Quality Assurance for Medical Devices in China

by

Ames Gross
Pacific Bridge Medical

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www.pacificbridgemedical.com

Overview of China

Source: CIA World Fact Book

China's Economy

- Ted Fishman author of China Inc. – "If the twentieth was the American century, then the twenty-first century belongs to China."
- Shanghai – 20,000 construction projects, 1 million construction workers
- Foreign direct investment about 5x more than India
- The place is still growing albeit at a reduced growth rate!

China Demographics

- Population—1.3 billion
- Per capita income—$2,200 in the countryside; $6,000 in major cities
- Life expectancy—73 years
- Investment—about $70 billion per year; five times the amount of investment as India

Health Statistics and Comparisons

	China	US	United Kingdom	Japan
Hospital beds per 1,000 people (2005)	2.4	2.7	3.1	8.2
Physicians per 1,000 people (2005)	1.5	2.4	2.4	2.0[1]
Total health expenditure per capita (2005)	$79	$6,400	$3,064	$2,803
Total health expenditure (% of GDP) (2005)	4.7%	15.3%	8.3%	7.7%

- Fifty percent of city dwellers in China have some basic health insurance.
- Ninety-five percent of people living in the countryside ***do not*** have health insurance.

[1]2004.

Source: WHO, *National Health Statistics Yearbook 2006. OECD Health Data*

China Medical Device Regulatory Authorities

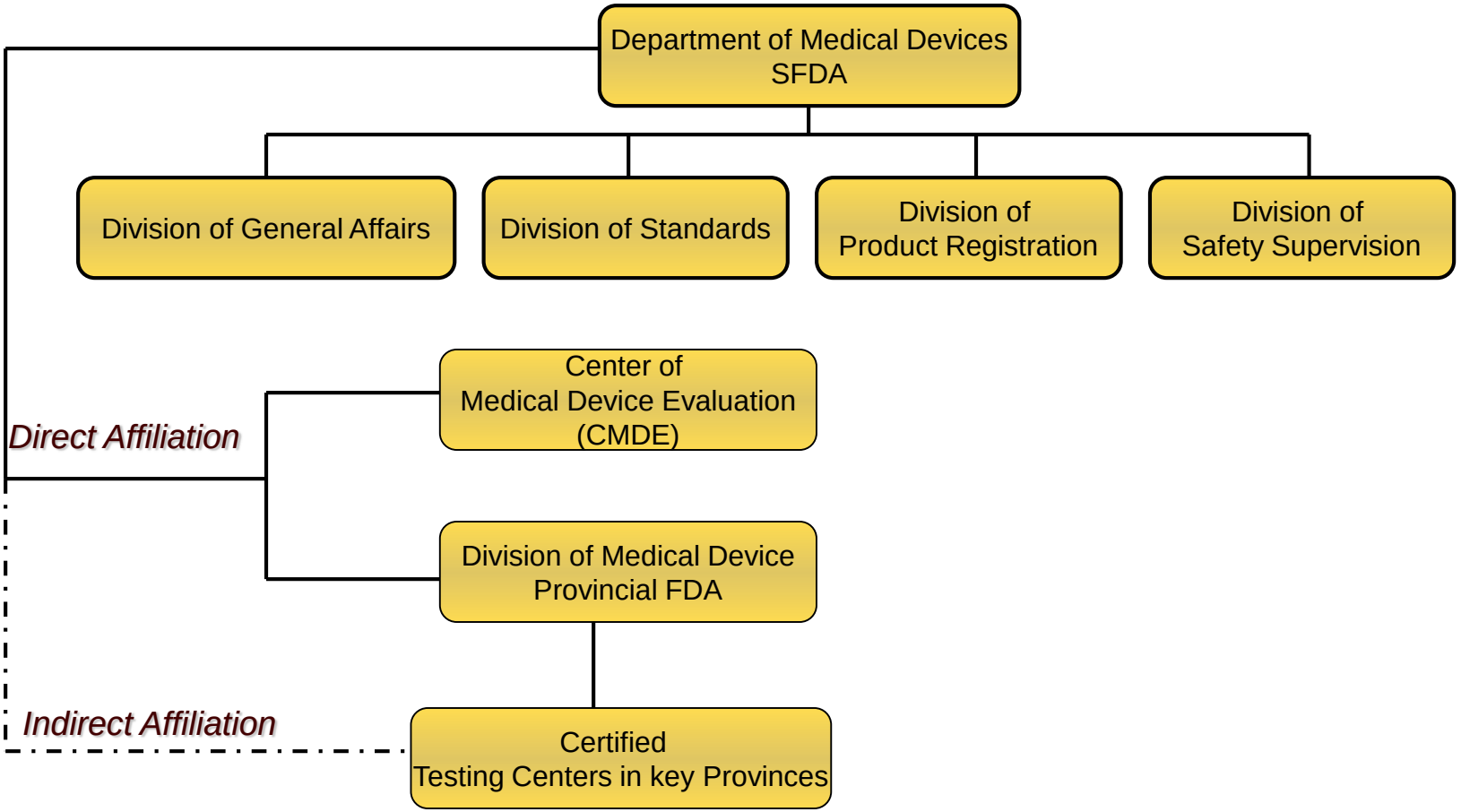
State Food & Drug Administration (SFDA)

