the need to analyze the patent

The relationship between technology and our products involved. WO2008002469 open on a biodegradable drug-coated stents

Layer, while WO2009099958 Disclosed is a slow degradation of the developing point care, Introduction to Table 5. If these two professionals

Lee technology is not our most critical technology product development, on this basis, or we can have a more significant improvement

It can be considered less likely infringement; greater likelihood of infringement and vice versa. From minimize the possibility of infringement angle

Departure, researchers should try to avoid using the same or similar like two patented technologies in the development process, in particular

When the structure and materials to avoid similar (similar mode of production is more difficult to evidence on).

Should the company has put the possibility in the future of biodegradable stent products to the United States or other markets, according to Table 5 Key

U.S. patent application patent status quo are even authorized to assess the need for further comparative analysis of whether there is infringement

Possibilities.

Table 5: Key patent abroad

International Publication Number	Name	Introduction	Specifies the country - state
WO2008002469	THIN STENT COATING	Belongs to the stent, drug coating thickness Degradable polymers or degradable gold Over 3 microns	United States - open Europe - open Japan - open Must have passed into the national phase Limit

WO2009155206	BIOABSORBABLE POLYMERIC STENT WITH IMPROVED STRUCTURAL AND MOLECULAR WEIGHT INTEGRITY	A process for the preparation of biodegradable stent France.	United States - open Must have passed into the national phase Limit
WO2009099958	BIOABSORBABLE STENT HAVING A RADIOPAQUE MARKER	Developing stand above the point care for Installation of one or more of the developing Points.	United States - open Europe - open Must have passed into the national phase Limit
WO2007105067	METHODS OF MINIMIZING STENT CONTRACTION FOLLOWING DEPLOYMENT	With developing point on the stand in order to Position of the stand, may be provided with 2 Developing a three-point or	United States - Authorization Must have passed into the national phase Limit
WO2007105068	METHODS OF MINIMIZING STENT CONTRACTION FOLLOWING DEPLOYMENT	Shape memory stent expansion can pass Over balloon dilation balloon or heating To achieve.	United States - Authorization Must have passed into the national phase Limit

In addition, from the perspective of the production process discovered a patent application (Application No. article with Division I: CN201110312261, Title: A new method for the processing of biodegradable stents, see Table 9) is very similar to the focus of the patent is as follows (Table 6).

Table 6: Key patent similar technology abroad

U.S. and international Publication Number	Name	Introduction	Designated countries - like State

US8,012,402	TUBE EXPANSION PROCESS FOR SEMICRYSTALLINE POLYMERS TO MAXIMIZE FRACTURE TOUGHNESS	Polymer scaffold production methods, increasing the The fracture toughness.	United States - Authorization Passed into the country Home stage must limit
WO2010017090			

Only the above patent is applied for and received authorization in the United States, so for our products in the Chinese and European market launch And will not have an impact. However, because of its similarity in high technology, is very likely to be my company apply for a patent Barriers to obtaining authorization to make our patent loss of novelty and creativity. Therefore, we also recommend our part by the Patent within three months of the conflict into the real trial stage after their claims, brochures and other proactive changes to minimize Distinguish it with the above patent.

All of the above Patent Document Foreign Key (Tables 5 and 6) belong to the following competitors: Abbott Cardiovascular Systems (Abbott), Medtronic Vascular (Medtronic), Arterial Remodeling Technologies (ART). Among them, in the European patent application WO2008002469 belong to Abbott Cardiovascular Systems; WO2009099958 belong Medtronic Vascular; WO2010017090 also belong Abbott Cardiovascular Systems. Therefore, in the course of the project, the proposal of several competitors in this patent case Continuous track and further analysis, especially Abbott Cardiovascular Systems. The figure below shows Abbott Cardiovascular (including Abbott Cardiovascular Inc. and Abbott Cardiovascular Systems Inc.) in a biological scaffold (biodegradable / bioabsorbable stent) related to the number of years the field of patents discloses biodegradable Weight distribution (see Figure 9). Thus, the peak of its development in 2007, although in recent years the number of patents in this field has Come down, but still maintain a high level, as of February this year, there have been four applications open.

Figure 9: Abbott Cardiovascular company in the field of biodegradable stent-related patent publication number distribution over the years:

In addition, according to information provided by the R & D project team, can have drug-coated stent surface, and the coating and
The stent body is biodegradable. At the same time, we note that the international application in Table 5 WO2008002469 patent disclosure
The polymer is coated with a biodegradable stent. In order to understand the biodegradable coating, the conduct of the project exists
The possibility of infringement, the company projects to apply for a patent if patentable, and whether higher WO2008002469
Authorized possibilities and thus become our obstacles, we WO2008002469 international search reports were analyzed. In
Its search report mentions the following several patents (Table 7), is likely to have a greater impact on their novelty, that is with us
The high degree of coating technology association. At the same time, we again on the domestic patent search results are compared, also found its
In several patents related to the drug coating (Table 8).

