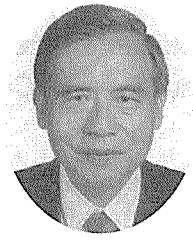
Demand and Strategy for Radiation Sterilization of Healthcare in China



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1. Status of healthcareproduct industry in China

China has a population of 1.3 billion and over 310 thousand medical institutions (hospitals) ; there is thus a high demand for healthcare products. It is one of the ten biggest 'sunrise markets' for healthcare products in the world, ranking just behind Japan in Asia. In 2000, the market for medical devices was worth 22.7 billion RMBs, corresponding to 3% of the global medical device market and showing an average annual growth rate of 15% [1]. Manufacturers are dominantly located in the Changjiang delta, Zhujiang delta and Yellow sea and Bohai areas where the labor resource is good. A significant proportion of their products are exported which need terminally sterilized. Some details of healthcare products manufactured in China are as follows.

1.1 Surgical (examination) latex gloves

Generally, surgical latex gloves are sterilized by radiation. There are over 30 large manufacturers in China that produce about 300 million pairs per year. Most of them are for export, but the proportion for domestic use has gradually increased in recent years. 〈Table 1〉 shows the data of glove yield in 2001 and 2002 from Latex Branch of China Rubber Industry Association.

1.2 Single-use medical devices (transfusion devices, syringes and others)

The radiation sterilization business was

〈Table 1〉 Surgical glove yield

Manufacturer	Yield (unit: 103 pairs)	
	Year of 2001	Year of 2002
Shanghai latex factory	41,203.8	34,322.3
Suzhou latex Factory (Jiangsu)	27,071.4	21,674.6
Guilin Latex Factory(Guangxi)	19,356	23,617.7
Qingdao Latex Factory (Shandong)	8,328	8,872.8
Ruijing Latex Factory(Beijing)	15,520	19,830
Shengyang Latex Factory(Liaoning)	6,216	4,352
Ningbo Latex Factory(Zhejiang)	10,292.2	8,480
Benbu Latex Factory(Anhui)	5,963.4	12,553.2
Zhanjiang Latex Factory(Guangdong)	1,490	314.2
Jingzhou Latex Factory(Hubei)	4,530	4,780
Tanggu Latex Factory(Hebei)	313	408
Total	140,283.8	139,204.8

started in China for the processing of single-use medical devices. However, currently 90% of such devices are sterilized by exposure to EtO due to its low cost. In 2002, there were 143 licensed manufacturers of such devices within China, more than half being located in the east of the country. These manufacturers are potential customers for radiation sterilization as they may have to use radiation as the sterilization method instead of EtO with the onset of the implementation of the Montreal International Agreement.The typical example is Organon (Nanjing) Co.Ltd, who has turned to radiation sterilization from previous EtO for its product (contraceptive devices)

1.3 Sanitary products

Sanitary products are medical dressings, surgical gowns and others made from cotton or non-woven materials. There are over 400 manufacturers in China, among whom 40% are located in Jiangsu, 40% in Huhei and the remainder in Zhejiang, Anhui and Shandong provinces. 43% of such products are intended for export. Previously, the exported product was in the form of an unfinished product, repacked and sterilized in the destination country. In recent years, some manufacturers introduced the automatic packaging machine and improved the quality of product. With improvement in compliance with quality systems, both by the

manufacturer and the irradiator, parts of products are being sterilized in China and then exported as finished product. It is one of the biggest businesses for radiation sterilization.

1.4 Packaging materials

According to China SDA data, there are over 700 manufacturers in China who produce packaging materials for food and pharmaceuticals. Such products include : plastic material, composite film, aluminium foil, vaccinal package, aluminium-plastic stopper for antibiotics and so on. Sterilization by irradiation is suitable for the products of 527 manufacturers, although only a few employ this form of sterilization because of inadequate knowledge of it. Thus it would appear that packaging materials constitute potentially a significant market for radiation sterilization.

1.5 Implantable devices

Many kinds of implantable devices are increasingly used in clinic. For example, the endosteal implant recommendedby IAEA is clinical applied ; Shanxi Tissue Bank has produced more than 100,000 bone tissues, which will be radiation sterilized with 25kGy before clinic use. In addition, the stainless steel artificial arthrosis has been widely applied in clinic. This is increasingly business for radiation sterilization.