- Founded in 1998
- Equivalent to the US FDA
- Responsible for medical devices, drugs, and healthcare services
- Headquarters is located in Beijing, with offices in each province also

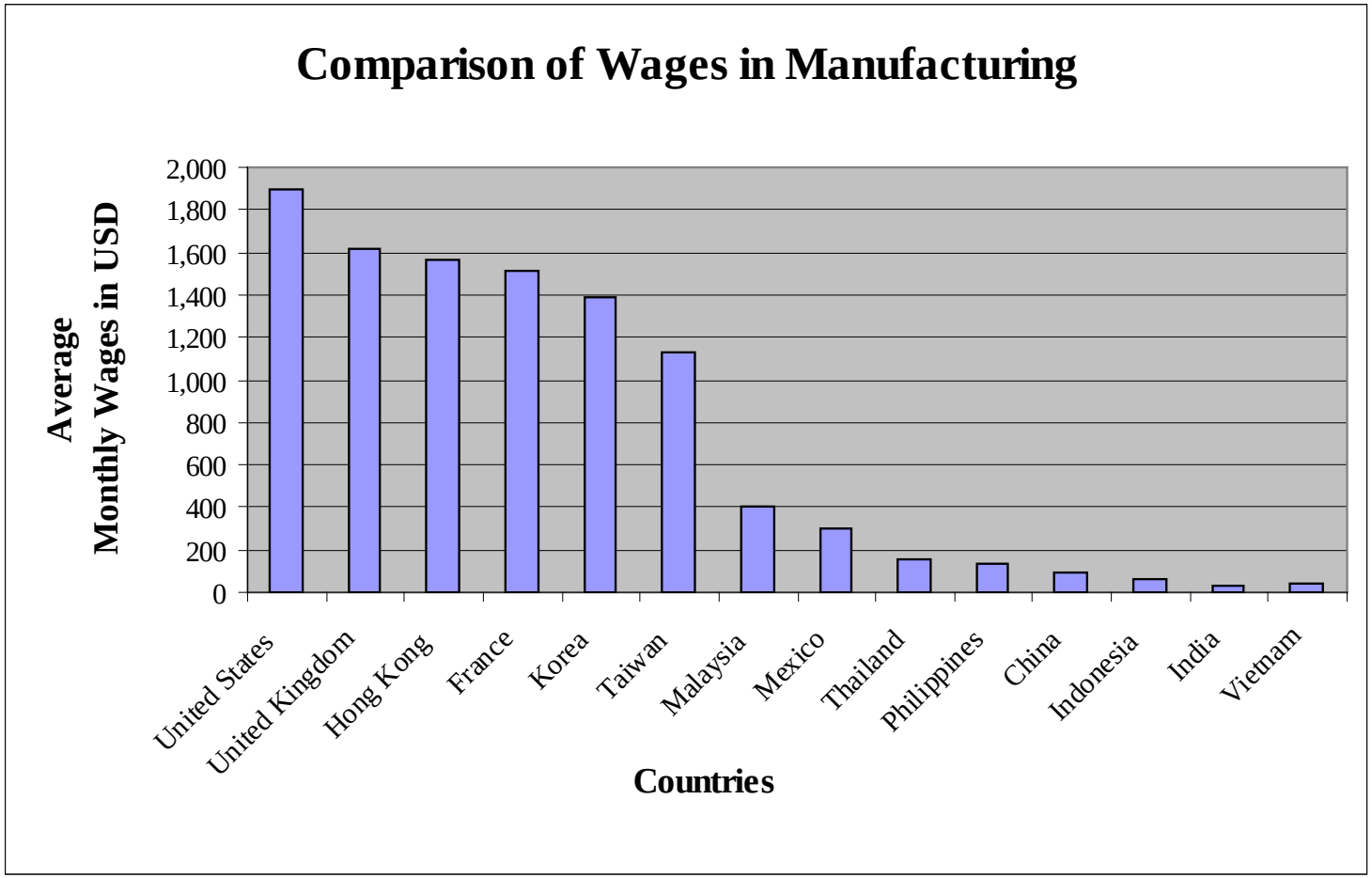
General Administration of Quality Supervision, Inspection and Quarantine (AQSIQ)

