

Deviation Management

偏差管理

Compliance or Continuous Improvement?
合规或持续改善?

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About this Presentation

关于本次演讲文稿

During this presentation I will be asking a number of questions and look forward to your responses
在本次演讲中，我将问若干问题并期待您的回应

Agenda 议程

- Introduction
简介
- Warm-up exercises
热身练习
 - Hydraulic Fluid 液压油
 - The Men's Room 男厕所
- GMP, Quality, and Deviation Management
GMP、质量和偏差管理
- So what is CAPA?
什么是CAPA（纠正和预防措施）？
- Q&A
提问与解答

Introduction 简介

- Who is your speaker?
演讲者是谁?
 - George Bernstein, Ph.D.
乔治.伯恩斯坦 博士

Who is George Bernstein?



- Principal with Double Dragon Consulting (Asia)
双龙咨询（亚洲）的公司代表
- Ph.D. in Chemical Engineering
化学工程博士
- 20+ years of Pharma experience
20多年制药领域的从业经验
- Wide range of experience:
在以下领域有广泛的经验：
 - Quality Systems Development, Audits, Documentation, Investigations
质量体系的发展、审计、文档、调查
 - Remediation 整改
 - Validation 验证
 - Project/Program Management 项目/ 程序管理
 - Facility Construction and Commissioning 设施建设和调试
 - Root Cause Analysis 根本原因分析
 - Business Process Re-engineering 业务进程再造工程
- Our website 我们的网址: www.doubledragonconsulting.com

Warm-up Exercises

热身练习

Root Cause Analysis

根本原因分析

- Hydraulic Fluid
液压油
- The Men's Room
男厕所

Hydraulic Fluid

液压油

This is an actual event that involves:
这是一个真实事件，涉及：

1. Automatic Elevator Co. of Durham
达勒姆自动电梯有限公司
2. Duke University Hospital System (DUHS)
杜克大学医院系统（DUHS）
3. Cardinal Health 卡迪那健康
4. DUHS Staff DUHS 员工
5. 3,650 Patients 3,650病人

Automatic Elevator

自动电梯

- Hired by DUHS in September 2004 to repair an elevator
2004年9月受雇于DUHS维修一部电梯
- Repair required replacement of hydraulic fluid
维修需要更换液压油
- Mechanics found empty buckets and used them to hold the used hydraulic fluid
维修工发现空水桶，并用它们来保存所使用的液压油
- The buckets used to contain detergent used by DUHS to clean surgical instruments
这些水桶是DUHS用来装用于清洁手术器械的洗涤剂
- Buckets now containing used hydraulic fluid were left by Automatic Elevator at the hospital
达勒姆自动电梯有限公司把装过使用液压油的水桶留在医院

Cardinal Health

卡迪那健康

- Buckets of hydraulic fluid were found and returned to DUHS central stores
液压油桶被发现并返还到DUHS中央仓库
- From central stores the hydraulic fluid was returned to Cardinal Health's distribution warehouse
液压油从中央仓库退回到卡迪那健康的配送仓库
- Cardinal Health later distributed the hydraulic fluid to two of DUHS regional hospitals – Durham Regional Hospital and Duke Health Raleigh Hospital
卡迪那健康随后将液压油分配到2个DUHS区域医院 -达勒姆地区医院和杜克健康罗利医院

DUHS Staff

DUHS 员工

- The hydraulic fluid was used by hospital staff to wash surgical instruments, prior to sterilization
医院工作人员用液压油在灭菌前清洗手术器械
- The hydraulic fluid was used for a period of 2 months
液压油被使用长达2个月之久



DUHS Staff

DUHS 员工

- The hydraulic fluid occasionally left the instruments feeling slightly oily
液压油偶尔会在手术器械上留下轻微的油腻感
“It is not uncommon for instruments to feel slick, as a lubricant is added during the normal cleaning process to prevent rust and ensure the instruments work smoothly during surgery.”
“感觉手术器械油滑并非异常，因为在正常清洗过程中会加入润滑剂来防止生锈及保证器械在手术中工作顺利。”
- Approximately 3,650 patients were affected.
大约有3,650个病人受到影响

The Question

问题

Whose fault was it?
这是谁的过错？

Whose Fault was It?