Table 7: Coating related foreign patents

International Publication Number	Name	Introduction
WO2001045763 A1	BIOCOMPTABIBLE COATING	The implant surface is coated ethylene - vinyl alcohol copolymer Coating, the coating may be provided with drugs. At least part Points above coating with heparin.
US 2002/123801 A1	DIFFUSION BARRIER LAYER FOR IMPLANTABLE DEVICES	Coating the surface of the implantable device, the coating particles in Substances, can play a controlled drug diffusion rate for With. This coating layer on the surface of the drug layer.
WO2004024201 A2	CALCIUM PHOSPHATE COATED IMPLANTABLE MEDICAL DEVICES AND PROCESSES FOR MAKING SAME	Implantable devices coated surface using calcium phosphate as Layers mainly refers to calcium hydroxyapatite, phosphorus Calcium in the form of particles deposited on the instrument microns Surface.
★ WO2002026281	COATED MEDICAL DEVICES	At least a portion of the medical device surface with a biocompatible Media, media agents can be treated due to the implant Biological response induced. Media can be PEV or

		By PBMA
	MORPHOLOGY PROFILES FOR	In the surface of polymeric medical devices (containing drug)
WO2007146049	CONTROL OF AGENT RELEASE RATES FROM POLYMER MATRICES	A method of forming a special surface topography - use Temperature, pressure, solvent, etc.

Table 8: Coating relevant national patent

China Application No.	Name	Introduction
★ CN200880011669	Drug-eluting stents and medical device coatings Degradation related to drug delivery	Treatment of disease, comprising: a catheter; set Stent on the catheter; coating disposed on the stent surface Layer and at least one therapeutic agent in the coating.
200910216008	An anti-restenosis coating arteries have Frame and its preparation method	Ultrasonic atomization method of spraying the surface of biodegradable polymeric Substance and drug on the stent.
03820105	Treating vulnerable plaque in coronary drug-eluting stent Stand off	There are drug-eluting stent surface coatings, drug-eluting coating The surface layer of a biodegradable sustained-release coating.
200580015085	For biological activity in patients with type II diabetes Stent and its application method	Biodegradable polymer coating is a bioactive, polymeric Comprising biological ligands and progenitor cells can knot Together.
200480005067	Bioactive stents and methods of using them	bioactive surface coating the stent.
★ CN200610014377	Coronary stents coated biodegradable drug-eluting	Biodegradable polymer coating constituted by drugs and drug Matrix, rapamycin or paclitaxel or Tucker, PLGA or PLA polymer, etc.

In Tables 7 and 8, with ★ patent No. focused patents. For example, the table of claim 7, WO2002026281 1,2,17,36,54,89 are very broad, covering a large part of our product technology, there is the possibility of infringement.

But we can also see that most of these key patent claims are too broad and difficult to obtain authorization, even if authorized,

We can also request to declare the patent invalid as needed. Moreover, our products are used by Firehawk coating technology

Very similar, and therefore is also not a problem. From the perspective of risk reduction, the project can Firehawk a

Since, further research and analysis in the special coating technology, at the same time to avoid the risk, you can develop the direction and Key play a guiding role.

5.6.2 Company summary of the project for the patent application of key technologies

Table 9: company to apply information technology in the key of the project ten articles patents

Patent Application No.	Name	Inventors	Filing date	Introduction	Legal Status
201010255641	An organism can be Degradable stent	Huang Chubo, Sau Feng Luo seventy-one, Wang Yihan, Juan Meng	2010-08-17	Reduce retraction rate, to avoid stent Collapse, displacement	Undisclosed
201010278678	An organism can be Degradable stent	Juan Meng; Shi Xiufeng; Luo seventy-one; Wang Han; Huang Chubo	2010-09-07	X-ray developer material coating On the inner wall of the stent.	Undisclosed
201110097517	Having a multi-Layer coating raw A biodegradable branched Rack	Shi Xiufeng, Juan Meng, Li Fei, Luo seven A	2011-04-13	Multilayer coatings, including drugs, Intima of developing	Has been made public Into the real trial
201110175411	A novel can Degradable stent and The preparation method	Chen love; Juan Meng; Shi Xiufeng; Luo seven A; Wang Yihan	2011-06-16	Is made of a composite material, with A corresponding supporting force and toughness Degradation, and can be regulated Rate.	Has been made public Into the real trial
201110219147	A new Health A biodegradable branched Frame processing side France	Juan Meng; Shi Xiufeng; Chen love; Luo seven A	2011-7-27	Effectively improve the radial bracket Supporting force, increasing the toughness, Efficiency to reduce rebound and expansion over Process of fracture.	Undisclosed