- Conducts mandatory safety registration, certification, and inspection for certain devices

Structure of Medical Device Department Under SFDA



Sourcing from China



Sourcing from China

- Chinese manufacturers are becoming increasingly sophisticated.
- Product quality has increased dramatically.
- Prices remain much lower than most other countries.
- Free trade/special economic zones
- Increased awareness of international standards
- Easier market access to growing demand in Asia
- Can customize products to local buyers' needs more easily

QA When Sourcing Devices/Components

- Check production line
- Samples from production line
- Test products in china
- Check packaging and container before shipping
- Test products in the US
- Return/default clauses

Other Key Factors

- Who owns the factory
  - Example, drainage bags
  - Need license
- Who owns the company -- what their % ownership is
- Who owns the mold/designs when things go bad
- Will your manufacturer copy your product over time and be your competitor?

Regulations for Quality Control

- *Provisions for Implementation of the Special Regulations of the State Council on Intensifying Safety Control of Food and Other Products*
- *Requirements on the Compilation and Revision of Medical Device Industrial Standards*
- *Eight Prohibitive Rules for Personnel Involved in Food and Drug Supervision*
- The SFDA's National Sampling and Testing of Medical Device Quality has increased in scope.
- Chinese government is investing the equivalent of over $1 billion dollars to improve the food and drug regulatory infrastructure, especially its underequipped testing centers.

Pictures of Chinese Factories


改正
制令No.
目標生出数
実際生出数
不良率(%)
備 註
第一節
第二節
第三節
第四節
加 班
TOTAL


HAN HUAZHONG LASER INDUSTRY

Quality Assurance/GMP

Quality/GMP in China

- Despite tainted toothpaste, milk, toys, the level of quality in China is improving, especially in the coastal area.
- As one goes more inland, the quality decreases, but the pricing will usually be more competitive.
- A factory may say they are GMP compliant, but WHICH GMP?
- Certain types of machining may not be available.
- Basic quality systems are usually in place, but may not be enough, especially for export purposes.
- Make sure to understand organization structure of facility – who does what? Is design, sterilization, packaging handled by another company?

GMP Development in China

- 2004 – SFDA initiated discussions and plans to set up medical device GMP certification
- 2005 – SFDA drafted GMP for sterile and implant medical devices
- 2006 – Experimental GMP certification was launched with orthopedic implant product manufacturers

Draft GMP Regulations

- SFDA issued GMP requirements for medical devices to solicit public comments in 2008
- These regulations would be for all medical devices
- Most likely, these will be revised and made mandatory in 2010 or 2011

Draft GMP Regulation Details

- When device companies apply to register their product(s) for the first time or for re-registration, they should apply for a China GMP inspection
- Also, SFDA will conduct an on-site GMP audit if device companies:
  - Apply or change their manufacturing license
  - Change their manufacturing site
  - Change their scope of manufacturing