〈Table 2〉 Opportunity of radiation processing in the future

Field	Opportunity (%)
Food radiation	45
Healthcare product sterilization	21
Packaging material sterilization	11
Flue gas treatment	7
Polymer modification	6
Nutracenticals	5
Pharmaceutics radiation	4
Molded parts sterilization	2
Wire and cable crosslink	0
Cosmetic radiation	0

〈Table 3〉 Estimation of annual increase rate of radiation processing

Annual increase rate (%)	Support rate(%)
〈5	25
5~10	39
11~15	18
16~20	7
21~25	5
〉25	5

〈Table 4〉 Obstacles for radiation processing

In the order of importance	Obstacles
1	Public acceptability
2	Cost
3	Technique of EB transformed to X ray
4	In-time Radiation
5	Changing regulation
6	Safety
7	Technology exchange
8	Supply of Co-60 source
9	Electricity supply

〈Table 5〉 Problems to be solved

In the order of importance	Problems
1	Technology Development
2	food radiation
3	Sterilization of Healthcare product
4	Application of high energy EB
5	Dosimetry
6	Application of low energy EB
7	Training and safety
8	Isotope
9	Facilities

2. Strategy for the radiation sterilization industry

As described above, there is in China potentially a high demand for radiation sterilization from the manufacturers of healthcare products. Exploiting and meeting this demandis an opportunity and also a challenge for the radiation sterilization industry, particularly in the current circumstances of economic globalization. Clearly, actions have to be taken to face up to this challenge.

Some key measures regarding the radiation sterilization were elucidated in author's previous paper[2] : establishment of modern radiation plant, establishment of good dosimetry system, dose setting, process validation, routine control, management by intranet, quality system, and radiation protection and safety. These are the spirit of domestic or international standards[3-13] and also our long-term practice in radiation sterilization.

In the IMRP2003 held in Chicago in Sept 9~12 of 2003, a poll was made for the radiation processing industry. The results are listed in 〈Table 2~5〉 which may be useful for us.

2.1 Developing modern industrial irradiator

A modern irradiator is featured:

(1) Industrial scale: larger than 37pBq, automatic face change and level change to reach the dose uniformity less than 1.5 at the density 0.4g/cm^3

(2) high energy utilization: the energy utilization efficiency can reach above 28% at the product density above 0.1g/cm^3

(3) high automatization, ease of main-

tenance, failure(malfunction) rate less than 1% ;

(4) radiation safety system : defence in depth and redundancy

Suzhou CNNC Huadong radiation Co. Ltd (SCHR)and Beijing Sanqiang Heli Radiation Engineering Co., Ltd(BSHRE) were cooperated to develop brand-new irradiator :

(1) Automatic conveyoring system (combination of mechanical chain and pneumatic driving), automatic face change and level change, high energy utilization efficiency, good dose uniformity, low cost ;

(2) automatic loading and unloading, ease of operation and maintenance ;

(3) multi radiation mode(6 paths mode, mixed mode of outer 4 paths and inner 2 paths) ;

(4) automatic control and monitor of process ;

(5) door-open source frame. It can accommodate nude source pencil and reduce self-absorbency. 6 patents were applied. These innovative designs have been applied in 11 irradiators. Currently some foreign companies intends to buy the design.

2.2 Implementation of quality systems

SCHR was awarded qualitysystem certificate from TUV ps in June of 1999, and passed FDA audit in April of 2004. Thus SCHR draws a lot of customers who exported their products to USA, Europe and Australia. SCHR' s boom is dramaticallyattributed to its firm implementation of quality system.

(1) Why establish the quality system?
Implementation of and compliance with quality systems are vital to ensure that irradiated products consistently meet the product manufacturer' s requirements. It is a precondition that an irradiator could be accepted by Europe or USA.

(2) How to establish and implement the quality system
SCHR started to establish the quality system from 1997. Considering the most of radiation products are for export, TUV ps, a notified body known world widely, was chosen. After strictly audit by TUV ps, SCHR was certified the quality system in 1999. Annual audit by TUV ps was conducted after that. In addition to TUV ps audit, SCHR also was audited by manufacturers and FDA. SCHR itself performs internal audit and management review twice and once a year respectively.

The 8 years' practice in quality system is summarized in follows :

(1) Internal auditor training

Internal auditors shall own the knowledgeboth on technical and management. They must own the license from competent institutes such as CNAT(China national Auditor and Training Accreditation Board) or TUV. At least 2 internal auditors areneeded for independent audit. Currently there are 7 in SCHR.

