



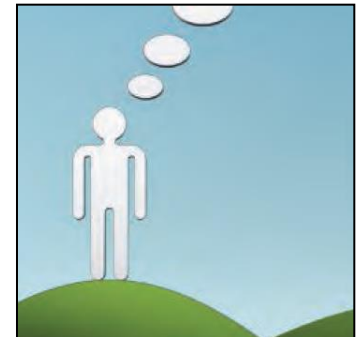
# 未来 智能化的 制药工厂 (制药 4.0)

## Smart Pharma-MFG Factory with Pharma 4.0



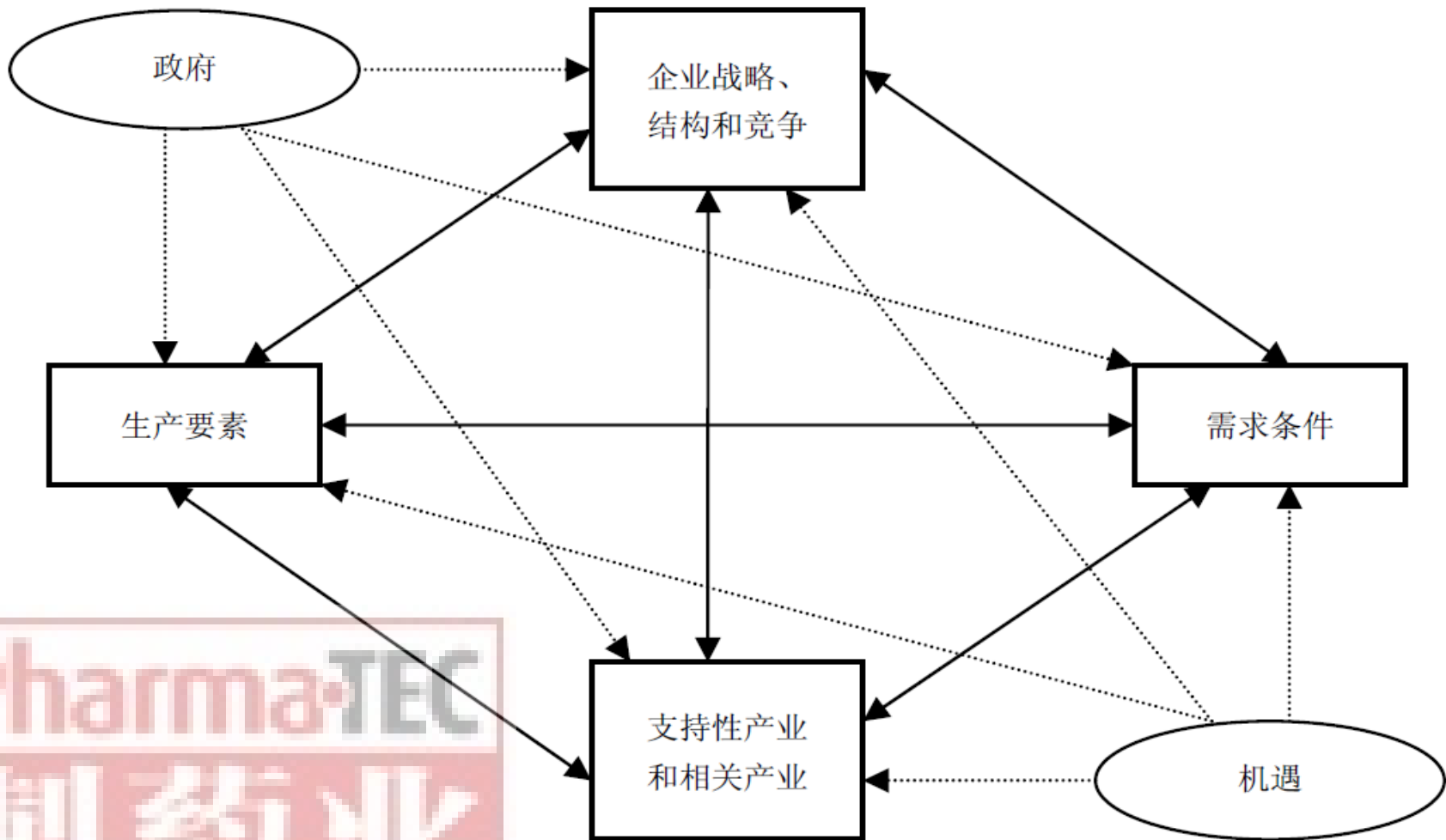
李树德 Michael Lee

Dec. 9, 2016



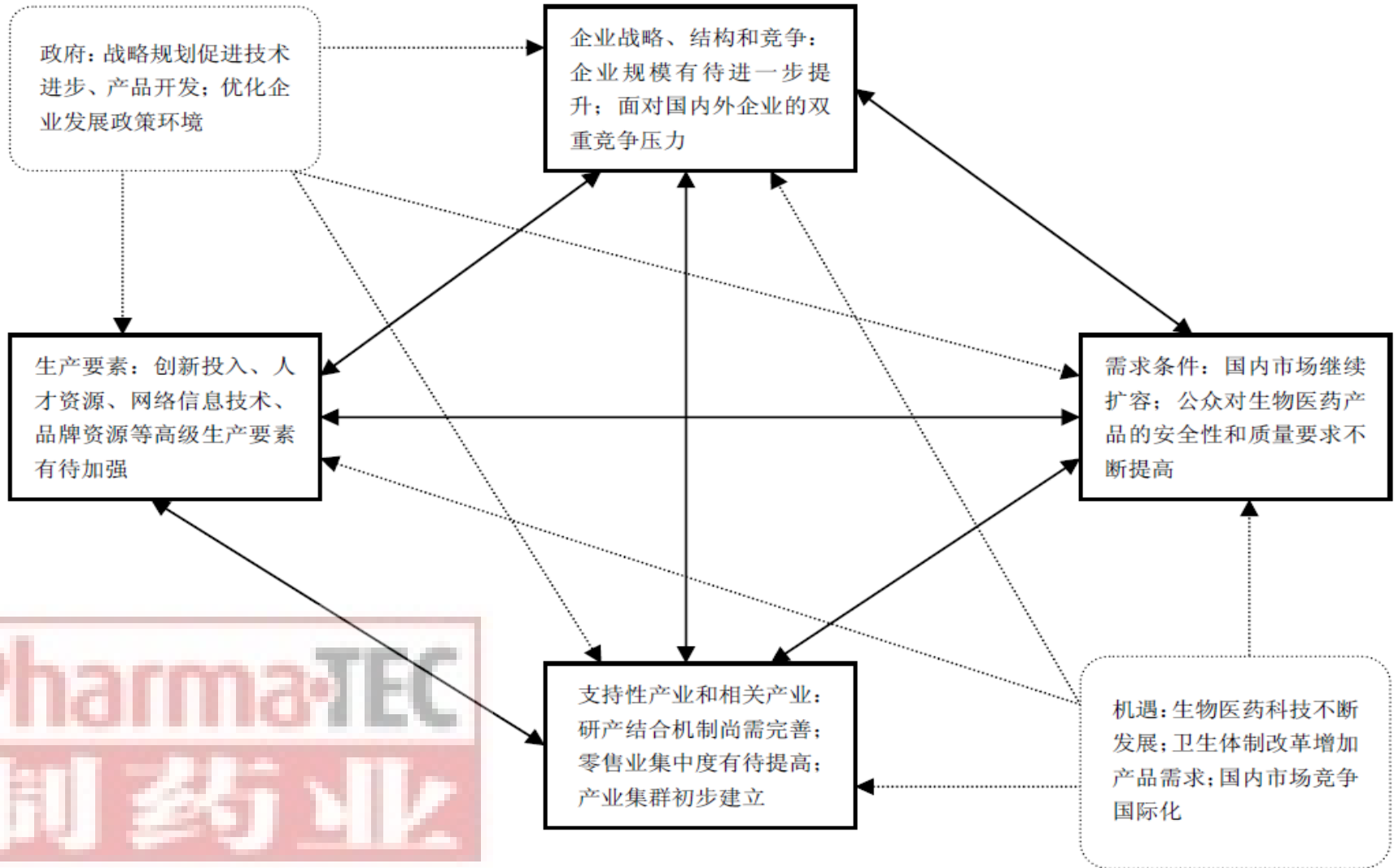
# 竞争优势理论

(波特的钻石模型)



PharmaTEC  
制药业

# 基于 竞争优势 理论的 我国生物制药产业 竞争力 分析图



# 合规的要求 Compliance

Medwatch Plus  
Risk Management  
FMEA ISO 14791 21 CFR 11  
Good Manufacturing Practice  
FDA Submissions Blood Services  
Regulatory Compliance Software  
Complaint Handling Risk Assessment  
Medical Device 21 CFR Part 1271 Compliance  
Failure Mode Effects Analysis ISO 14791  
Life Sciences Blood Services  
21 CFR 11 eValidation  
Quality Assurance Software  
ISO 13485 Good Manufacturing Practices  
Pharmaceuticals 21 CFR Part 1271  
Risk Management FDA Submissions  
Medical Device Regulatory Compliance  
Complaint Handling eValidation

eMDR  
Risk  
FMEA  
GxP  
cGMP  
FDA  
cGxP  
CFR 11  
eMDR  
GMP

Quality  
GMP  
Pharmaceuticals  
Life Sciences  
FMEA  
Pharmaceuticals  
Biotechnology  
eValidation  
CFR  
FDA  
GMP  
Risk  
FMEA  
eVal  
GxP  
ISO

Good Manufacturing Practices  
MedWatch Plus 21 CFR Part 1271  
Risk Assessment Quality Assurance  
Change Management  
Regulatory Compliance FDA Submissions  
Medical Device Reports  
21 CFR Part 11<sup>cGMP</sup>  
Failure Mode Effects Analysis  
Complaint Handling  
Medical Device FMEA  
FDA Regulations  
Biotechnology  
Electronic Submissions  
FDA  
CFR 11  
Biotechnology Life Sciences  
21 CFR Part 1270 cGMP FDA Submissions  
Medical Device FMEA MedWatch Plus

CFR  
FDA  
GMP  
Risk  
FMEA  
eVal  
GxP  
ISO

GMP  
21 CFR  
11  
ISO  
13485  
eMDR  
FDA  
CFR 11  
21 CFR  
1270  
cGMP  
FDA  
Submissions  
FMEA  
MedWatch  
Plus

合规是竞争力，别打擦边球！



**新产品的开发**  
**New Product**  
**Development**

PharmoTEC  
是竞争力

未来的发展，靠现在的规划

THE FUTURE IS NOW  SEPARATED FROM THE PAST.



Pharma-TEC

制药业

竞争力

# 竞争力

Expertise, Resources and Technology  
Brought Together for Your Success

MULTIPLE  
SOLUTIONS

未来发展的 规划 与 解决方案  
专业、资源 与 技术

# 医药产业的发展趋势

## 商业机会



Population  
to increase by



Additional  
50+ year olds



Chronic  
diseases

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~1 billion

>500 million

>70% of all illnesses

2015 - 2025

医药产业



# 医保费用的加倍投入



Healthcare spending to double<sup>1</sup>

2x

商业机会

Pharma·TEC

制 药 业

2015 - 2025

# 更多新产品的 开发成功



More breakthrough  
drugs and devices

商业机会

Pharmaceutical  
制药业

# 更多新产品的 开发成功

OPTIMIZED API  
PERFORMANCE

DRUG  
DELIVERY  
ROUTE

Improve the  
bioavailability

ENHANCED  
DRUG DELIVERY  
SOLUTIONS



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## Trends in drug portfolios