Draft GMP Required Documents

- Documents such as the following will be needed while applying for GMP inspection:
  - Medical Device GMP Inspection Application Form
  - Medical Device Manufacturing License and a copy of the business license
  - Corporate organizational chart
  - Copy of resumes, academic degrees and titles of production supervisor, technology and quality control managers

GMP Inspection Process

- When SFDA approves application materials, they should finish on-site audit within 40 business days
- SFDA will notify company 5 business days prior to audit date
- After on-site audit, GMP inspectors will compile report with any issues or problems noted
- Inspection conclusion will be made within 20 business days after SFDA reviews the audit report
  - Conclusion falls in either Approved, Conditional Approval, or Failed

SFDA Inspection Focus

- Review corrections of failed projects from past inspection
- Any changes of corporate leaders, supervisors, and staff of key responsibilities
- Any changes and maintenance of major manufacturing facilities, inspection equipment, or manufacturing environment
- Finished product inspection, OEM product inspection
- Status of products that failed the sampling inspection (corrective action)
- OEM information (if you're the actual OEM or the final manufacturer)
- Adverse effect reporting and handling
- Other GMP regulated content

Plans For Quality Control

- *Interim Requirements for Further Intensifying and Standardizing the Registration of Medical Devices*
- New industry standards for medical devices
- Strengthening risk management for medical devices
  - *Provisions on the Adverse Events Monitoring and Re-evaluation of Medical Devices (Draft)*
  - *Provisions on Medical Device Recalls (Draft)*
  - *YY/T0316 Application of Risk Management to Medical Devices; equivalent to ISO 14971 (2007 version)*

Adverse Event Reporting

- Adverse event reporting and monitoring has only become regulated in recent years
  - It was not always routine for hospitals or manufacturers to report adverse events to monitoring authorities, and adverse event reporting does not always happen when it should
  - However, an official network of adverse event monitoring institutions does exist and the reports that the network receives have increased dramatically in the recent years

AE Reporting -- New Regulations

- The SFDA released new regulations *Provisions on Medical Device Adverse Event Monitoring and Re-evaluation* on December 30, 2008 to significantly increase manufacturers' reporting requirements
- Medical device manufacturer must report adverse events in the following timeframe:
  - Adverse event involving death: within 5 working days of learning about it
  - Adverse event involving severe injury: within 15 working days
  - Other adverse event: no mandated timeframe

AE Reporting – New Regulations (cont'd)

- Additionally, Class II and III medical device manufacturers must file an "Annual Report on Medical Device Adverse Events" with their local adverse event monitoring institution by the end of January each year
- The new regulations also impose penalties for failing to properly report or respond to medical device adverse events

Case Study

Background on Project – Acquisition

- US medical device company planning to acquire Chinese factory
- Company wanted to conduct appropriate audits to make sure China factory complied with standards and had a quality system in place
- PBM checked for compliance to – (1) Chinese standards and (2) international standards (two different auditing teams)
- Details on China Factory:
  - Manufacturing site in Shanghai
  - Distribute products to USA, EU and China
  - Make Class 1 and Class II devices
  - Design and Development outsourced to related company

Due Diligence/Acquisition

- Determine who owns company you are considering working with.
- Determine if Chinese company really understands Western business values.
- Find a company that's not just looking to make a quick buck.
- Make sure legal documents done according to Chinese law NOT US law.

Due Diligence

- Have local consultant / regulatory person do due diligence and quality assurance.
- Do a factory visit to make sure the company is trustworthy and makes quality products.
- Face-to-face meetings are key in building trust and relationships.
- Clear, concise contracts -- try to avoid legalese.
- Staged payments.

Quality Systems in Place at China Facility

- Have STED Technical Files for most EU products
- Have Declarations of Conformity for most EU products
- Have 510(k)s for USA Class II products
- Have SFDA product registration certificates and SFDA Medical Device Manufacturing License
- ISO 9001 qualified
- ISO 13485 qualified

Quality – China Audit Team

- Good:
  - Quality Management System Inspection Report granted by SFDA stating that facility complied with Chinese GMP
  - Products were registered correctly with appropriate testing to comply with Chinese national standards
  - Has a valid Medical Device Manufacturing License approved by provincial SFDA
  - No record of failed quality inspection report in SFDA National Quality Announcement Database for past 8 years
  - Internal audits conducted every 6 months with appropriate CAPA
  - Management Evaluation conducted every 6 months with appropriate CAPA
  - Production records and QC records are maintained and traceable based on SOPs
- Bad:
  - Facility seems too small as all production, QC testing and final release are done in the same room.