这是谁的过错？

- Automatic Elevator? 自动电梯？
- Cardinal Health? 卡迪那健康？
- DUHS staff? DUHS员工？
- Surgical nurses? 手术护士？
- Surgeons? 外科医生？

Whose Fault was It?

这是谁的过错？

Everyone is responsible
每个人都有责任

The Men's Room

男厕所



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The Men's Room

男厕所

- What's wrong?
问题在哪里？
- Can we improve on this situation?
我们能改善这种状况吗？

The Men's Room

男厕所



The Men's Room

男厕所

Communication is critical in the pharmaceutical business

在医药行业，沟通是关键

⇒ It must be clear 沟通必须清楚

⇒ It must be complete 沟通必须完整

It must be written down
沟通必须记录下来

Deviations

CAPA, Root Cause

偏差

纠正和预防措施、根本原因

- Definitions 定义
- Motivation 动机

Definitions

定义

Deviation 偏差

- Results when a written procedure is not followed or an unexpected result is obtained
没有遵循书面规程的结果或获得意向不到的结果
- Any deviation must be recorded and product impact evaluated and justified
任何偏差都必须记录及评估和解释对产品的影响

Root Cause 根本原因

- In terms of cause and effect, Root Cause is the fundamental reason(s) for the failure of a procedure which, when resolved, prevents a recurrence of the problem.
就因果而言，根本原因是一个程序出现错误的基本原因，解决后可以防止问题重复发生。
- For a particular product problem, Root Cause is the factor(s) that, when you fix it, the problem goes away and doesn't come back.
对于一个特定的产品问题，根本原因是要素，当你纠正它后，问题消失且不再回来。
- Data collection and analysis are usually necessary to determine the root cause, and therefore guide decisions about the corrective and preventive actions needed for improvement.
数据收集和分析通常是必要的，以确定问题的根源，并且引导做出用于改进的纠正预防措施的决定。

CAPA 纠正和预防措施

- Corrective Action(s) – action(s) taken to **correct** or fix a failed procedure
纠正措施 – 用于**纠正**或修复失败程序的措施
- Preventive Action(s) – action(s) taken to **prevent** similar issues from occurring in the future
预防措施 – 用于**预防**将来发生类似问题的措施

Deviations

偏差

- Must be documented
必须记录
- Must be investigated
必须调查
 - to identify root cause 来找出根本原因
 - to assess product impact 来评估对产品的影响
- Investigations must be completed in a timely manner (usually within 30 days of occurrence)
调查应及时完成（通常事件发生后30天内）
- Must be closed before a batch can be released
必须在批次可以放行前关闭

Question

问题

Are deviations:
偏差是:

- A GMP compliance requirement?
GMP合规要求?
- A part of a continuous improvement process?
持续改善程序中的一部分?

Root Cause

根本原因

Root Cause Categories include:

根本原因的种类包括:

- Materials 材料
- Manpower 人员
- Machine / Equipment 机械/设备
- Environment 环境
- Management 管理
- Methods 方法
- Management system 管理体系

Root Cause

根本原因

What is the root cause of the hydraulic fluid mishap?

什么是液压油事故的根本原因？

- Hint: the root cause is not always training
提示：根本原因不仅仅是培训

Hydraulic Fluid Root Cause

液压油事件根本原因

- Management
管理
 - Inadequate supervision of outside contractors
对外部承包商的监管不当

CAPA 纠正和预防措施

- In order to identify an effective CAPA, the deviation investigator must have:

为了找出最有效的预防措施，偏差调查者必须具备：

- Good investigator skills 良好的调查者技能
- Good documentation/reporting skills 良好的记录/报告技能
- Good working relationship with production workers in order to identify, fix, and prevent reoccurrence
与生产工人保持良好的关系，以找出、修复并预防事故重复发生
- Reduce product risk
降低产品风险

Motivation 动机

Why CAPA?