## 新产品的多样性



Therapeutic competition



Orphan drugs



Personalized medicine



Complex medicines

Pharmotec

制药业





PharmTEC  
制药企业

人类如何看见 未来的进步？



**制药业如何看见 它未来的进步？**

# WAVE OF INNOVATION

后浪 推 前浪  
人类的进步 靠创新



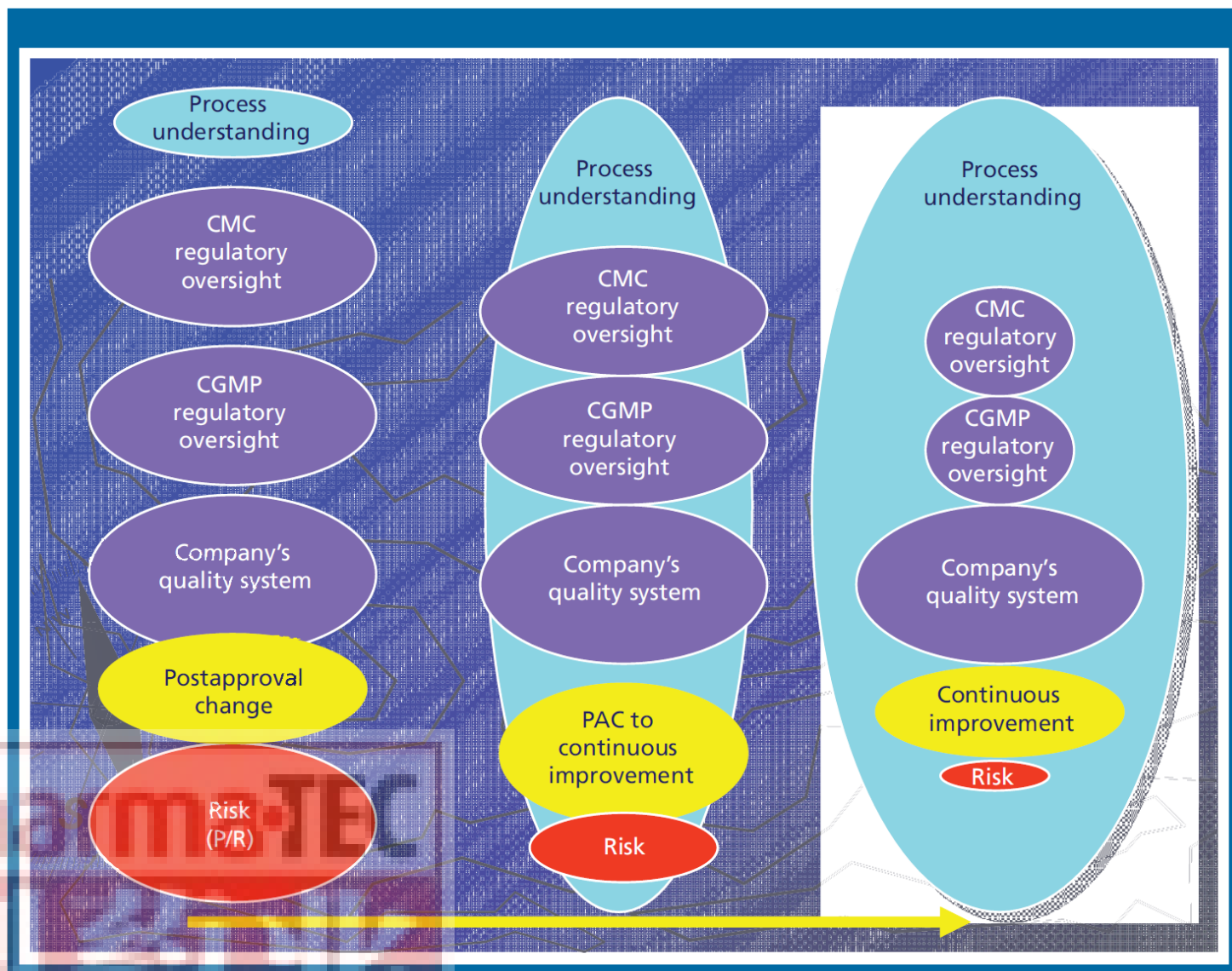
Future Incorporated

## WHAT'S NEXT?

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制药行业

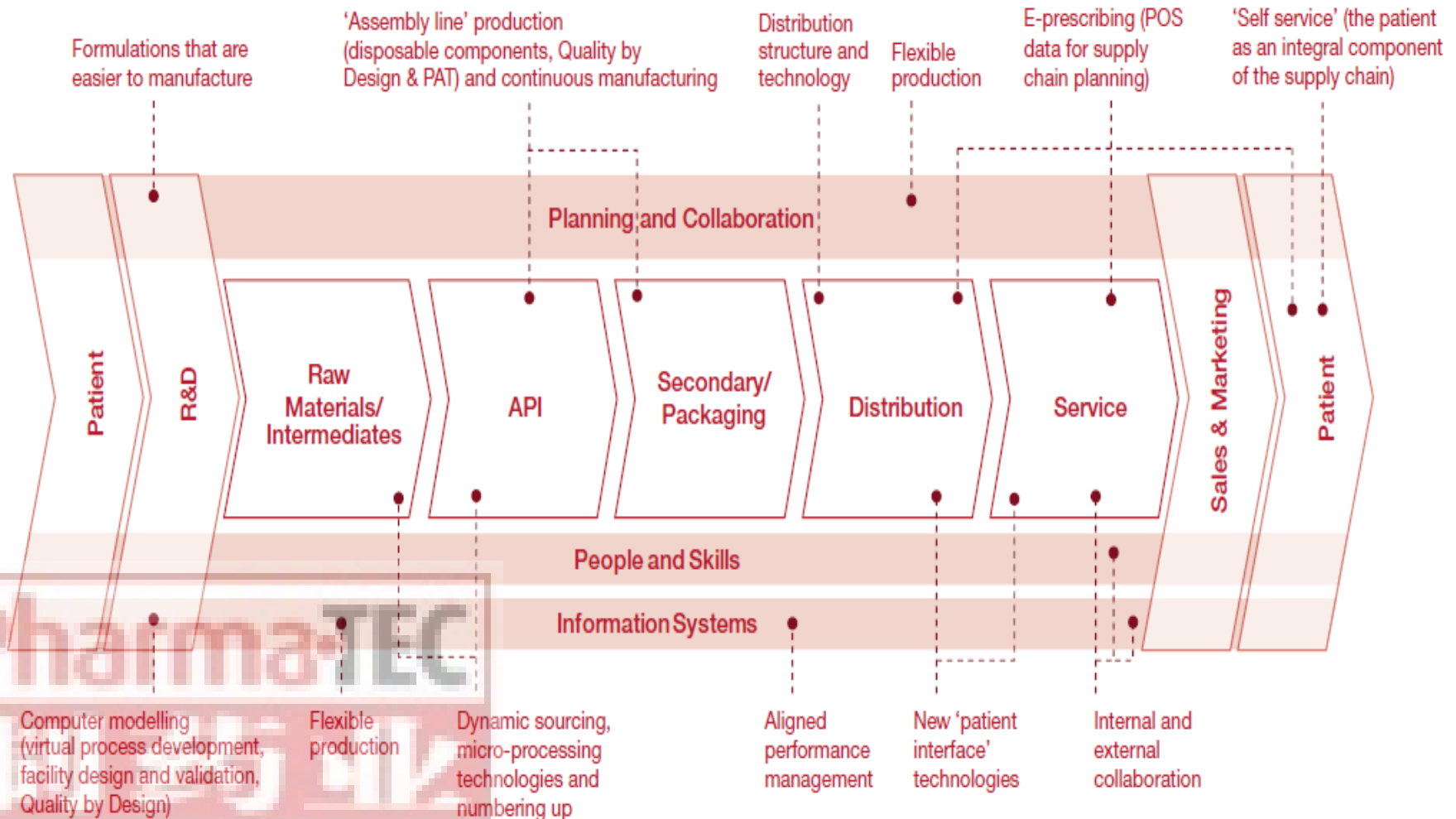
# 工艺开发与 风险管理





# 供应链管理的创新

## 竞争力



# 生产工艺 与 技术 的创新-1

## 竞争力

Primary (bulk drug substance) manufacturing

Secondary (drug product) manufacturing



Small molecule

Continuous manufacturing<sup>1</sup>

Process analytical technology

Green chemistry

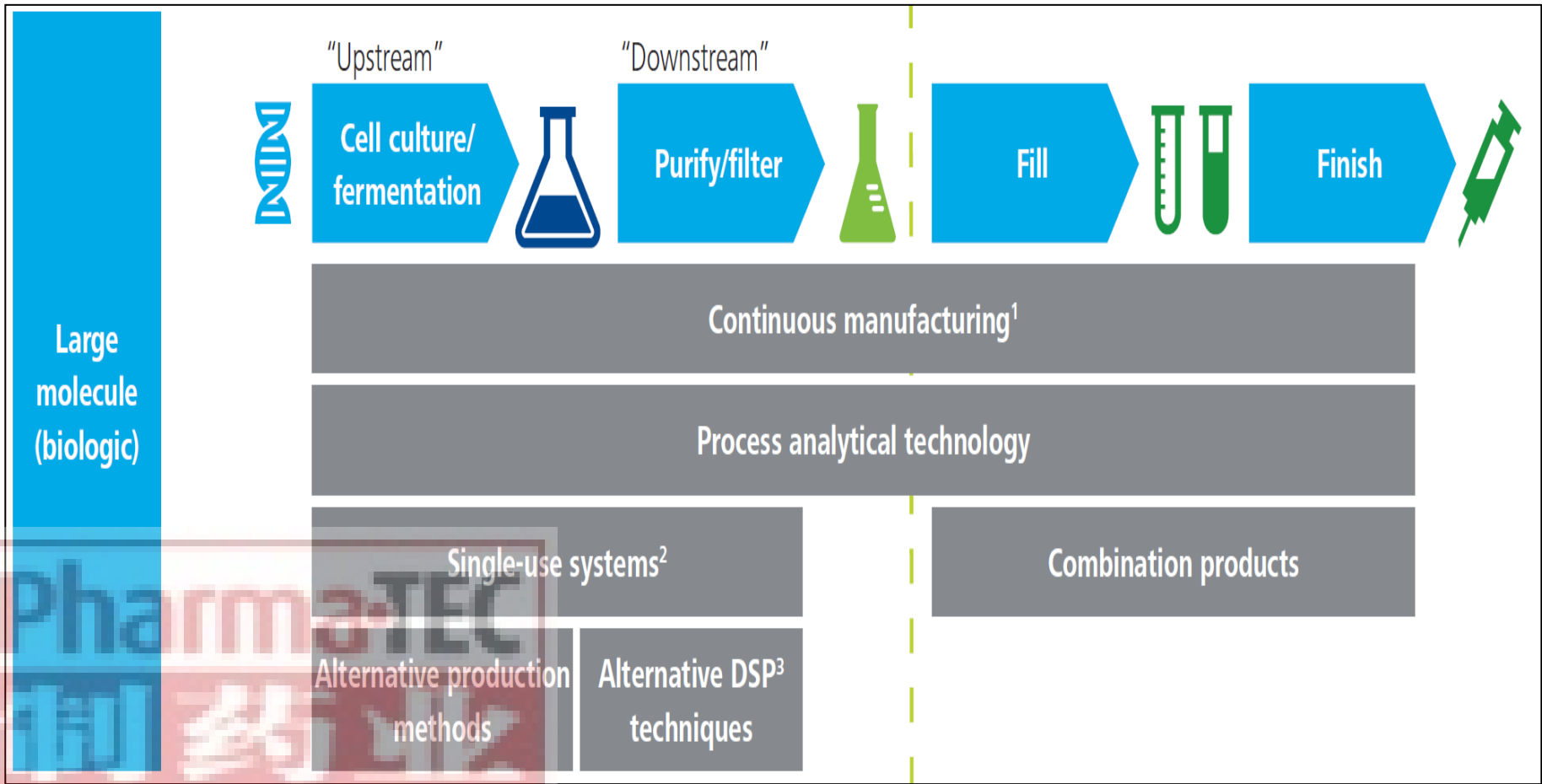
Products with improved drug delivery systems

PharmaTEC

PharmaTEC

# 生产工艺 与 技术 的创新-2

## 竞争力



# 竞争力



PharmaTEC

制药技术

**FoF**

**竞争力**

# Facilities of the Future

**制药企业的未来新厂**

**When change  
is the only  
constant,  
are your facilities  
up to speed?**

**竞争力**

**行业变化多，未来新厂  
如何及时应对未来的挑战？**

Pharmaceutical  
制药业

# 产品、自动化、 工艺、验证、合规

Product  
Solutions

Automation  
Solutions

Process  
Systems

Compliance  
& Validation

## 竞争力

**Impact of FoF**  
未来工厂的影响

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制药业

## PROCESS TECHNOLOGY

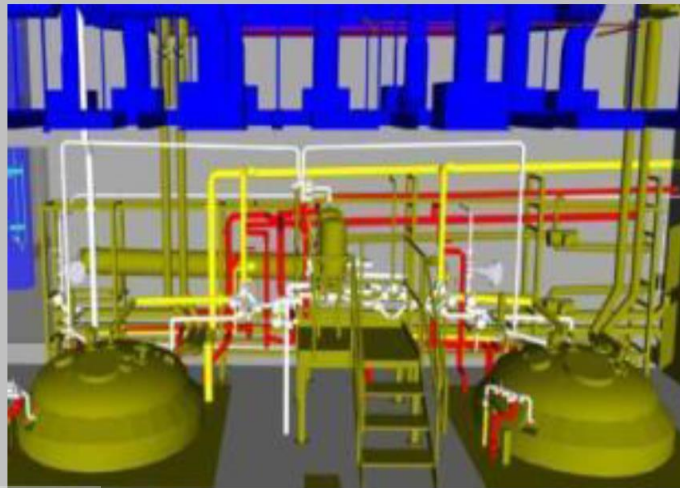
Process equipment, process infrastructure (clean utilities, CIP-/SIP-systems, chemical supply), piping technology, emission control, waste water treatment, waste handling

## CIVIL, ARCHITECTURE

Structural works (concrete, steel), civil construction, finishes, cladding, site development

## LOGISTICS

Warehouse- and storage-management and -control, transportation systems



## BUILDING SERVICE SYSTEMS

Cleanroom technology, ventilation, utilities, fire protection installation, building automation, electrical and communication systems

## PROCESS CONTROL ENGINEERING

Instrumentation, process automation, manufacturing execution system (MES), vertical integration

## LAB FACILITIES

Equipment and furniture

Pharmatec  
竞争力

未来新厂的挑战



**Higher titers, smaller batches, higher potency products, complex delivery forms all challenge the traditional paradims in the way we design and operate manufacturing facilities.**

**未来新厂的挑战：  
设计、建设与营运的新思路；  
产品多、交货快、  
质量好、成本省。**

# 未来新厂：软硬件的匹配。

## 产品多、交货快、 质量好、成本省。

### Air Handling

- Make-up air handling
- Filtration
- Clean air
- Decontamination
- Air showering
- Special solutions

### Environments

- Ceilings, floors, walls, accessories
- Isolators
- Compounding solutions
- Weighing solutions
- Biosafety (BSL) containment solutions
- Modular construction
- Mobile solutions

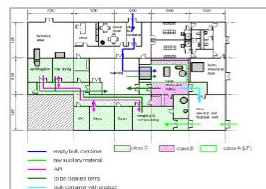
### Solutions

- Design & engineering
- Production
- Installation & service
- Validation
- Monitoring
- Maintenance

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制 药 业

Sampling Area →  
(Goods receiving)



- Design and construction of entire process manufacturing steps to total production lines.
- GMP-Layouting