Quality – International Audit Team

- Good:
  - Quality Manual and EU Technical Files with about 20 SOPs (in English) – balance of documents in Mandarin
  - Lots of quality sampling, testing, and traceability and product quality delivered by intensive (and often 100%) inspection
  - Vendor defects are inspected out
- Bad:
  - More than 20 - 50% of the components are defective on a regularly basis but all are 100% sorted and rejected
  - Vendors/suppliers are unreliable and indifferent to quality standards
  - Difficult to return faulty items
  - Process validation is not conducted
  - No computerized systems to co-ordinate and analyze multi-country events

Overall Points for Case Study

- Facility was very good in complying with Chinese SFDA standards
- There are some points with Design Control and post-marketing surveillance with adverse events that are not up to international standards

Other Quality Issues Seen at Chinese Facilities

- Sterilization issues
- Manufacturing facility is not closed off enough
- Disorganization, good products not properly separated from defective products
- Modernized parts too quickly
- Little to no understanding of international standards
- Lack of communication between QA and Production or Sales Department
- Lack of records and lack of product numbers, leading to issues of traceability
- No follow up with post-marketing surveillance

Upgrading your China Facility

- Provide adequate training programs for all employees
- Centralize documents and create a document control system
- Do appropriate facility construction changes as needed
- Label everything, create a system to track all components, products
- Have everything written down, from procedures to processes to SOPs and make sure employees have access to this information
- Employ someone who coordinates between facility and HQ and is fluent in technical Chinese and English – make sure s/he is locally based to see what is going on every day

Quality Control in China

- Quality inspections are routinely performed during product registration and factory registration.
- IEC 60601 standards exist for medical electrical equipment.
- For some advanced products, non-SFDA regulatory bodies enforce more demanding China Compulsory Certification (CCC).

Coordinating with your HQ and China Office

- Make sure to centralize all files
- Organize all product registration information, certificates, expiration dates in one comprehensive database
- Keep track of any changes to the product, such as manufacturing address changes, product names changes, what's been discontinued, etc.
- SFDA drafted proposed regulations in regards to product registration renewals and changed official device standards – make sure your China office is up-to-date on all regulations and has prepared accordingly!

Regulatory Personnel in China Office

- Where do you put your regulatory or quality people in your Asian operations?
- How many regulatory or QA people do you put in your China office?
- Company conferences/outings to foster trust between US and China regulatory people.
- Have Asian regulatory people work in US for 6 months to a year; and US people live/work in China.
- Cross-cultural training for both sides.
- Many regulatory issues are really people issues and lack of trust.
- Can hire people who have trained at large device companies or train local Chinese people

Other Updates on Regulations

- Revision of *Provisions on Medical Device Registration* (2009)
  - Compared to the current *Provisions*, the revised *Provisions* emphasize legal responsibilities and intensify the punishments on illegal activities
  - Applicants of medical device registration should conduct research on devices with relevant risk analysis, verifying the devices' safety, effectiveness and control of quality
- Import Testing (Type Testing) Revisions (2008)
  - The SFDA reviews and approves medical devices for the China market while the General Administration of Quality Supervision, Inspection, and Quarantine (AQSIQ) inspects and certifies devices to be physically imported into China
  - AQSIQ administers the China Compulsory Certificate (CCC) for certain medical devices like X-ray equipment, pacemakers and previously AQSIQ conducted tests while the SFDA also conducted sample testing
  - Now CCC marking and SFDA medical device registration will share a single testing process

Other Updates on Regulations (cont'd)

- *Methods for Review of Medical Device Advertisement* (2009)
  - Any type of advertisement whether it be print or electronic whose content contains device name, application scope, performance, structural composition as well as mechanism, should be reviewed and approved in accordance to the new regulation
  - Only medical device manufacturers or distributors are allowed to apply for publishing medical device advertisement

Other Opportunities in China

- Clinical studies
- R&D

Clinical Trials in China

- All clinical trials (if necessary) for medical devices must follow China Good Clinical Practices (GCP).
- Regulation on Medical Device Clinical Trial Requirements became effective April 2004.
- Can only draw on previous clinical trial experiences of similar products.