201110227994	A tape groove Creatures may drop Xie bracket and Preparation	Huang Chubo; Sau Phoenix; Luo seventy-one; Tian Hao; Wang Yihan	2011-08-02	Retraction rate can be reduced to 10% in Under avoid collapse, displacement, Minimum reduction of vascular Wall heat damage.	Undisclosed
201110236013	One kind have shaped Shape memory properties Multilayer may drop Xie bracket and Preparation	Chen Love, Juan Meng, Shi Xiufeng, Luo seven	2011-08-17	multilayered, and shape memory properties	Has been made public Into the real trial
201110298398	An organism can be Degradable stent and The preparation method	Shi Xiufeng; Juan Meng; Chenshu Guo; Chen Love; Luo seventy-one	2011-09-28	Stent has shape memory properties Energy, as well as sufficient mechanical strength School performance.	Has been made public Did not enter the real Trial
201110312261	A new Health A biodegradable branched Frame processing side France	Juan Meng; Chenshu Guo; Shi Xiufeng; Chen Love; Luo seventy-one	2011-10-14	Biodegradable improve Stent strength and toughness.	Undisclosed
201110409747	An x light Visible creatures Biodegradable stents Preparation	Chenshu Guo; Sau Phoenix; Juan Meng; Luo Seventy-one	2011-12-09	The main layer and the developer layer pairs Layer formed by melt extrusion;	Undisclosed

At present, these patents are still open and before entering the actual trial stage, not related to the official's review comments or authorization through Know. We will make the appropriate analysis and processing according to the official follow-up notification. Has applied for a patent 201 110 312 261 PCT.

Minimally Invasive Medical Devices (Shanghai) Co., Ltd. Management System

Biodegradable stent product development projects | File Number

5.6.3 Patent Analysis Conclusion

In summary, for the company's biodegradable stents in China and Europe, these two products on the target market, purpose Ago in China and no significant patent barriers, while in Europe, you need to avoid as far as possible from a technical and WO2008002469 and WO2009099958 these two PCT international applications entering the European patent applied for similar, and the choice of other R & D direction as heavy Points. For the future market expansion in markets outside of these two objectives, we will need depending on the area and the country at the time Outside the patent application for further comparative analysis of the situation, to be able to make appropriate judgments. For the company has for the project Patent application, the portion of the patent (particularly Application No. CN201110312261, entitled "A new biodegradable branched Frame processing method "in a), because it is possible to focus on the above-mentioned patents have lost one or more of the patent, the more Difficult to obtain authorization. But in view of the patent examination has certain subjectivity, according to the review comments received on the patentability of futur Argue or make some modifications. In addition, the drug coating technology, the project will follow the Firehawk coating method, There may be the risk of infringement. We recommend that this project can be targeted research and analysis together with the Firehawk on drug coating technology.

Finally, it should be added that this patent is based upon analysis of the feasibility study currently disclosed in patent offices Patent Currently limited by the available patent search tools offer, as well as my intellectual property room. Has applied for but did not open (Chinese patents After the application open within 18 months) of the patent, or retrieval software and websites can not retrieve patent search is not included Analysis category. Meanwhile, in the progress of the project process, the proposed R & D and intellectual property room with, according to the progress and developm Layout of the market on a regular basis or periodically updated patent information, especially for major competitors (such as Abbott Cardiovascular Systems) patent track and further data analysis in order to avoid possible tertiary Lee risk of infringement, reduce development costs, and enhance market competitiveness.

Attachment: patent search tool

http://www.soopat.com/

http://www.wipo.int/patentscope/search/en/search.jsf

http://www.drugfuture.com/

http://www.orbit.com

5.7 Analysis of the economic feasibility study

5.7.1 intends to develop products or technical sales forecast

According to market research content, complete the table next to estimate the content. Sales price estimates should be considered promotional price cuts and nati

Sales estimate factors should be considered sales model and team building. If you think the product life cycle is short, you can only do three-year forecast.