Weighing Area →



Compounding Area →



Filling Area →



Packaging Area →



Storage / High Bay Warehouse →

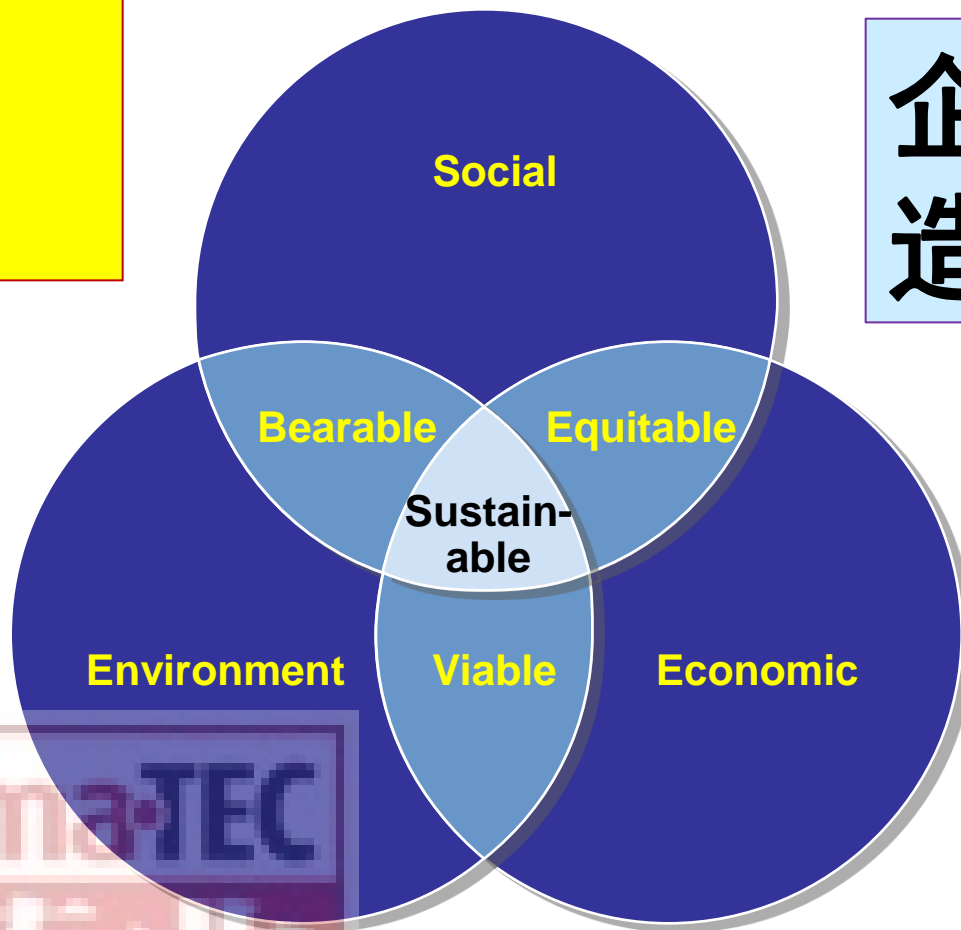


未来新厂的考虑与选择

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制药工业

# 可持续发展

- 经济
- 环境
- 社会

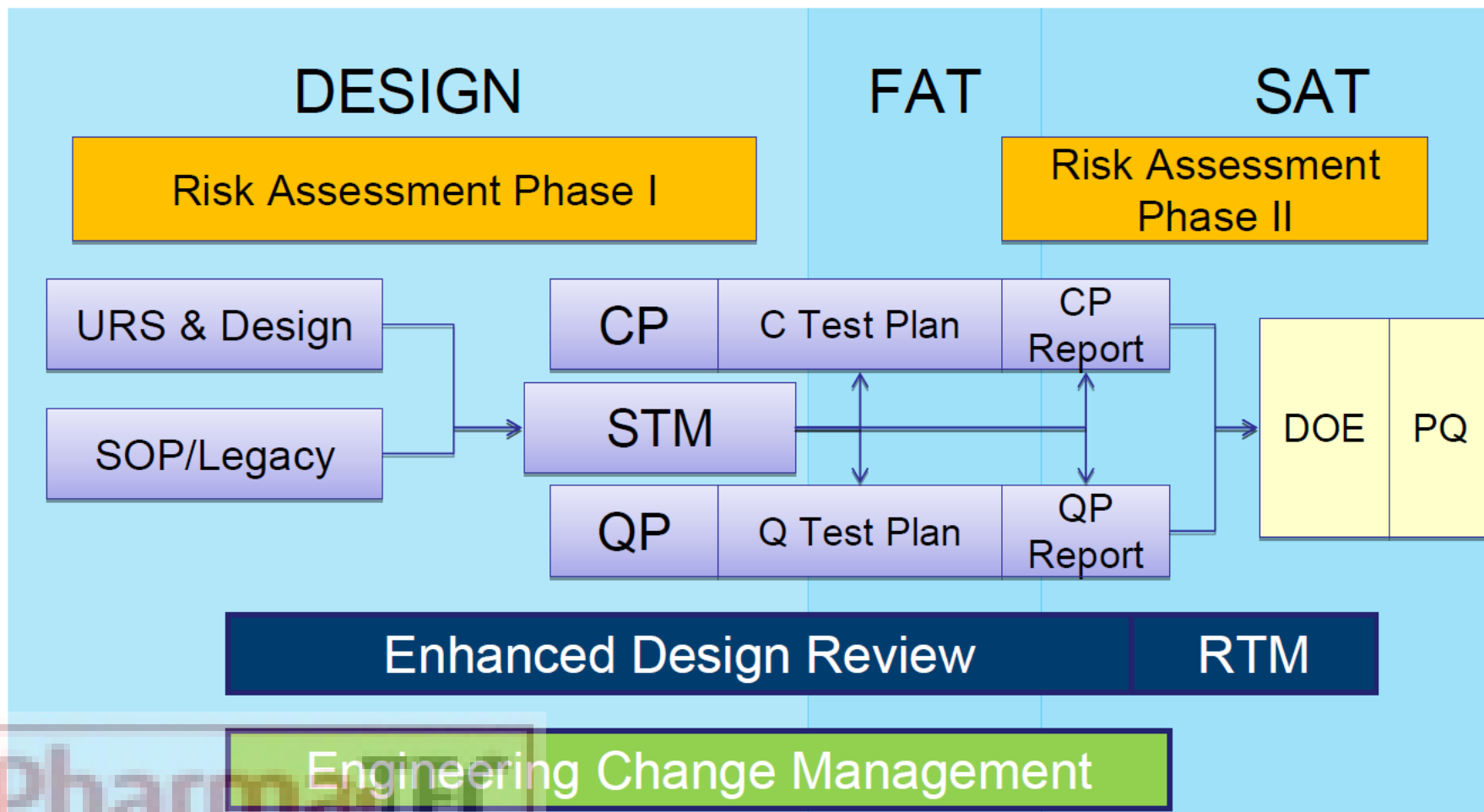


企业良心，  
造福子孙。



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制药业

# Process Flow Supporting C&Q



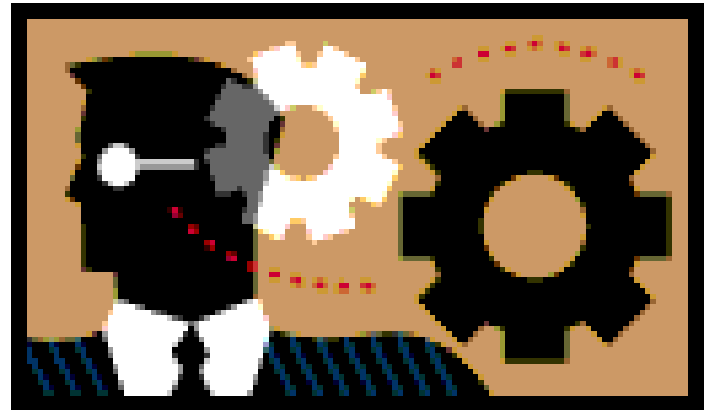
Pharmaceut

制 药 业

支持验证的 设计与测试

# 制药业 的发展 路在何方？

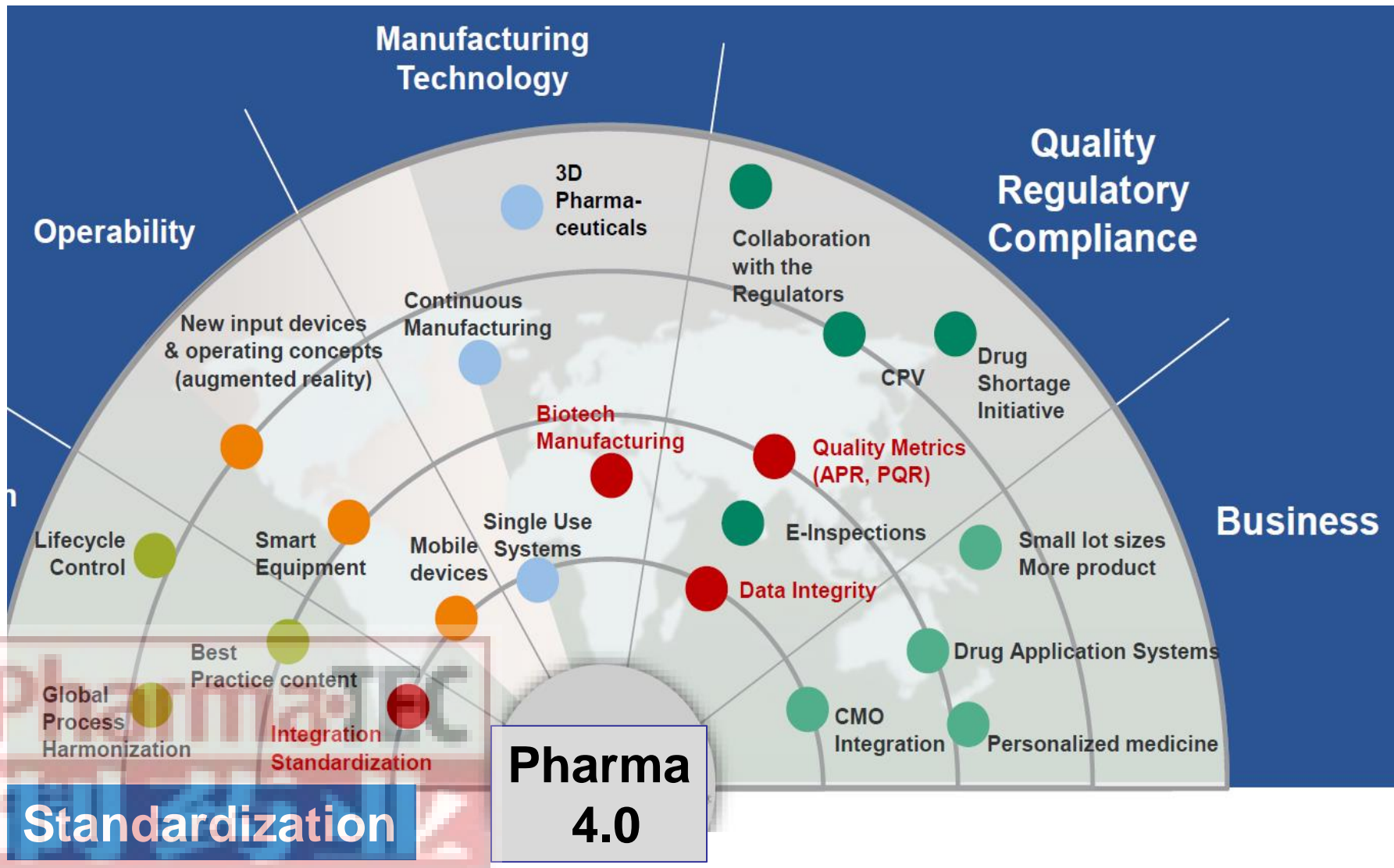
Pharma·TEC  
制 药 业



**More companies expect that their production processes will be largely or completely automated/computerized in the years to come.**

- **自动化的程度 持续提升**
- **（德国 → 欧洲）工业4.0**
- **中国制造2025**
- **智能化 制造**
- **制药业 向 制药4.0 迈进**

# 智能化药厂 Pharma 4.0





# 智能化药厂 Pharma 4.0

人、机、料、法、环  
各个介面的信息  
及时化、可视化

Pharmatec  
制药业

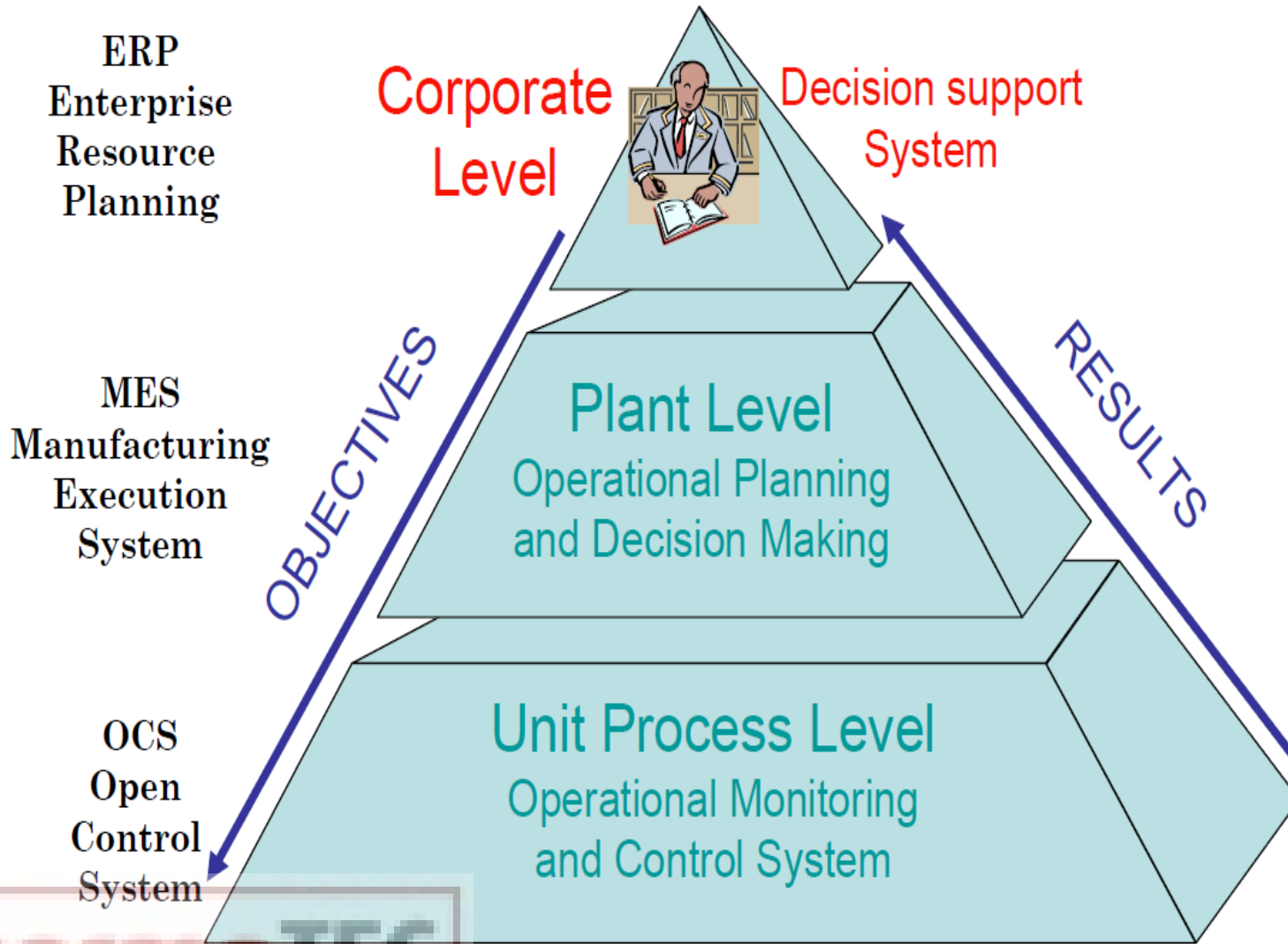
**More manufacturers will invest  
over 25% of their  
New plant total budget for plant-floor  
IT/Operation systems.**

**Process Automation\***

- Instrumentation
- PLC systems
- SCADA systems
- PCS/DCS systems
- MES/ERP systems (SAP)
- LIMS systems

**未来工厂的投资，  
用于 资讯系统 及 作业系统  
的软件投入  
将高达 25% 或 更多。**

**PharmaTEC**  
**制药业**



PharmaTEC  
制 药 业

公司的 作业体系

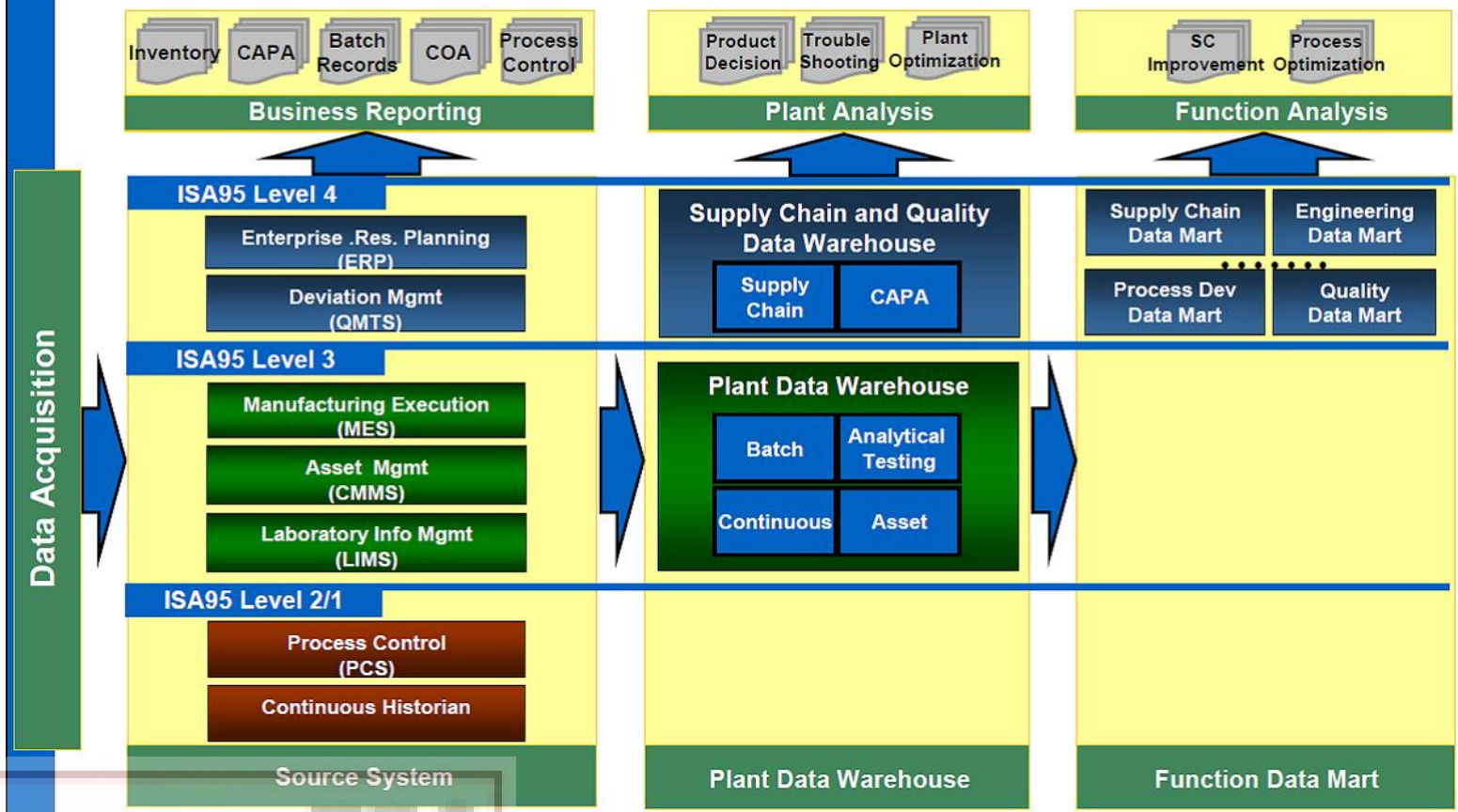
**More and more companies will give up to  
make-to-stock (MTS)  
and will be heading toward  
make-to-order (MTO).**

**未来工厂 的生产计划  
从 MTS 安全库存 导向  
转为 MTO 订单生产 导向。**

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制 药 业

# Plant Data Warehouse Is the “Single Version of Truth” of Plant Data Integration

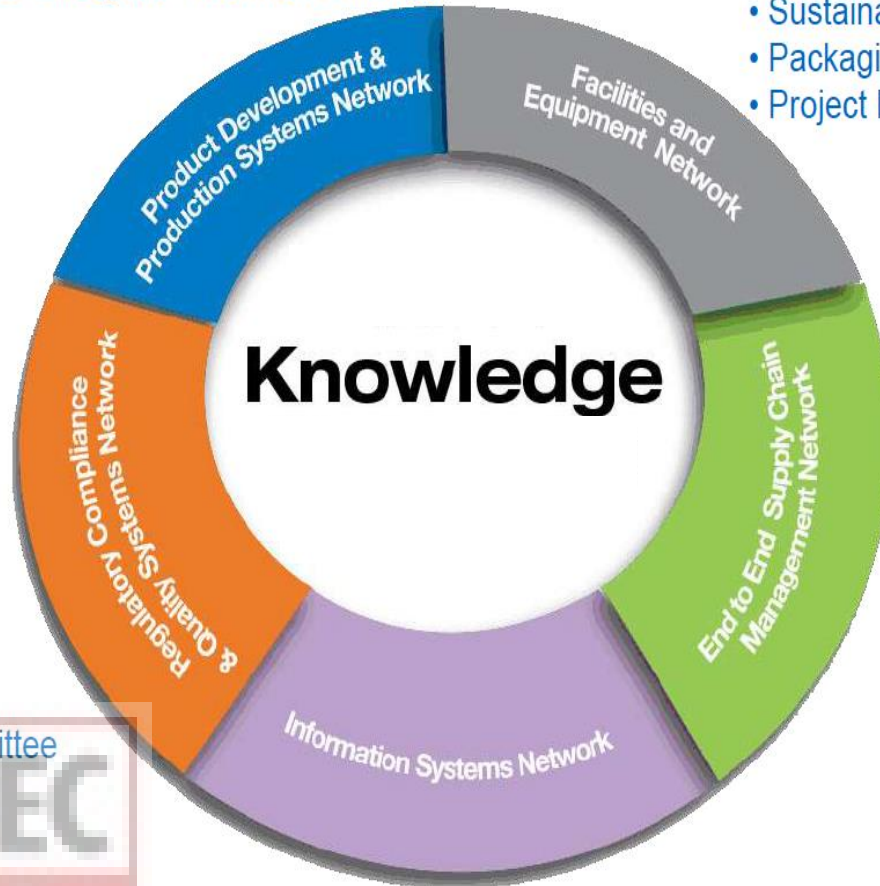


工厂的单一数据库

数据完整性

- Active Pharmaceutical Ingredients
- Biotechnology
- Disposables
- Oral Solid Dosage
- **Process Analytical Technology & Lifecycle Control Strategy**
- Product & Process Development
- Sterile Products Processing