GCP (Good Clinical Practice)

- The SFDA plans to revise the current Provisions on Clinical Trials for Medical Devices (2004).
- The revised Chinese GCP will be in accordance with international GCP standards.
  - Strengthening management of technical aspects of clinical trials.
  - Establishing quick and effective mechanism to coordinate trails with medical device registration.

Picking the Right CRO

- Local CROs may have more time and focus to dedicate towards your trial.
- China Clinical Trials Centre Ltd.
  - www.chinahealthcareltd.com/principal/clinical.htm
  - Located in Beijing, wholly owned subsidiary of a Hong Kong-based company.
- Accelovance, Inc.
  - www.accelovance.com
  - Beijing location; began conducting clinical trials in 2006.
- Tigermed
  - www.tigermed.net
  - Established in 2002, has completed 110 clinical trials.

R&D Trends

- Major multinational companies conducting R&D in China.
- Also allows for establishment of relationship with Chinese physicians and government officials, helpful in registration and product launch.

R&D Advantages and Disadvantages

- Lower salaries in China compared to counterparts in US, Europe.
  - However, these researchers may require additional training.
- Lower costs to build R&D centers in China.
- Spread out research so no one knows how the pieces fit together.

IPR Protection

- Protecting one's IPR is one of the most difficult challenges of doing business in China.
- China's legal system guarantees adequate protection of IPR, but enforcement is lacking.

Your China Office

Setting Up in China
Options For Foreign Companies

- Representative office
- Branch office
- Joint Venture
- Wholly Foreign Owned Enterprise (WFOE)

Representative/Liaison Office

- Simplest form of business structure
  - Usually one person with assistant
  - Established in preparation for future expansion into branch or subsidiary
- Functions:
  - Advertising
  - Market research

Branch Office

- Requires some form of registration process.
- Usually must appoint an official representative responsible for local operations.
- Branch offices can earn income and remit to parent company.

Joint Venture Structures in China

- Chinese-foreign equity joint venture (EJV)
- Chinese-foreign cooperative joint venture (CJV)
- Previously, joint ventures were 50/50 (foreign/Chinese) but now 80/20 or 90/10.

Joint Venture in China (cont'd)

- Chinese-foreign equity joint venture EJV
  - Limited liability company with Chinese legal person status.
  - Parties invest together, manage together and share risks, losses and benefits in proportion to their contribution to registered capital.
- Chinese-foreign cooperative joint venture CJV
  - Parties determine manner of operation and management, obligations, risk and profit sharing, etc through contract at beginning of venture.

Wholly Foreign Owned Enterprise (WFOE)

- Wholly foreign owned enterprises -- permitted to register where at least half of annual output is exported or if operations relies heavily on advanced technology and the application of technology is beneficial to China.
- A wholly foreign owned enterprise is considered a Chinese legal entity and must abide by Chinese laws.
- More management control and more autonomy with operation.

Some Important Cultural Issues

Western vs. Asian Approaches

Western Approach	Asian Approach
Do a deal	Build relationships
Maximize short-term profits	Establish long-term foundations
Be frank	Don’t deliver bad news
Make changes quickly	Move when ready

Intercultural Communication

- Personal Connections (*Guanxi*)
  - Earning respect and trust should be considered first step to business interaction.
  - Find a mutual friend to serve as intermediary to introduce you to potential business associates.
- If you have a strong relationship with your Chinese partner, everything is possible.

The Chinese Mentality

- Gaining “face” – Helping someone avoid an embarrassing situation can help him/her save face; this person will not forget the favor.
- Praising or thanking someone for a good job in front of peers or superiors will help the person gain respect, but overly effusive praise can appear insincere.
- Chinese in China are different than Chinese in Taiwan, Hong Kong, or Malaysia. Know the differences!

Thank you for your consideration!

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www.pacificbridgemedical.com

contact@pacificbridgemedical.com

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