Market sales forecast

No.	Project	1st year	2nd year	3rd year	4th year	5 years	Total
1	Market capacity (million)	386.27	459.66	547.00	650.93	774.60	
2	Stent sales (million units)	229	269	316	371	436	
3	The market share (%)	3%	4%	5%	5%	4%	
4	The product sales (sets)	70000	110,154	162,580	186,967	172,010	
5	Market excluding tax selling price (yuan)	3,288	2,959	2,663	2,397	2,157	

6	Sales revenue (RMB)	230,132,479	325,928,739	432,944,287	448,097,337	371,024,595	

5.7.2 Product development investment forecast

5.7.2.1 Analysis of new product development critical resource requirements:

Demand for R & D engineers, process engineers, quality engineers, clinical engineers, registered engineers and other staff positions;: human resource needs

Venue Requirements: R & D and production sites and the area occupied by the basic requirements;

Demand for key materials and equipment research and development, testing, production and other aspects of use;: key raw materials, equipment needs

Other requirements: project may take the Association or dedicated special resource requirements.

5.7.2.2 According to the critical needs analysis, R & D investment budget summary form the following:

		R & D investment budget (million)							
No.	Project	2012	2013	2014	2015	2016	2017	2018	2019
		(Year 1)	(Year 2)	(Year 3)	(Year 4)	(5 years)	(6)	(Article 7)	(Article 8 years)
1	Direct material cost consumed in R & D activities, including Including materials and consumables	166.40	300.00	300.00	300.00	400.00	400.00	400.00	200.00
2	Directly engaged in R & D activities of personnel costs, including Wages, salaries, allowances, subsidies, bonuses, its His remuneration and social insurance	300.60	360.72	432.86	519.43	623.32	747.98	897.58	1077.09
3	Depreciation related R & D activities devoted (by Provisions once or apportioned management fees instruments And excluding equipment), including instruments, equipment and housing House	91.00	101.00	111.00	121.00	131.00	141.00	151.00	161.00

4	About the rental fee dedicated to research and development activities, including Including instruments, equipment and housing	11.40	13.68	16.42	19.70	23.64	28.37	34.04	40.85
5	Related intangible assets dedicated to R & D activities Amortization charges, including software, patents and non-patent Technology	0.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
6	Related expenses for research and development results of the application of intellectual property rights Use, including fees, registration fees and attorney's fees	5.00	6.00	6.00	5.00	4.50	4.00	4.00	4.00
7	R & D results demonstrate, identification, assessment and acceptance fee Use, including the test sample production, outsourcing testing, Animal tests, biological performance testing, the process does Recognize, series production, technical cooperation, clinical, Registration submission, review and other experts	15.36	114.43	294.52	1825.62	1836.25	1546.40	1547.07	1047.29
8	Other costs directly related to R & D activities, including Including technical drawings fees, document translation fees, special Home insurance consultancy and high-tech research and development, but also Including the need to purchase new equipment / devices / software, Compare products, technology exchange, market research, people Training, etc.	34.14	98.73	109.47	121.37	129.64	141.57	173.48	187.78
9	Total	623.9	995.56	1271.27	2913.12	3149.35	3010.82	3208.17	2719.01
10 *	R & D investment in fixed assets (including instruments, equipment And Housing)	118.40	100.00	100.00	100.00	100.00	100.00	100.00	100.00

Note: Item 10 R & D investment in fixed assets, has been considered in the previous paragraph 3 after depreciation, it is not included in the totals.

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5.7.3 product cost and cost projections

Content includes but is not limited formal stage in the production and sale of products to predict costs and expenses, including the purchase cost of raw materials Manufacturing costs, management and sales expenses, maintenance and service costs as well as fixed asset investment. This section lists the inputs and costs required Like historical financial data products. The following table:

Cost forecast table (yuan)

No.	Project	1st year	2nd year	3rd year	4th year	5 years	Total
1	Cost of raw materials	23,668,400	37,245,270	54,971,550	63,217,282	58,159,899	237,262,402
2	Artificial	5,160,000	7,920,000	11,400,000	13,320,000	11,640,000	49,440,000
3	Manufacturing costs	4,690,000	7,198,605	10,361,628	12,106,744	10,579,767	44,936,744
4	Management and sales expenses	57,533,120	81,482,185	108,236,072	112,024,334	92,756,149	452,031,860
5	Product routine maintenance and Upgrading R & D expenses	11,506,624	16,296,437	21,647,214	22,404,867	18,551,230	90,406,372
6	Production equipment and other fixed Assets investment	69,413,800	42,546,800	47,506,000	15,078,800		174,545,400
7	Collector in Hong Kong Financing costs	218,713,133					
8	Total	390,685,077	192,689,297	254,122,464	238,152,027	191,687,046	1048,622,778

5.7.4 Benefit Analysis

See earnings forecast template, long considered the project cycle, using 20% of the risk discount. Domestic economic benefits calculated according to the above sales f

(1) Project IRR (Internal Rate of Revenue, IRR): 21%

(2) The payback period (Payback Period): 10.31 (including initial investment of eight years, the actual payback period of 2.31 years)

(3) ROI (Return On Investment, ROI): 38%

(4) Project gross margin (GrossMargin, GM): 74%

5.7.5 Project Economic Analysis Conclusion

Based on the above analysis shows that the domestic market (20% risk discount), the project economically viable in the domestic market.