- Commissioning & Qualification
- Containment
- Critical Utilities
- Sustainable Facilities/HVAC
- Packaging
- Project Management



- Investigational Products
- Operations Management

- Process Validation Teams
- PQLI
- Regulatory & Compliance Committee

**知识 对  
制药企业  
未来新厂  
的影响**

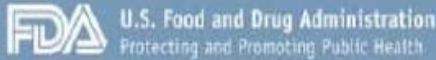
GAMP®



# FDA & ICH Roadmap

## QbD / Risk & Science based Approach of the FDA & EMA

- ❑ ICH Q 8 (R2) Pharmaceutical Development
- ❑ ICH Q9 Quality Risk Management
- ❑ ICH Q10 Pharmaceutical Quality System
- ❑ ICH Q 11 Development and Manufacture of Drug Substances (planned end 2016)
- ❑ ICH Q 12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management (planned for June 2018)



## FDA Quality Related Guidance and Initiatives

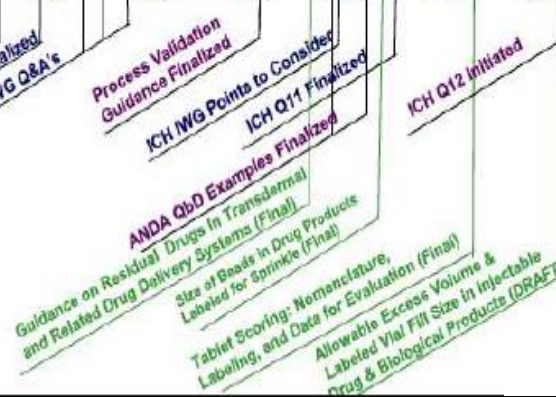
### Initiatives



### Guidance/Documents



**FDA  
Office  
of  
Pharma  
Quality**



**法规的发展  
对  
未来新厂  
的影响**

# Process Control Strategy

## Scope & Aspects

# 工艺控制 与 合规



## Regulatory

Regulatory Filing Management

Knowledge Management



Quality Metrics



E-Inspections

APR/PQR

## Compliance

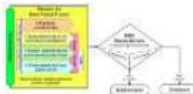
# Process Control Strategy

## Performance

Data Integrity



CPV



OEE/KPI



## Integration

ALCOA+

Operator & Equipment

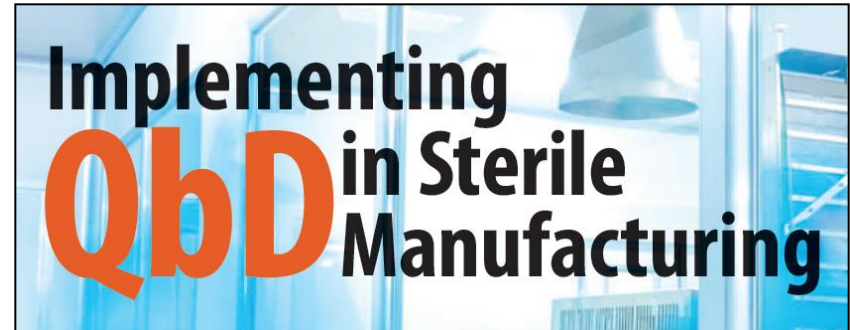
manual / automatic data capture via HMI, PLC, DCS, SCADA

# Pharmaceutical Manufacturing

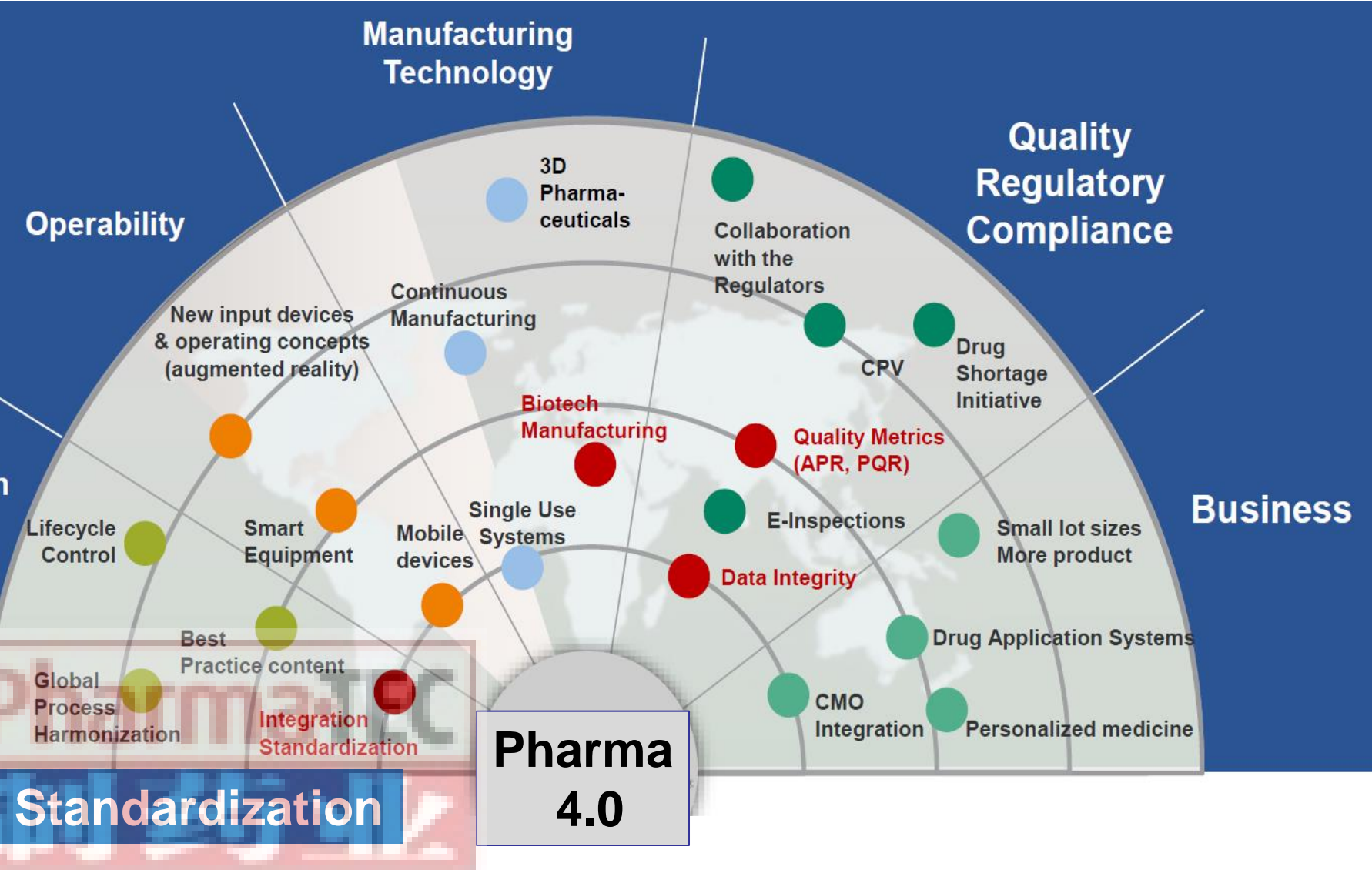




# 全球化的标准与能力



# FoF -- Smart Factory – Pharma 4.0



technologies.  
better outcomes.

竞争力



PharmaTE

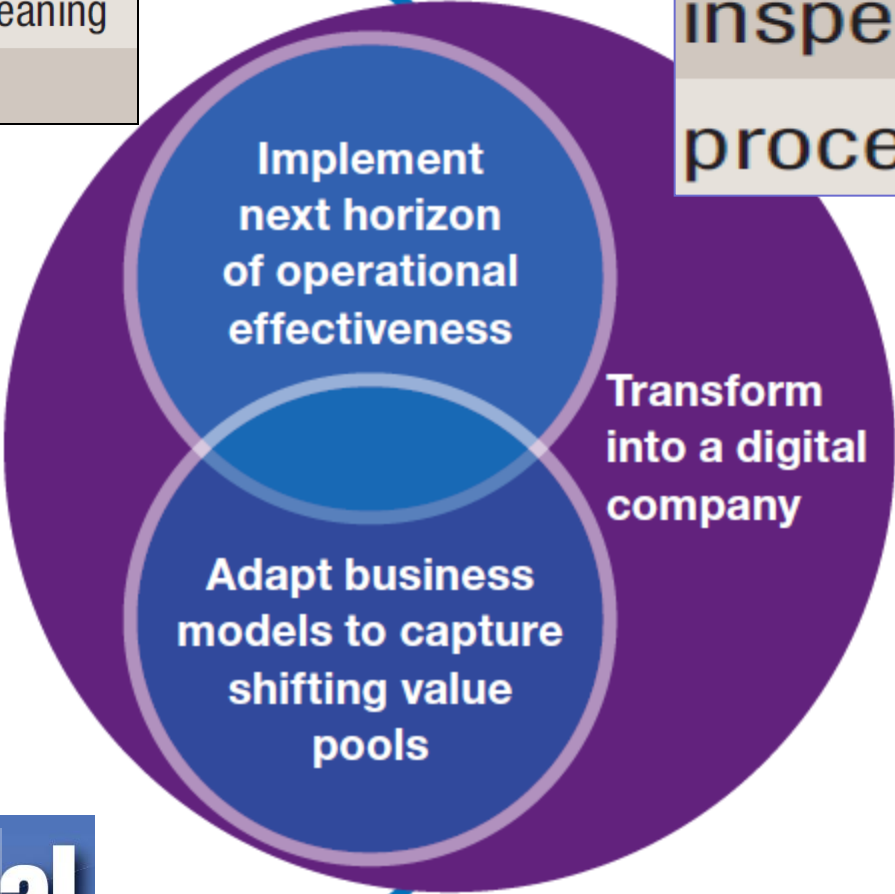
制药业

Automated systems	Sterilization
Water systems	Depyrogenation
Process utilities	Automated cleaning
Automated inspection	

cleaning  
inspection  
processing

Disruptive technologies

竞争力



Pharmaceutical

制药业

Pharma 4.0

### Data, computational power, and connectivity

- Big data/open data
- Internet of things/M2M
- Cloud technology



### Analytics and intelligence

- Digitization and automation of knowledge work
- Advanced analytics



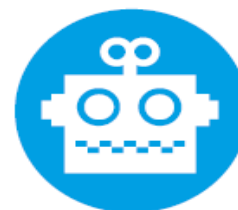
# Pharma 4.0

## 竞争力



### Human-machine interaction

- Touch interfaces and next-level GUIs
- Virtual and augmented reality



### Conversion to the physical world

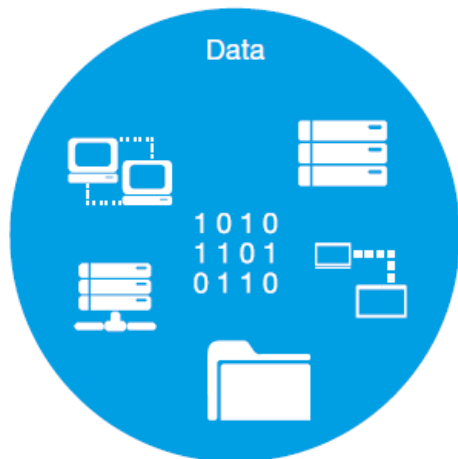
- Additive manufacturing (i.e., 3-D printing)
- Advanced robotics (e.g., human-robot collaboration)
- Energy storage and harvesting