为什么要纠正和预防措施？

- Quality risk management (see ICH Q10)
质量风险管理（参考ICH Q10）
- Cost
成本
- Regulatory Actions
法规措施

(see www.FDA.gov for examples)

（例子请参考www.FDA.gov）

About Double Dragon Consulting

关于双龙咨询

About Us

关于我们

What We Do
我们咨询什么

- We provide a diverse range of consulting services to Life Sciences companies in Asia.
给亚洲生物科学公司提供多元化得咨询服务

Details
细节

- DDC incorporated in 2010 成立于2010
- 2 offices 两个办事处
 - Shanghai, PRC 中国 上海
 - RTP, NC, US 美国 北卡罗来纳州
- Sister company MAI Consulting incorporated in 1992 姐妹公司MAI咨询成立于1992年

How We Do
Business
我们怎样开
展业务

- We fill our client's needs 满足客户的需求
- We provide consultants from our network to meet that need 提供自由的咨询人员以满足需求
- We charge reasonable rates 收取合理费用
- We are flexible 可以灵活调整

What Services does DDC Offer?

双龙咨询可提供怎样的服务？

- **Quality / Compliance 质量/合规**
 - Procedures, Processes, Documentation, Inspection preparation, Remediation
程序、流程、文档、审查准备、纠正
- **Training 培训**
 - Aseptic Operations including Gowning Qualification, Environmental Monitoring, Investigations, Root Cause Analysis, CAPAs, Change Control, Internal Audits
无菌操作包括更衣合格认证、环境监控、调查、根本原因分析、纠正和预防措施、变更控制、内部审计
- **Regulatory 法规**
 - ANDA Submissions 新药简略申请书 (ANDA) 提交303030
 - CMC Development 化学，制造和控制 (CMC) 的发展
 - Analytical Method Validation 分析方法的验证
- **Engineering/Maintenance 工程/维修**
 - Class A/B Cleanroom Design A/B级别洁净室的设计

How Do We Differ From Other Consulting Companies?