5.8 The overall conclusion of the project feasibility study

Corporate Strategy: coronary stent is one of the company's flagship product, as a new generation of coronary stents, biodegradable stents developed

In line with the company's strategic direction. If this product successfully developed, not only as a product of the current coronary

One of interventional treatment of congenital heart disease, peripheral vascular areas, gastrointestinal and neurological involvement and so have a good

Boost.

Market: Currently on the market is not biodegradable stent products, but has a large market potential.

Technology: biodegradable scaffolds after two years of pre-development, has identified some of the feasibility of the key technologies. But as

For a new product, there are still some risks that need attention.

Patents: Biodegradable Stent is currently in China and no significant patent barriers in Europe need to pay attention to two technically

Xiang PCT international application; technical aspects of the drug coating, although the project will use a similar drug-coated and Firehawk

Layer technology, but there may be risk of infringement, it is recommended together with the Firehawk on drug coating technology for targeted

Research and analysis.

Economy: The project economically viable in the domestic market.

In summary, the development of biodegradable stent is feasible. As previously described, the product is delivered and fully

The biodegradable polymer scaffold composition, the stent surface can carry the drug, the balloon-expandable, the implant can be effectively after 6 months

Support the narrow blood vessels, 1-2 years degradation completely absorbed by the body. Product is expected to be listed in 2020, the first year listed on the market

Share of 3%, and gradually increased to 5% in three years. Project payback period is 10.31 years (including the initial investment of eight years, the actual recovery

Period of 2.31 years), the return on investment was 38%. Important milestone in the progress of the planned projects are as follows:

Table 10, an important milestone in the project

Time node	Project Progress
2012.01-2012.12	Sample design bare stents, drug dispensing begin research
2013.01-2013.08	DES sample review
2013.09-2014.06	Type test and design validation (including animal experiments)

2015.07-2018.06 Clinical and design transfer phase
2018.07-2019.12 Registration information submitted and reviewed

Currently SFDA biodegradable stent for no particular provision, however, the project development cycle is longer, in the development process With SFDA standards, clinical requirements of some policy changes may lead to the development of our current milestone node in advance or Delayed implementation.

5.9 Project Risk Analysis

Technical Risk Analysis in 5.4.10 "technology risk assessment and response measures" have been described in some detail, and its It analyzes the risk categories as follows:

Category	Risk	Coping strategies
Market Risk	There better alternatives during the project development Completely dominate the market	Focus on technology developments, if the direction of the development of better Timely follow-up
Production Risk	Supply shortages of raw materials	Development of a number of qualified suppliers
Clinical Registration	State regulations require more stringent for new products, Making clinical and product registration period longer	And SFDA close communication, always pay attention to the new policy requirements. Reasonable arrangements for project development progress, in parallel fashion Some work to save time
Patents	Has applied for but not disclosed specifically in China, the European Union Lee and the project uses technology conflict, then Sales of the affected products	In the project development process, developed for the new technology and Patent applications to protect our products
Financial Indicators wind Insurance	Long project development cycle, due to technological development Uncertainty in the process, resulting in the production costs Inaccurate estimates	Periodical review of the project, initiated into the new technology The additional timely accounting, project accounting as a result of progress An indicator.

Long project development cycle, due to national policy,	Market research on a regular basis, in a timely manner in accordance with the market price of nuclear	
Competition and other factors, resulting in product price significantly	Calculate project benefits, accounting as a result of the progress of a project	
Decline	Indicators.	
The actual increase in sales volume is small, because the project	Because the longer the project cycle, the future market share may	
* Impact on the profitability of	Achieve a higher market share. Considering the market share	
	Factor, sum up the state of the market, analyze profitable projects	
	Capacity.	

6 transitional measures

No

7 related records

No

8 References

8.1. MP / QS7.3 "passive product lifecycle management control procedures."

8.2. MP / AS7.3-13 "product development project management and decision-making review regulations"

8.3.MP/AS7.3-15 "key technical feasibility of regulations"

8.4.MP/AS7.3-06 "Passive Product Design History File (DHF) regulations"

9 Revision History

Revisions	Revision Date	Amendment Description	Modified
A version	2012-5-22	Biodegradable stent product development project feasibility study report	Juan Meng