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制药业

# Pharma 4.0

Technology driven

People driven

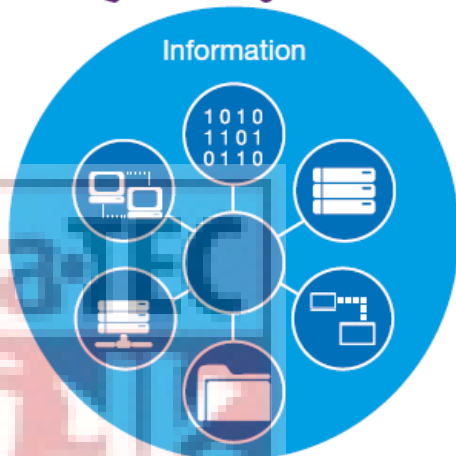


Translate and connect

Identify value driver

Derive action plan

Track progress and financials

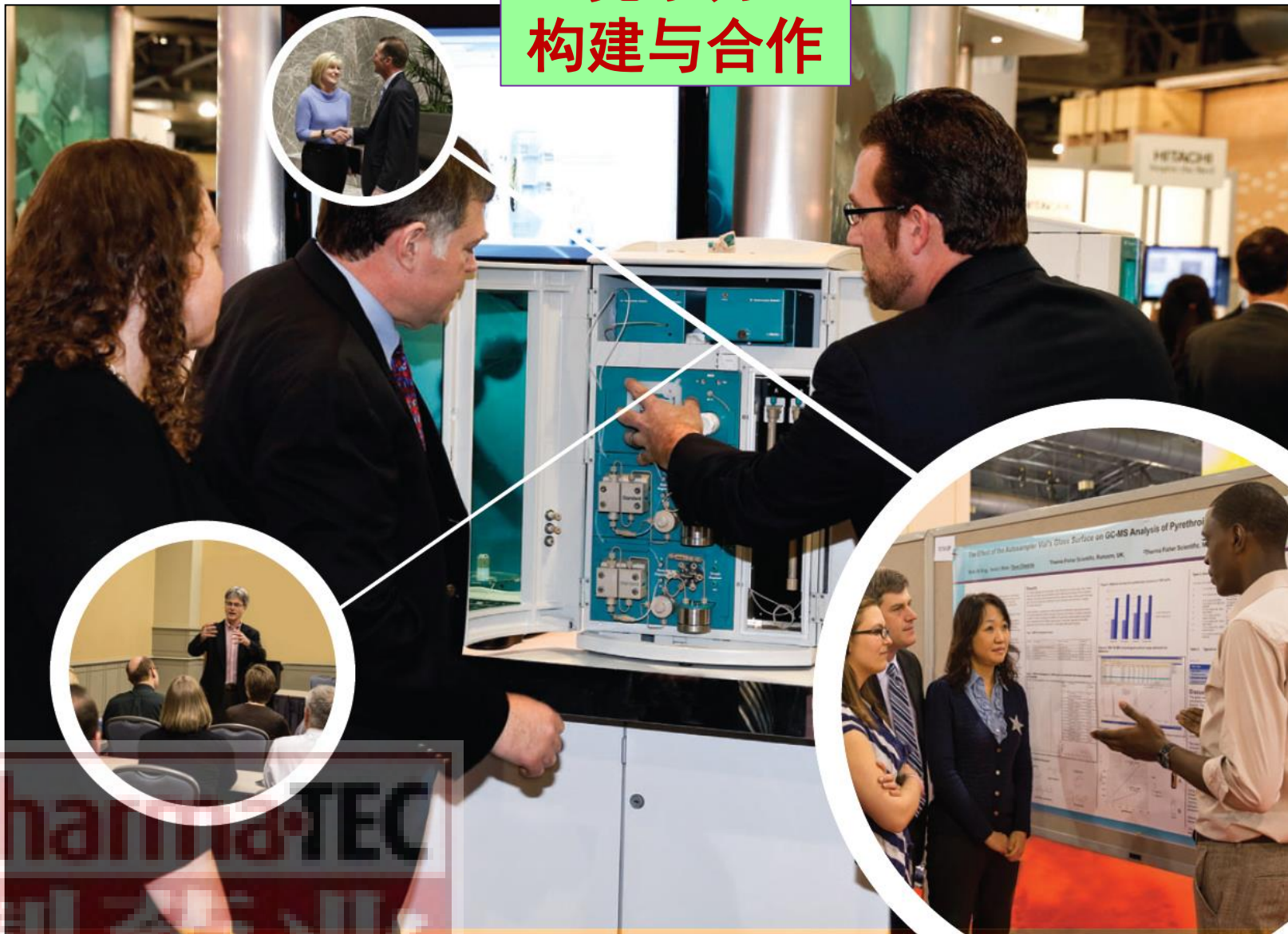


竞争力  
构建

Pharma 4.0

制药工业

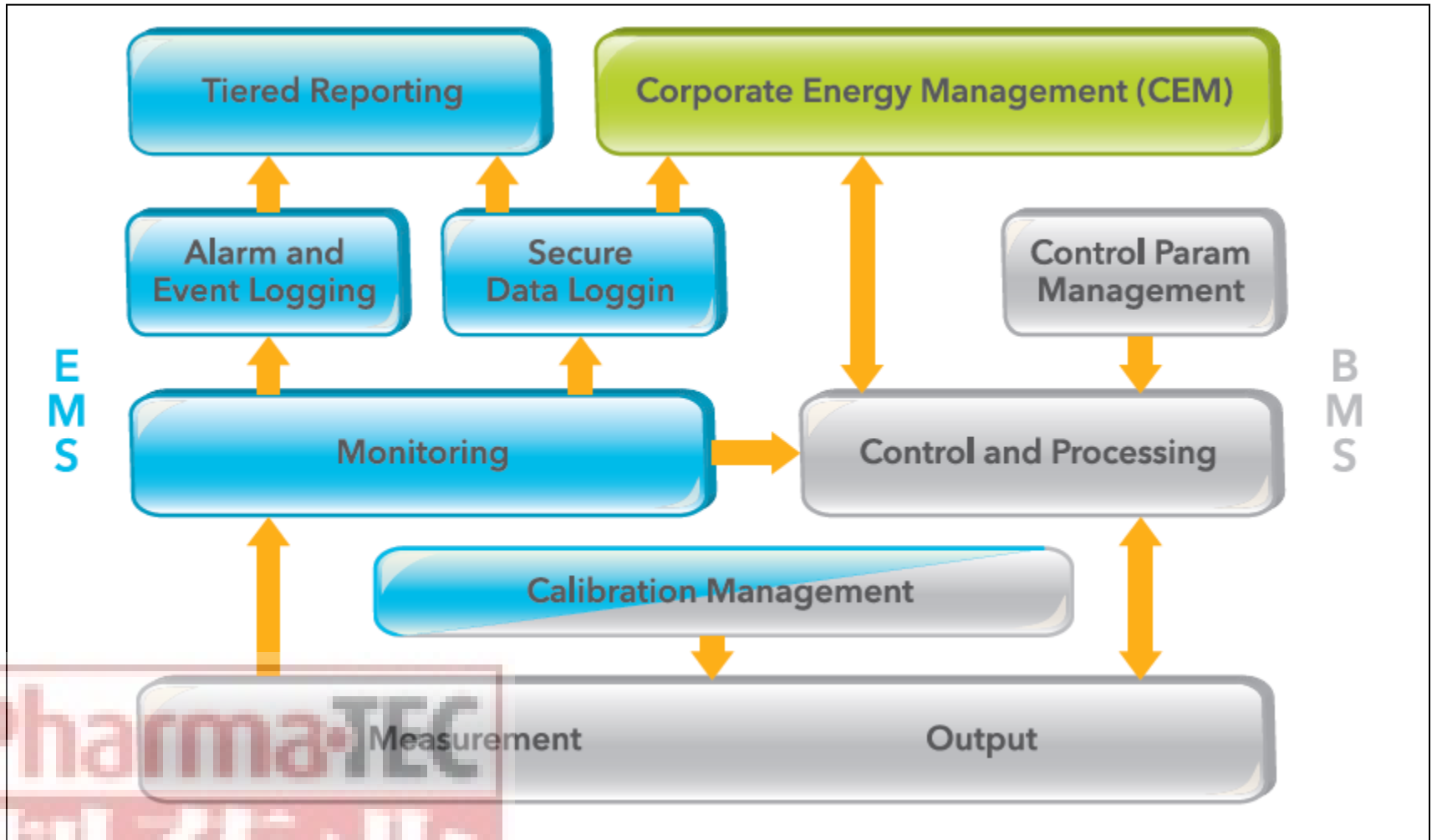
# 竞争力 构建与合作



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# Environmental Monitoring System (EMS)