我们跟其他咨询公司有哪些不同？

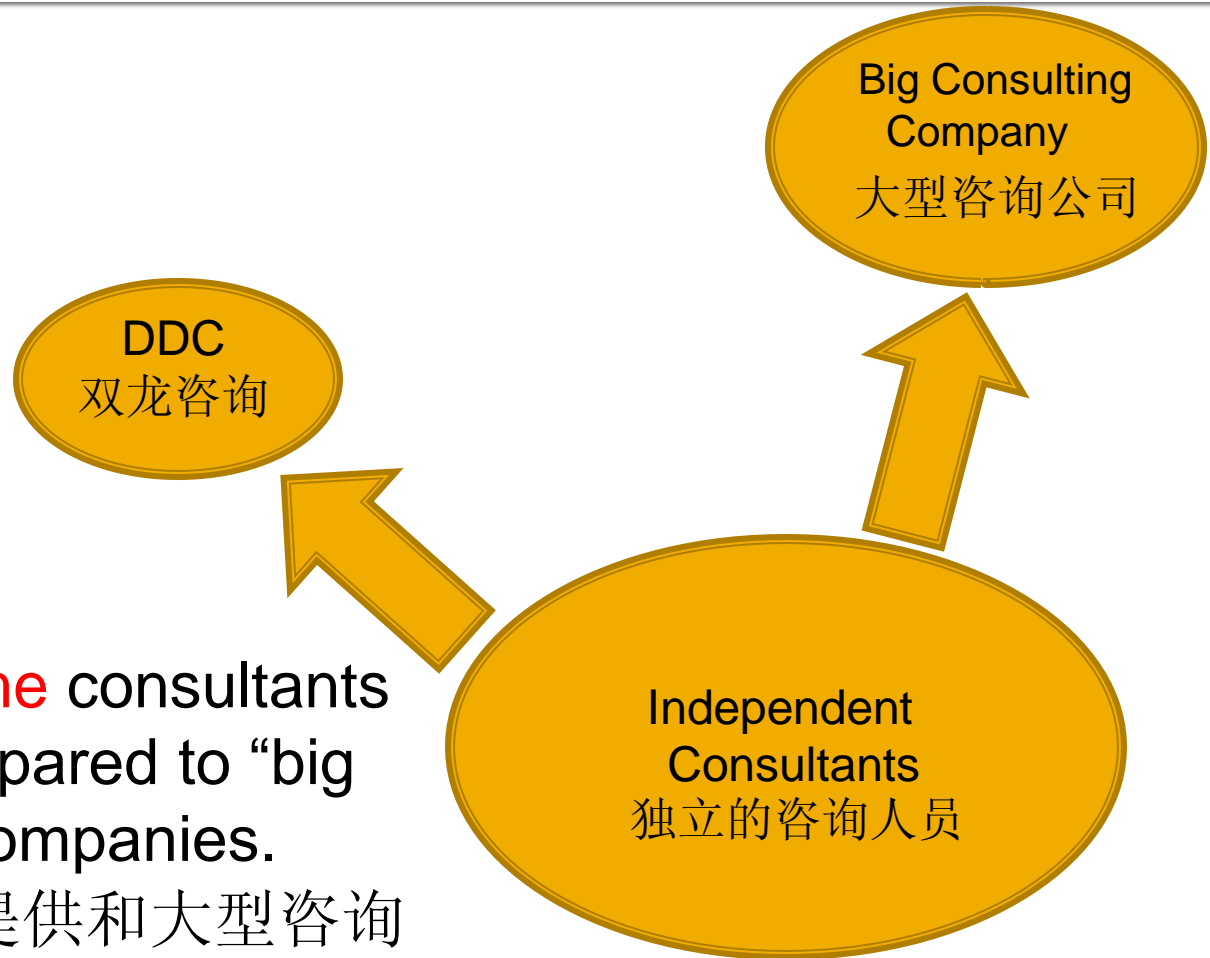
COST 成本

- The consulting / consultant relationship
咨询公司 and 咨询人员的关系
- Low overhead business model 低成本商业模式
 - Exclusively use independent subcontractors
使用独立咨询人员
 - Maintain small office staff 维持精简组织架构
- Strategic alliances 战略联盟
 - Expand service offerings 扩大服务范围
 - Provide single interface to client 提供一站式服务

Why DDC?

为什么选择双龙咨询？

TALENT
人才



We provide the **same** consultants at a lower cost compared to “big name” consulting companies.

我们以较低成本，提供和大型咨询公司**一样**的咨询人员。

Our Clients

我们的客户

- CibaVision 视康
- Novartis Pharma 诺华制药
- Novartis Vaccines and Diagnostics
诺华疫苗和诊断
- sanofi pasteur
赛诺菲巴斯特
- Bayer Biologicals 拜耳生物
- Cardinal Health 卡迪那健康
- WHP
- Stiefel 施泰富
- Forest Research Institute
福斯特研究中心
- F. Hoffmann LaRoche
罗氏
- URL Pharma
URL制药
- Merck 默沙东
- MedImmune 阿斯利康子公司
- Hospira
- West Pharmaceuticals
西部制药
- Luitpold
- Teva
- Marianna
- Sandoz 山德士

How We Do Business

业务方式

FLEXIBILITY

灵活性

- **DDC will:**
我们可以:
 - Work with you directly
直接与您合作
 - Will partner with in-country consultants as a team member, to supplement their expertise, or to review their work
与国内咨询公司/人员合作，以加强和监督他们的工作能力和表现
 - Will work remotely via Internet or in-country
在国外（互联网）或国内展开工作
 - Work on an hourly or retainer basis
按小时或长期模式收费

In Summary

总结

Regarding CAPA, remember:

关于CAPA，请记住：

- Retraining isn't always the preventive action
重复培训不是永远的预防措施
- To set realistic goals and timelines for implementation
为实施设立符合实际的目标和时间
- To implement promised corrective/preventive actions
执行计划的纠正/预防措施

**CAPA is a part of the continuous
improvement process**

CAPA是持续改善程序的一部分

Resources

来源

- **ISO 9004** “Quality Management Systems – Guidelines for Performance Improvement”
ISO 9004 《质量管理体系 – 性能提升指南》
- **ICH Q9** “Quality Risk Management”
ICH Q9 《质量风险管理》
- **ICH Q10** “Pharmaceutical Quality System”
ICH Q10 《制药质量体系》

Questions?

问题？

DoubleDragon
双龙咨询 Consulting

The Final Word...

最后...

- For additional information:

更多信息请咨询:

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