(2) Document of quality system

- Follow documents shall be available according to ISO13485 :
  a) quality objective and quality policy
  b) quality manual
  c) procedures
  d) documents for planning, operation and control
  e) record
  f) standards and regulatory document
- Thus, follow documents shall be available in one company :
  a) quality manual
  b) procedure documents
  c) work instruction
  d) master device record
  e) record
  f) standards , regulatory file and external document.

(3) Quality manual

- In ISO13485, concept "process control" is introduced instead of previous "20 quality elements". SCHR' s quality manual includes:
  a) company introduction and organization
  b) referenced standard
  c) term and definition
  d) quality management system
  e) management responsibility
  f) management resource
  g) product realize
  h) measure, analysis and improvement
  i) qualitypolicy and objective

(4) Quality policy and objective

Quality policy concerns about the quality goal and long-term direction. It is commitment to continuing effectives of quality management system, meeting customer and reg-ulatory requirements. I shall be incorporated into the enterprise culture and well understood by all staff. It shall be reviewed periodi-cally for its applicability.

Quality objective includes the contents to meet product requirements. It is measurable, accorded with the quality policy.

Ten objectives are stated in SCHR :

a) The delivered dose shall fall into the dose range provided by the customer. The dose uniformity shall be less than 1.5.
b) Installation re-qualification andprocess re-validation shall

be performed once the radiation source is replenished. Irradiation time compensation related to the decay of radioactivity shall be conducted once a month by increasing 1% irradiation time length.

c) Contract review shall be conducted timely. Customer requirements shall be met to the maximum extent.

d) Dosimeters shall be calibrated to National Metrological Institute once a year at least. Dosimeter batch calibrations shall be performed. QC Dept shall be appointed at least two licensed persons.

e) Measurement instruments such as timer, balance, spectrophotometer and platform scale shall be calibrated once a year as minimum.

f) Maintenance shall be done regularly to ensure less than 1% of malfunction rate.

g) Management review and internal auditshall be performed, as minimum, once and twice a year respectively.

h) Training plan shall be made strictly. Employees shall qualify the training courses.

i) Technical documents shall be retained for 5 years, and job record for more than 2 years.

j) Regular inspection on radiation safety devices shall be performed to ensure they are in good conditions, to secure the personnel and environmental safety.

2.3 Developing radiation sterilization market

Radiation sterilization accounts for about 60% of the output of the total sterilization industry in developed countries. China has become the international base of healthcare manufacture. As mentioned above, many manufacturers are located in Changjian delta, Zhujiang delta and Bohai coast. Just in Jiangsu-Shanghai-Zhenjiang area, approximate one million cubic meter medical devices (dressing, transfusion, surgical glove and packaging material) are produced per year, which need to be terminally sterilized. Meanwhile, attention shall be paid to radiation sterilization of the Class? medical device which can bring about added value.

Food radiation is another big market in China. Currently 6 food categories are approved to be radiated. Radiation sterilization is also extended to the food packaging material.

2.4 Training

Training of qualified personnel is key issue in current times of knowledge

explosion and severe competition. Radiation processing is of "complex", needing specialists not only in nuclear physics, radiationchemistry, automatic control, and mechanical engineering, but also in management who knows the state-of-art and owns ability to make scientific sound decision.

The irradiator enterprise shall establish training plan. Only the qualified personnel can be appointed to suitable job. Additionally, due to the unique safety requirement of radiation facility, psychologicalexamination shall be conducted for operator. Anyone who shows mental defect shall be excluded in operating the radiation facility.

2.5 Establishing modern financing system

Construction ofirradiator needs high invest, afterwards the replenishment of source costs a lot. In generally, it takes 4 years at least to retract the investment. Thus, financing system is quite important to maintain the radiation enterprise.

SCHR experienced two reforms in stockholder. The first happened in 1996 to avoid the bankruptcy, the second happened in 2000 to collect funds for modification of hardware.

Experience told us that bank support is very useful both in the construction phase and afterward operation (for example, purchasing Co-60 source). Of course radiation enterprise must consider the relationship of input-output, scale-benefit.

Employee as shareholder is the future plan in SCHR to encourage the employee to actively participate the operation of enterprise.

Being listed in stock market is another good approach to operate a modern enterprise.

3. Conclusion

In conclusion, radiation enterprise is encountering the chance to develop. We must get rid of the status of "small-but-many", showing us in the world in the gesture of good assurance of quality, high efficiency, faithfulness and safety. KRIA