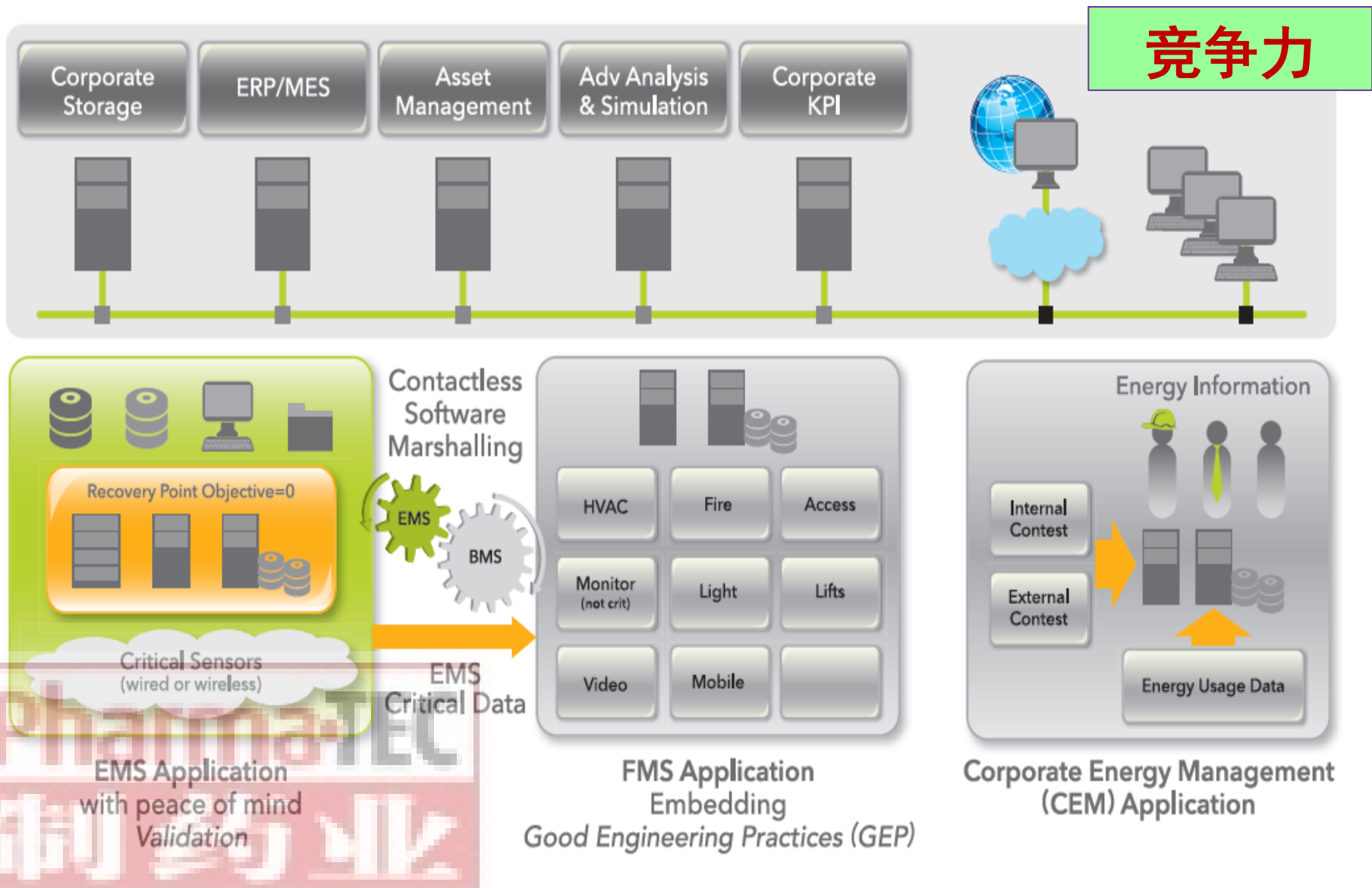


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# Operation Systems

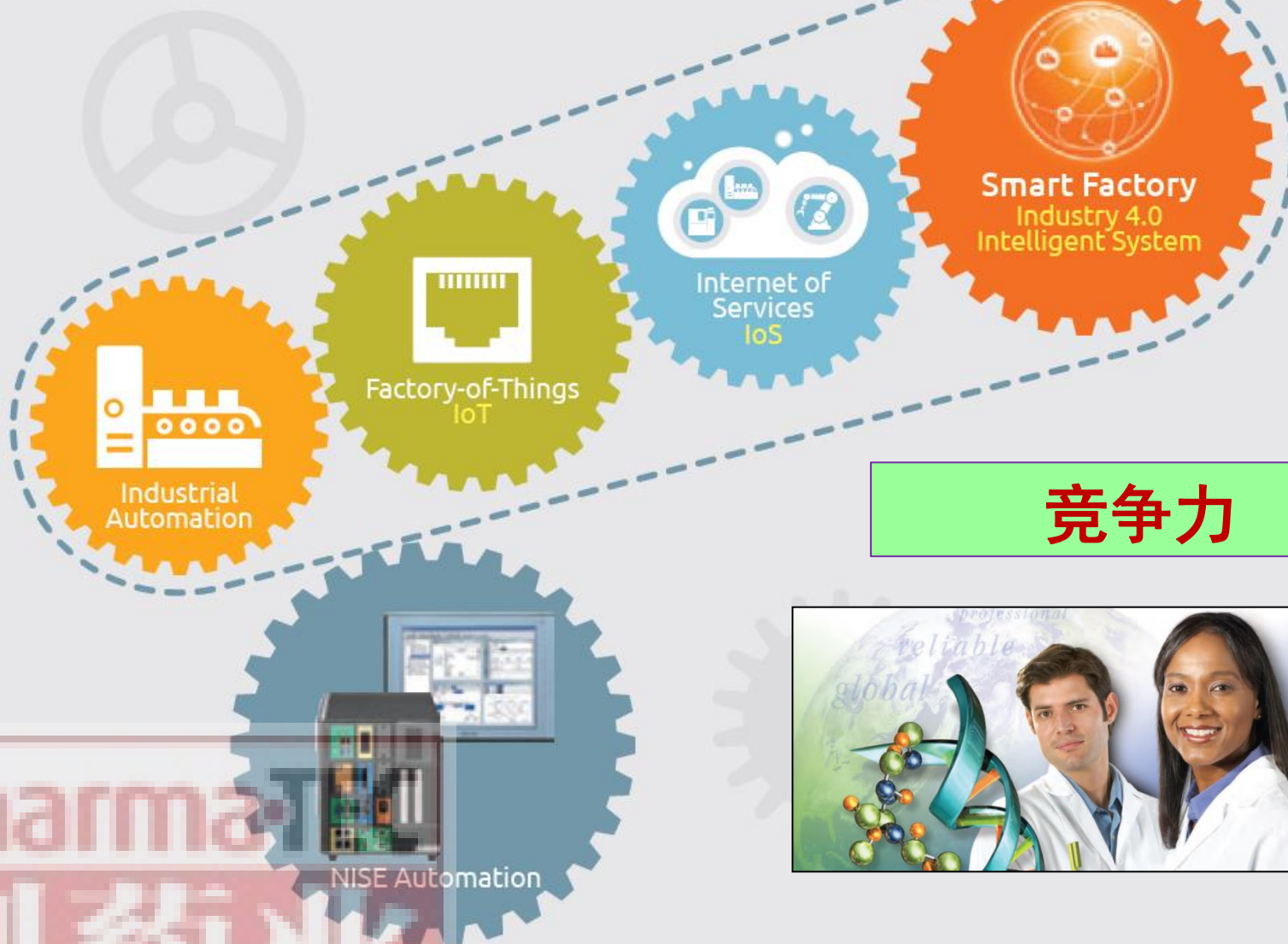


# 信息化、自动化

竞争力



# 信息化、自动化



竞争力



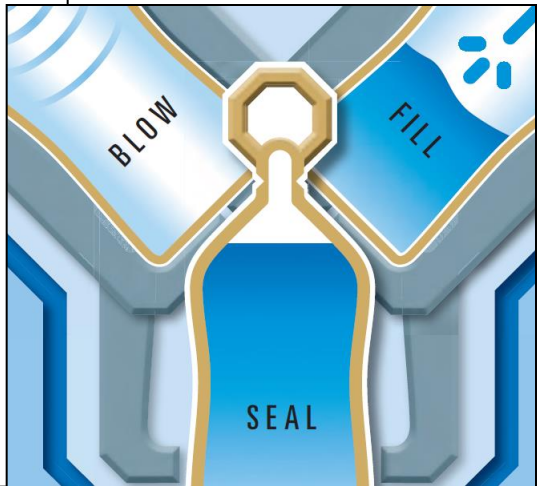
Pharma

制药



竞争力

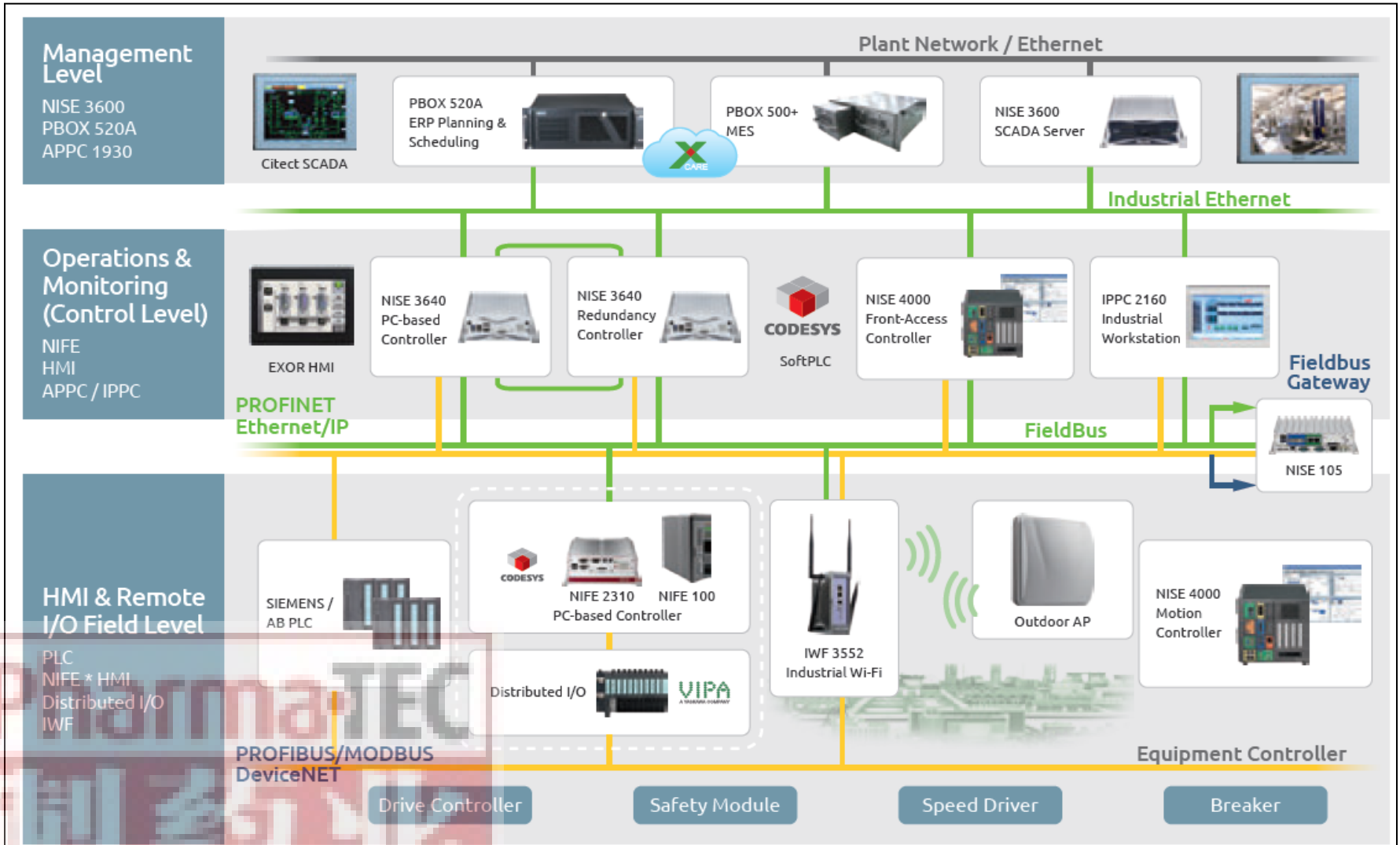
信息化、  
自动化



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智能制造

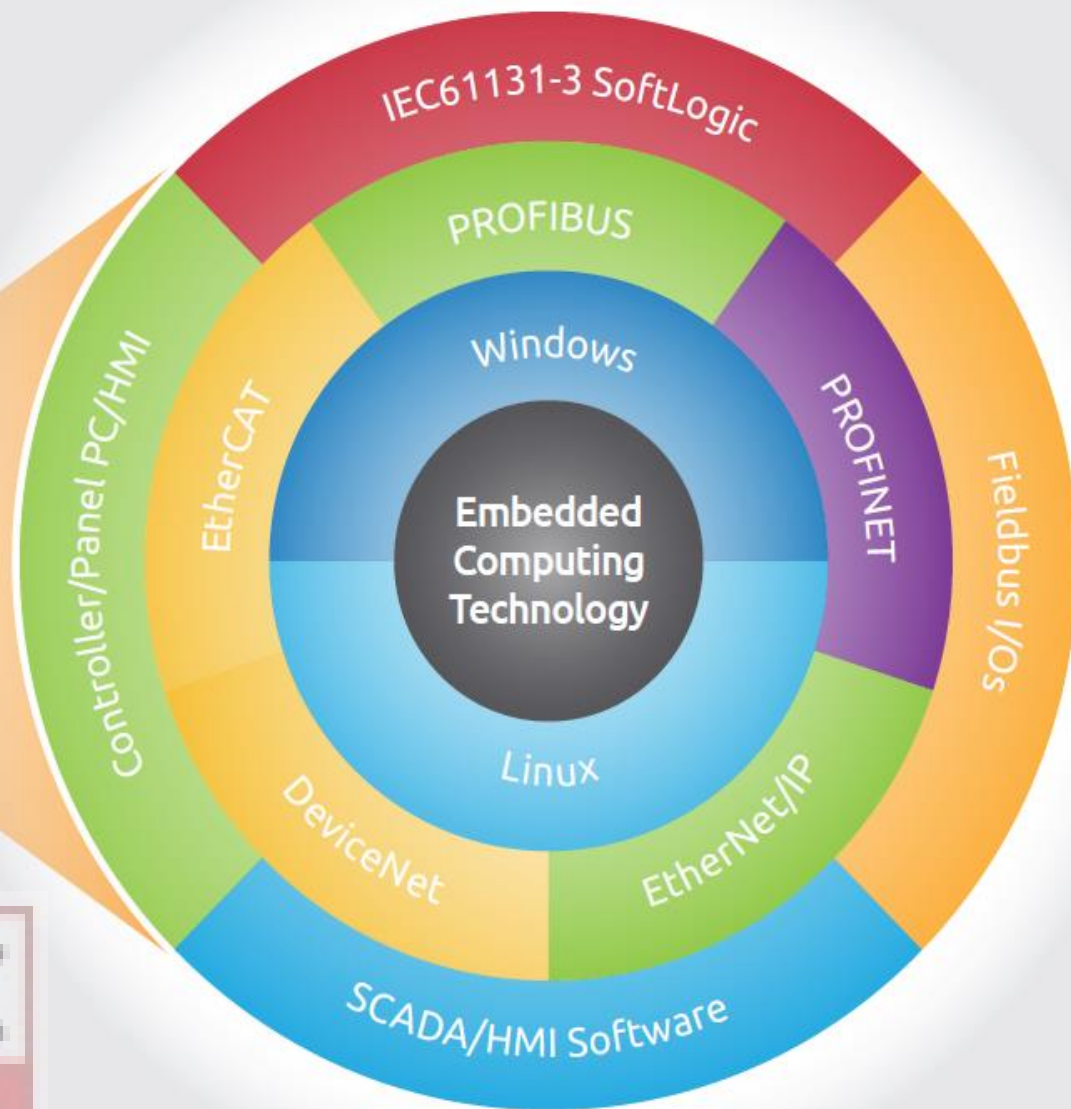
# 自动化 方案 路线图



# 自动化 方案



NISE Automation



PharmaTEC

制药业

# SCADA/HMI

WinCC®

Wonderware®

Intellution®



## NEXCOM Factory Automation Solution

APPC  
IPPC



NIFE



IEC61131-3 SoftPLC



CODESYS



## PLC & Remote I/O

SIEMENS

Allen-Bradley

BECKHOFF

ABB



▲ NEXCOM PC-based Factory Automation Building Blocks

自动化  
方案

# 系统整合



Panel PC  
Citect  
Industrial Through Solutions



NISE 3600  
SCADA/HMI  
Station

Ethernet Network



Fieldbus  
Concentrator

PROFI  
BUS



NIFE PC-based Controller

PROFI  
NET



EtherNet/IP



DeviceNet



EtherCAT



Fieldbus Remote I/O & Fieldbus Devices

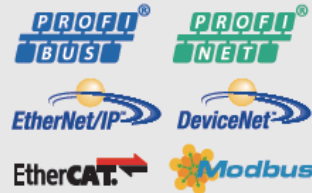
PharmaTEC

▲ NIFE Series Fieldbus Integrated Solutions



# PC-based Automation Controller

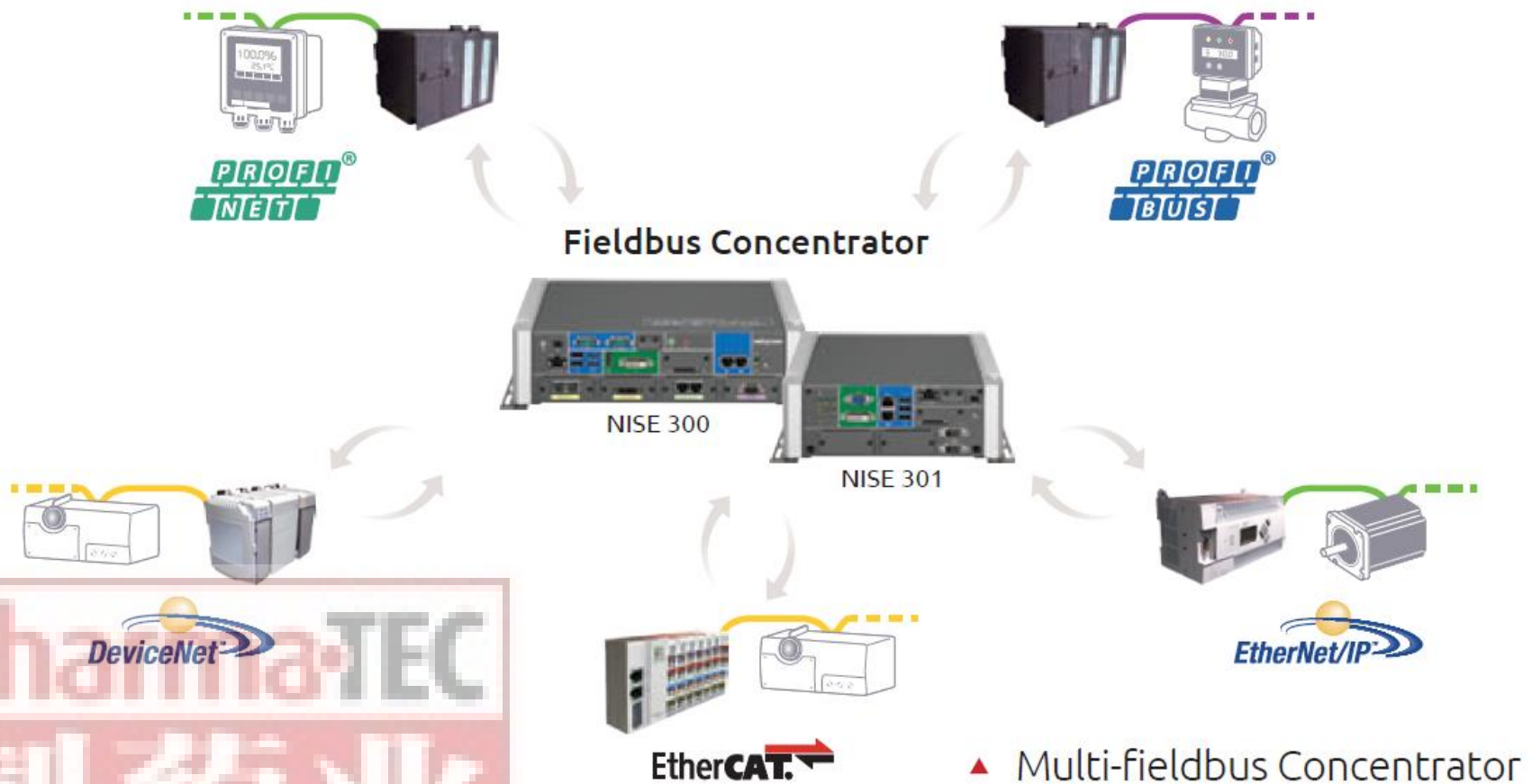
## 控制系统的解决方案



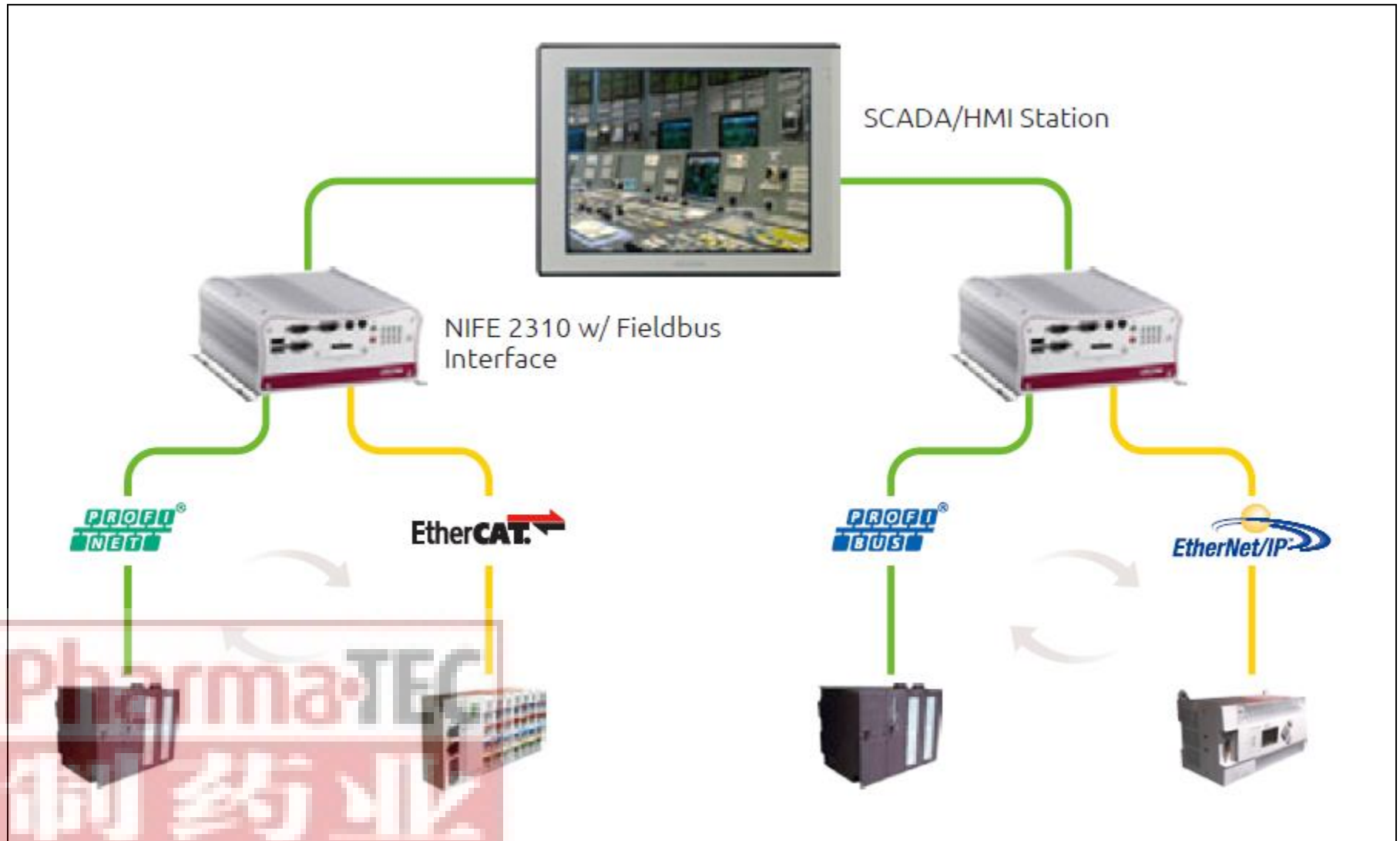
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制 药 业

# 控制系统的整合



# 控制系统的人机介面

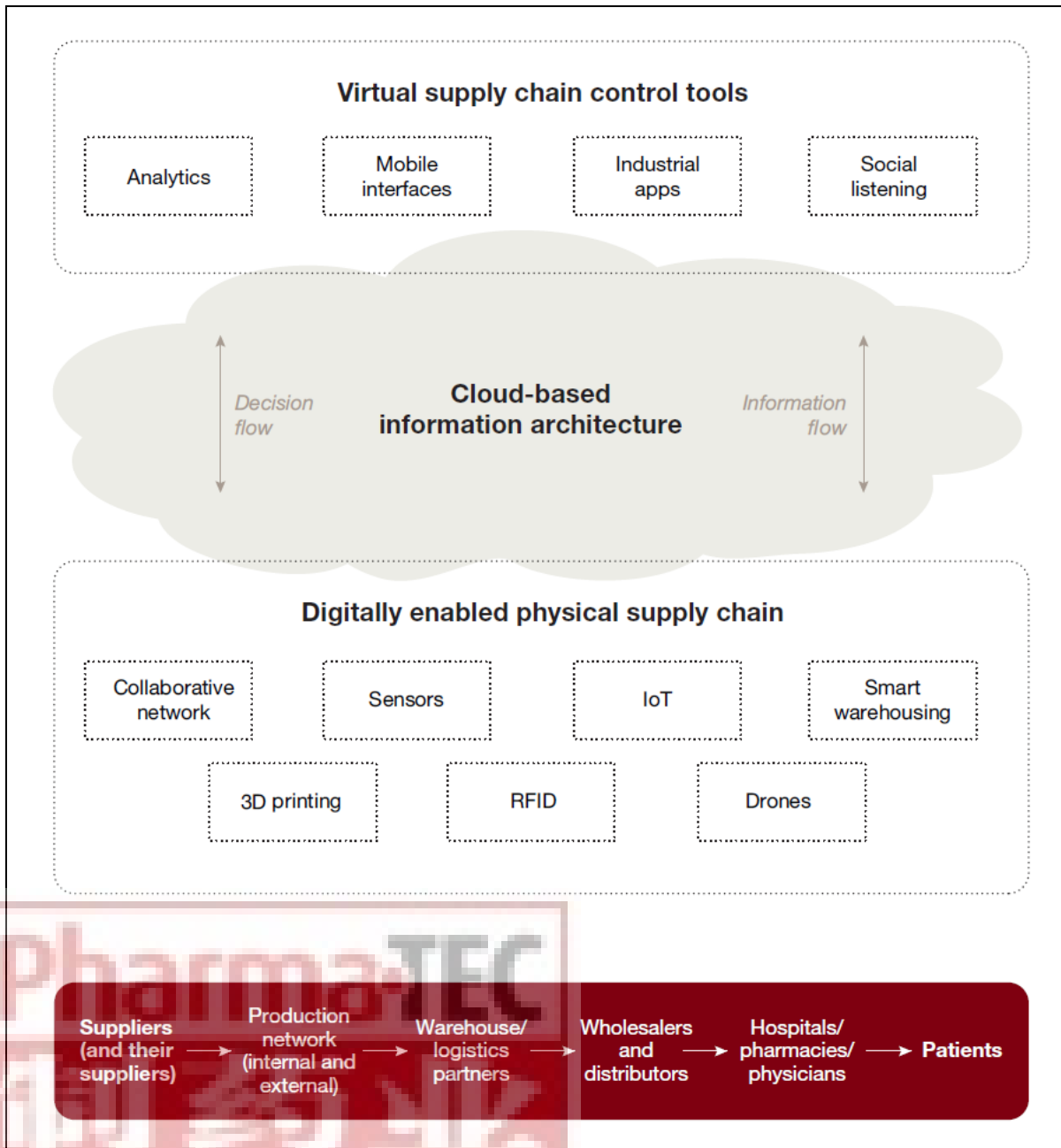


# NEXCOM SCADA/HMI Solution



Pharma-TEC

控制系统的人机介面



# 可视化 及时化的 供应链 管理系统

# 可视化、及时化的 供应链 管理系统

竞争力

## Step 1

Scout the  
technology  
landscape for  
opportunities

## Step 2

Define digital  
strategy and  
prioritize  
opportunities

## Step 3

Design  
solutions and  
launch pilot  
projects

## Step 4

Scale up  
successful  
projects and build  
capabilities

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# 可视化、及时化 的 生产 管理系统

Pharma·TEC

制药业

## Plan

- Real-time supply chain monitoring
- Near-real-time scheduling
- Demand management
- Inventory replenishment
- Compliance management
- Supply chain optimization
- ...

## Source

- Automated order processes
- Online/mobile approval
- Enterprise-level spend analysis and dashboards
- Supplier relationship and quality management
- Contract management
- ...

竞争力

## Make

- Real-time shop floor and production flow monitoring
- Automated, real-time process analytics
- Equipment downtime monitoring
- Predictive maintenance
- Additive manufacturing/3D printing
- ...

## Deliver

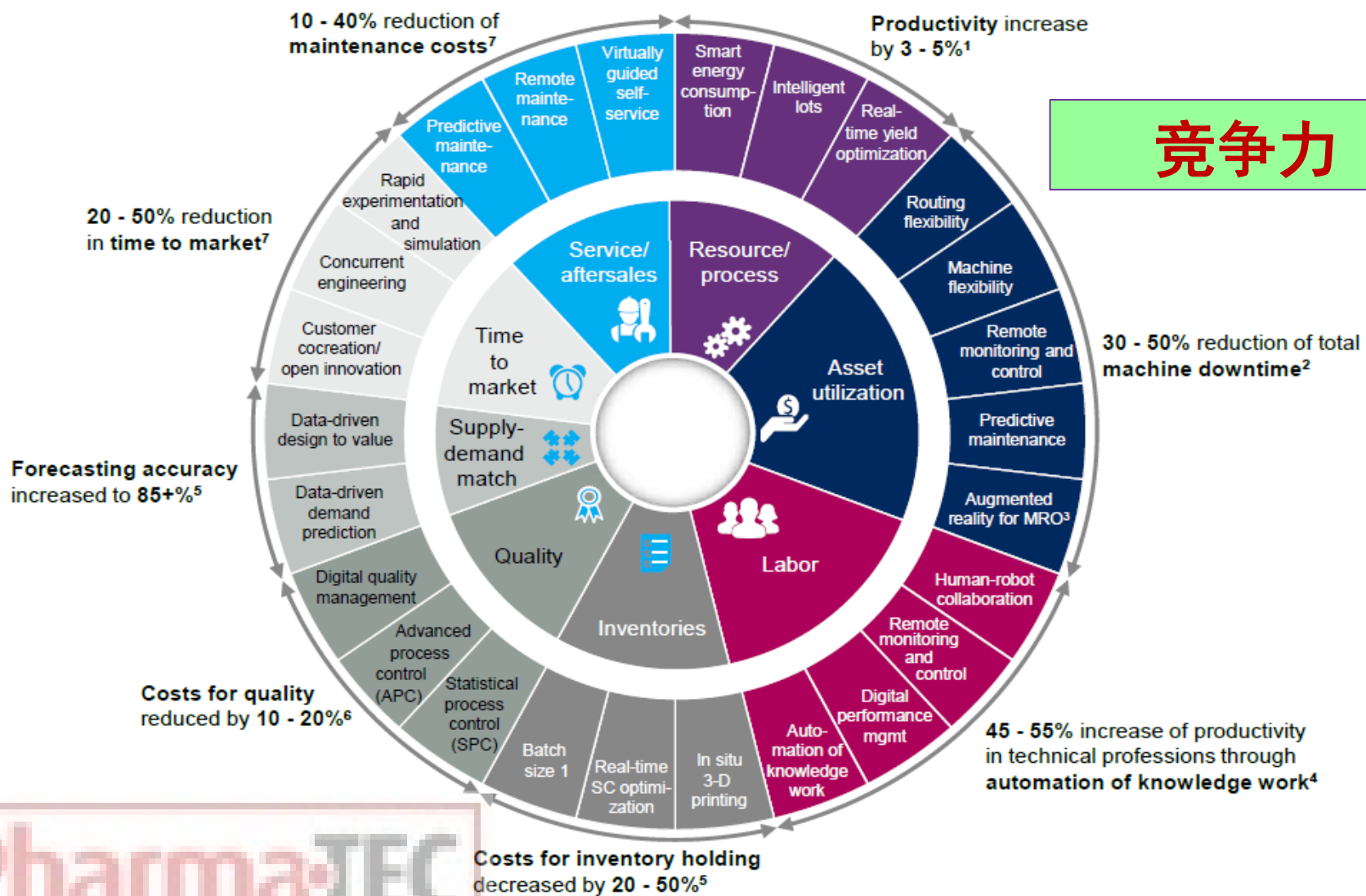
- End-to-end product visibility (supporting track-and-trace initiatives)
- Automated product stocking
- Automated inventory and delivery via drones
- Improved internal logistics via automated guided vehicles
- ...

Pharmatec

制药业



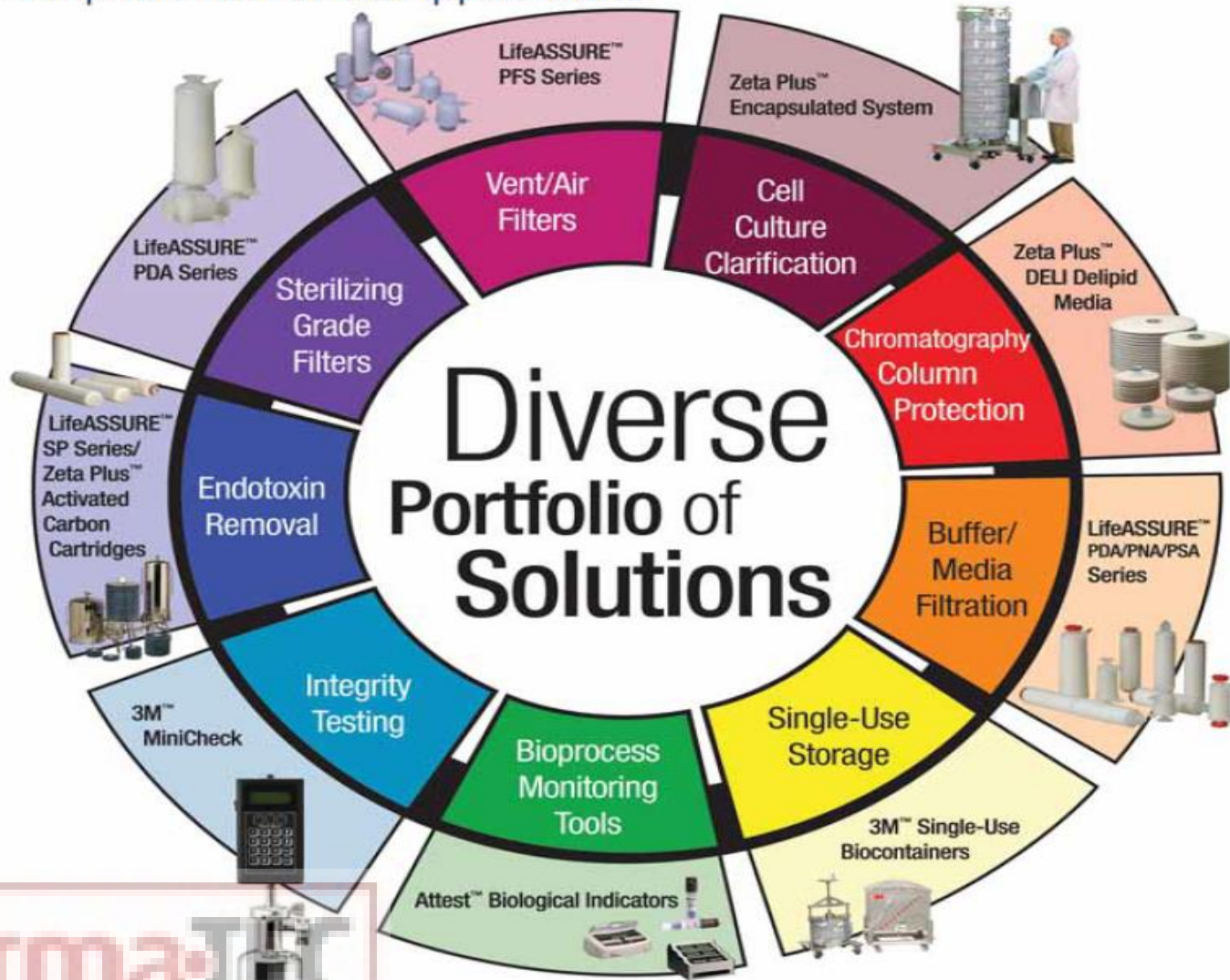
# 竞争力



# Pharma 4.0 的效益目标



for Biopharmaceutical Applications



Pharma·TEC

生物制药的解决方案

# 未来 制药工厂 的 弹性

Product

Process

Timeline

Capacity

Regulatory

Location

弹性化的工厂：

生产、工艺、

效率、产能、

合规、运销。

Pharmatec

制

***„In God we trust, the rest bring data!“***

W. Edwards Deming

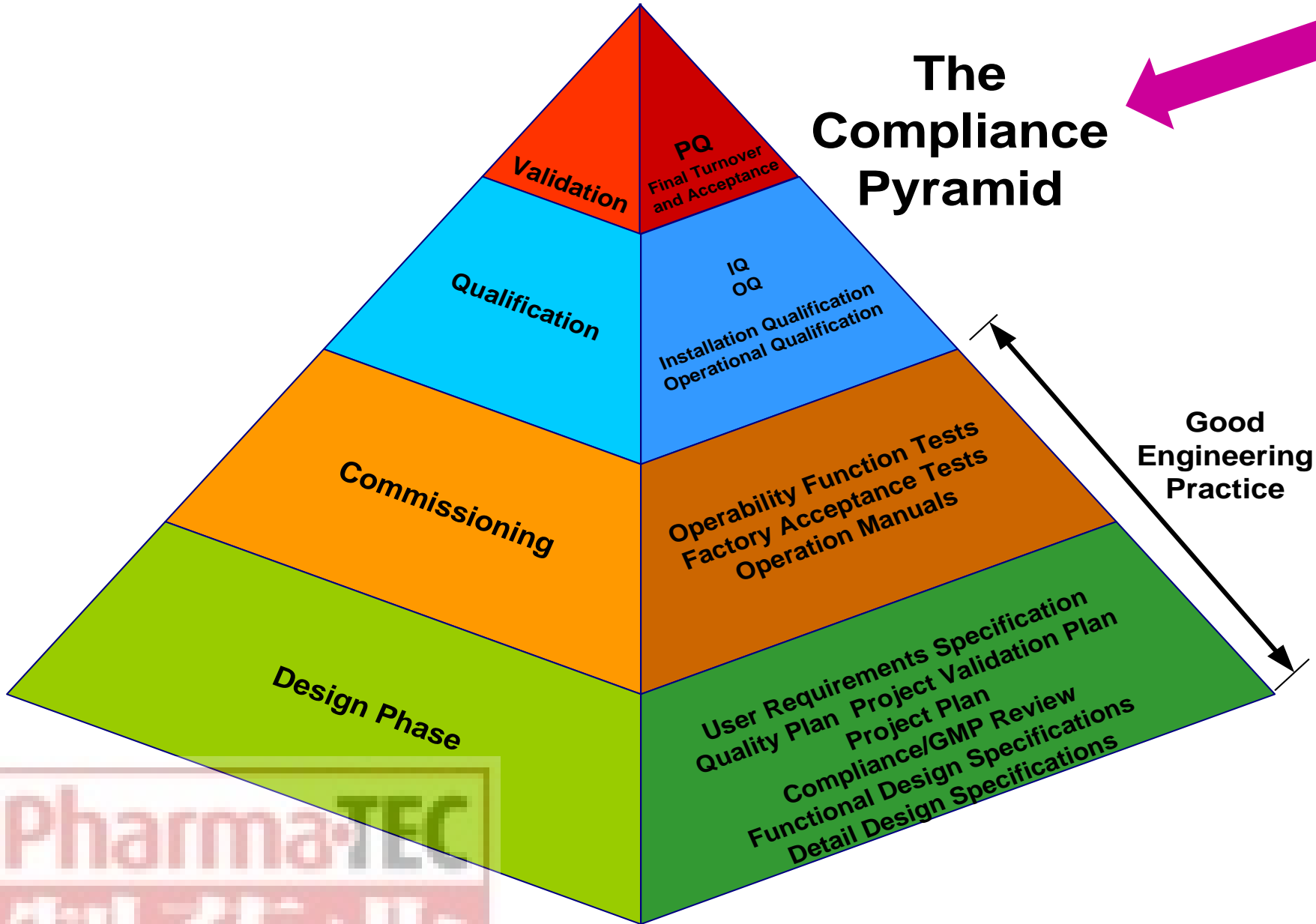
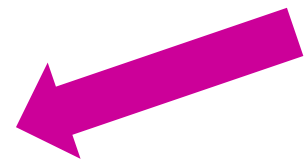
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Pioneer in Quality Philosophy, W. Edwards Deming is widely held to have been one of the leaders who helped create the **Total Quality Movement**. Deming's 14 points and his book "Out of the Crisis" are key documents in the development of Quality Systems for Business management. Dr. Deming is best known for his revolution in the quality and economic productions in Japan where from 1950 onward he taught top management and engineers, methods for management of quality. These teachings dramatically altered the economy of Japan. In recognition of his contributions the Union of Japanese Science and Engineering (JUSE) instituted the annual Deming prizes for achievement in quality and dependability of product.

<http://www.resourcesystemsconsulting.com/blog/reference/glossary>



# The Compliance Pyramid



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**The factory of the future will be measured according to its production capability and flexibility.**

**车间设计的 产能规划  
与 调整 弹性 。**

Pharma·TEC

制 药 业

**Manufacturers will have to achieve the globally- standardized plant floor, harmonizing, supervising, and coordinating execution activities across the company's and suppliers' global SCM network .**

**全球一致化的车间设计、**

**全球一致化的  
供应链管理网络。**

Pharma-TEC

制药业

**More companies expect that their  
production processes will be  
largely or completely  
automated/computerized  
in the years to come.**

**自动化、系统化 对生产工艺很重要。  
未来工厂中，自动化、系统化  
的生产工艺 其比重  
会逐年提高。**

PharmaTEC

制药业



**More manufacturers will invest  
over 25% of their  
New plant total budget for plant-  
floor IT/Operation systems.**

**未来工厂的投资，  
用于 资讯系统 及 作业系统  
的软件投入  
将高达 25% 或 更多。**

Pharm

制药业

# Pharma 4.0

## Related to Pharma Industry

- **Importance to Pharma Industry**
- **The Role of Innovation in FoF Development**
- **The Role of Enabling Technologies**
- **The Next Generation of Pharmaceutical Manufacturing Facility**



PharmaTEC 制药 4.0 的角色  
创新的工厂设计、新技术的应用

PharmaTEC  
制药行业

# Driver for Pharma 4.0

- To be efficient & cost effective.
- FoF is a contributor to the overall Pharma Business.

**Patient safety and efficacy.**

病人安全、业务发展

**Pharma Business success.**

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## *Safety, Efficacy Imperatives:*

Product Quality

Excellence and Compliance

## *Business Drivers:*

Capital Investment

Utilization

Operating Costs

Flexibility and Resilience

New Markets

# 固定成本、运营成本

**In terms of pharmaceutical manufacturing facilities, the overall cost of manufacturing a product can be viewed as a combination of operating and capital costs.**

**With the current cost pressures on the industry as a whole, understanding and controlling both of these costs via Pharma 4.0.**

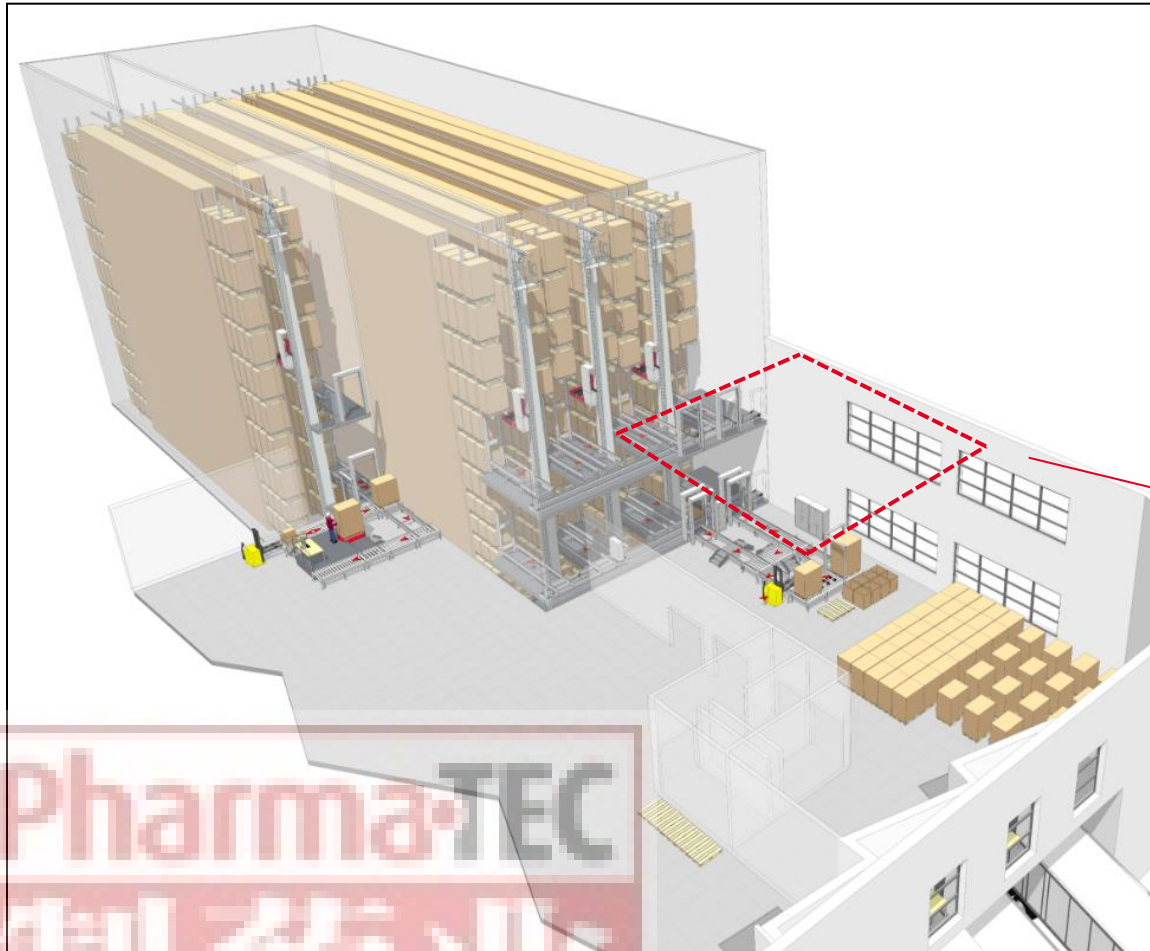
Pharmaceutical  
产品质量

制药业



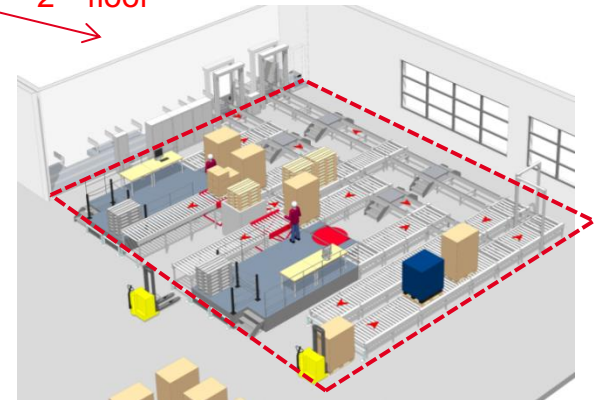
# 供应链 管理

# Solutions



- 1 storage aisle for frozen storage
- 3 aisles for ambient storage
- Goods to Person picking in ambient and in frozen
- AGV's to / from production
- **Goal: cold storage and safety under control**

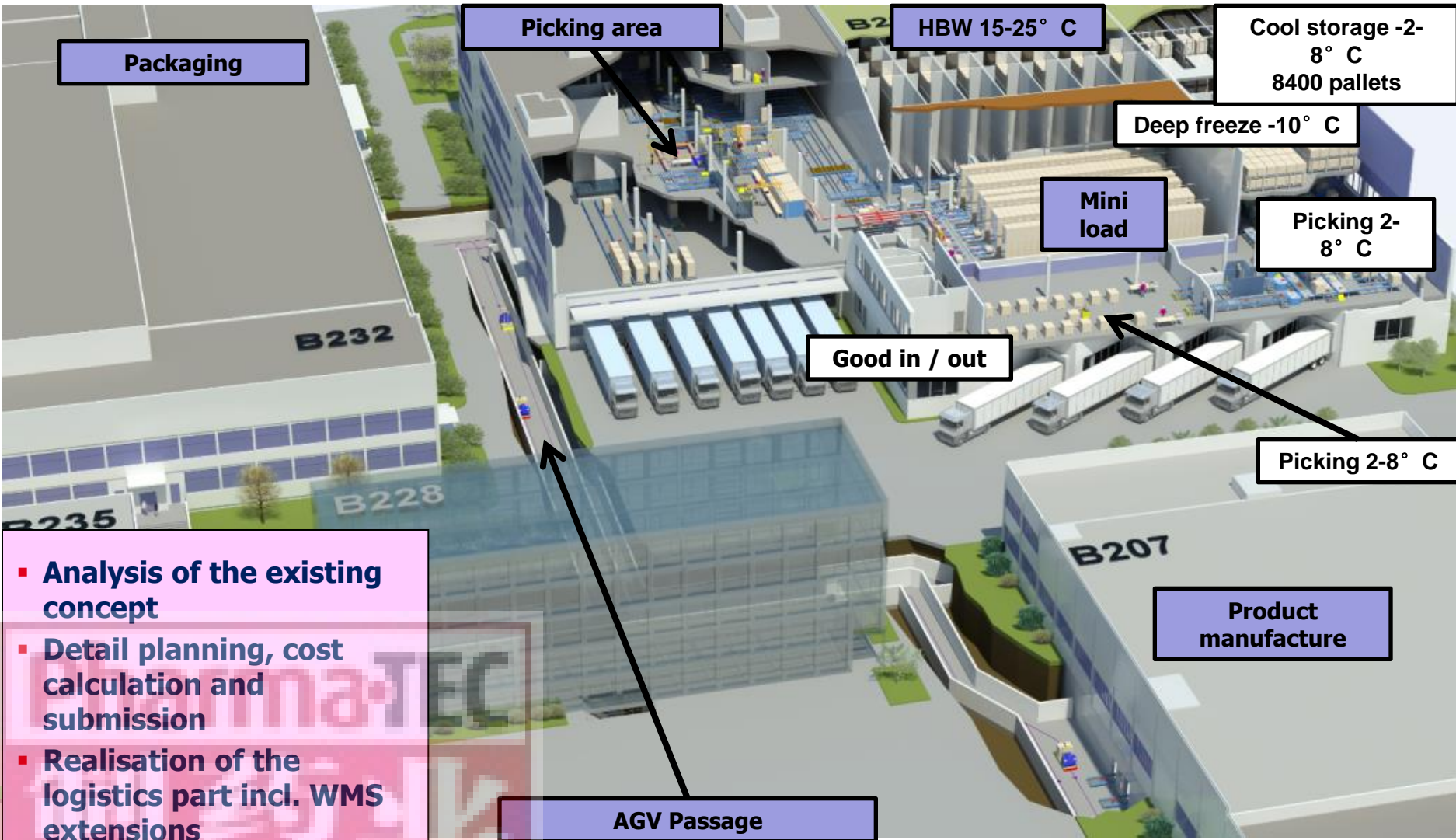
2<sup>nd</sup> floor



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# 供应链管理

# Solutions



- Analysis of the existing concept
- Detail planning, cost calculation and submission
- Realisation of the logistics part incl. WMS extensions

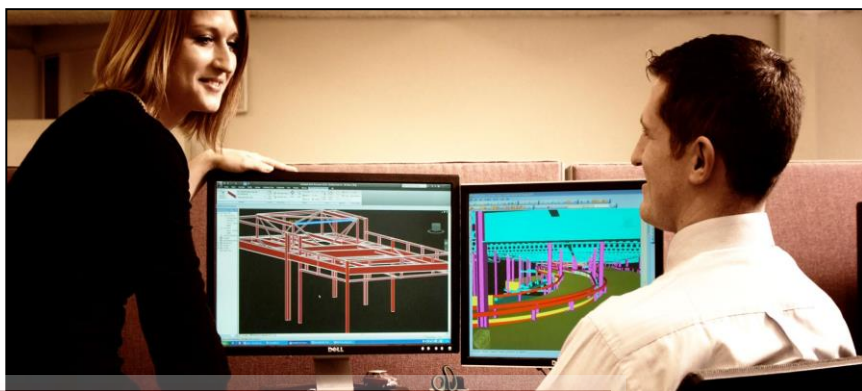
**Despite the growing  
plant automation,  
the flexibility,  
People,  
With the  
decision-making  
capabilities  
will stay as  
the core competency.**



**Pharma 4.0 与 人才**

PharmaTEC  
制药工业

自动化、系统化 很重要。  
**Pharma 4.0 成败在决策，决策在人才！**  
**人才在哪里？**

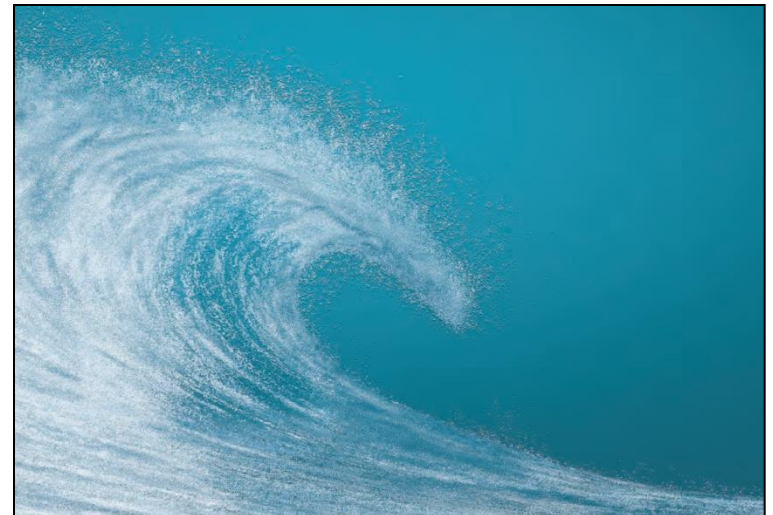


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# 未来的药厂 Pharma 4.0 迈向未来



# 中国高铁 的 成功经验

在全球的范围里  
寻找  
自动化、系统化  
的  
最适合的创新  
与  
最佳的搭配



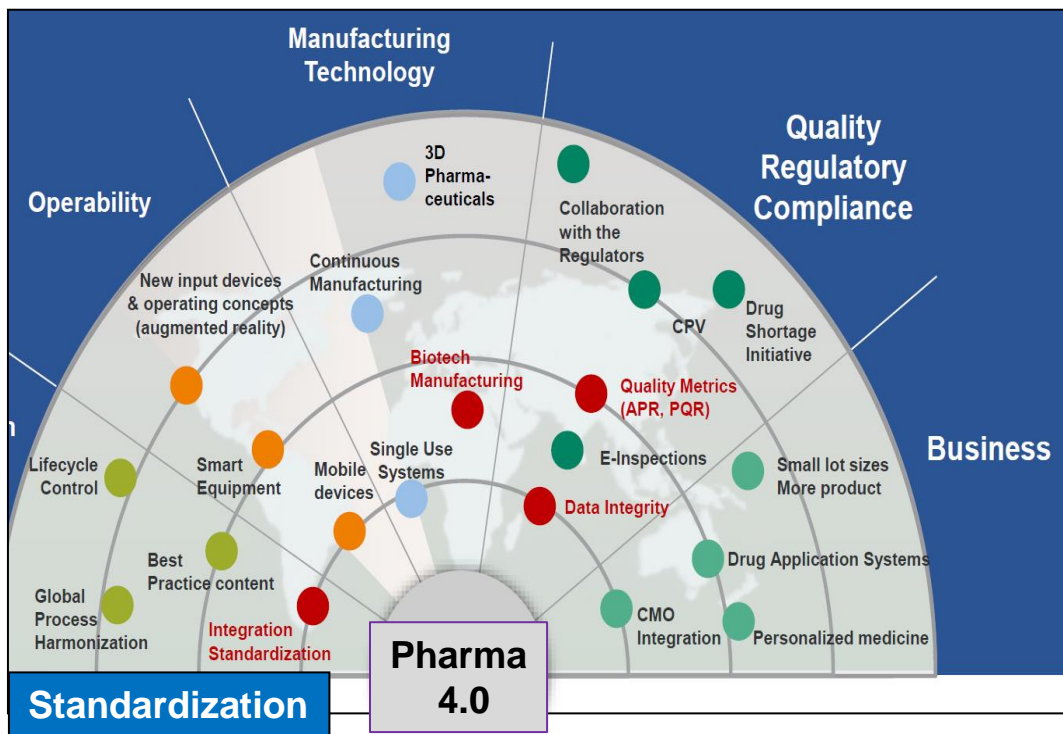
PharmazTEC  
制药业

# Pharma 4.0 的成功

在全球的范围里  
寻找  
自动化、系统化的  
最适合的创新  
与  
最佳的搭配

Pharma 4.0

制药业

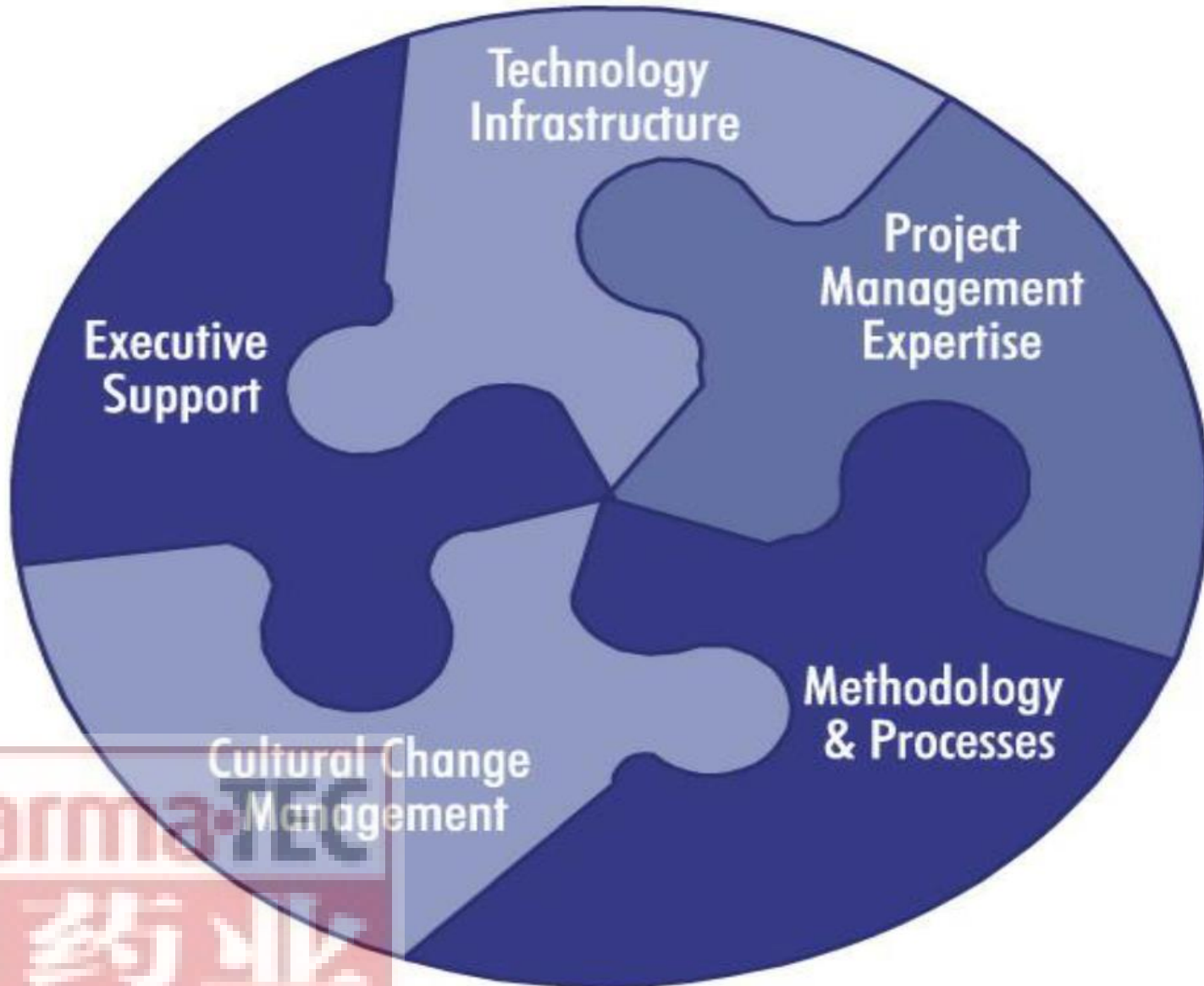




向未来 启航

PharmaTEC  
制药业

# Critical Success Factors



鲤鱼跃龙门，再创新辉煌！



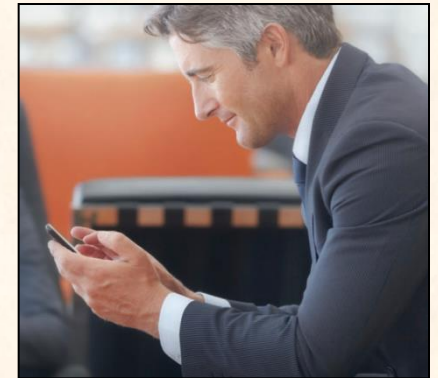
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감사합니다 Natick  
Danke Ευχαριστίες Dalu  
Thank You Köszönöm  
Grazie Tack  
Spasibo Dank Gracias  
谢谢 Merci Seé  
ありがとう



**mikeleeok@126.com**



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