疫苗生产相关 GMP 知多少？

什么是 GMP？

GMP 全称（Good Manufacturing Practices），中文含义是“生产质量管理规范”。GMP 要求制药、食品等生产企业应具备良好的生产设备，合理的生产过程，完善的质量管理和严格的检测系统，确保最终产品质量符合法规要求。

中国从什么时候开始执行 GMP 要求？

从 1988 年国家卫生部颁布了中国第一部《药品生产质量管理规范》(1988 年版)，到目前已有整整 30 年，期间的一系列 GMP 规范与执行工作影响着中国几千家制药企业的发展与命运，GMP 的要求也在不断的完善。

过去对 GMP 观念的认知问题？

其实国内外对 GMP 的认知差异不在于 GMP 原文上, 主要在法律意识和文化观念上的差异或理解与执行上的差异， 过去国内人员常常担心硬件达不到要求, 怕机器不够先进，而未重视书面程序和书面证据， 对控制管理的重要性没有充分认识。

目前中国使用的是什么版本 GMP？

目前疫苗行业使用的是新版 GMP《药品生产质量管理规范(2010 年修订)》, 2011 年 3 月 1 日起施行，并要求在规定期限内未达到新版 GMP 要求的企业将不得继续生产药品。GMP 认证由非强制转变为强制认证。

新版 GMP 重点要求哪些方面？

新版 GMP 更要求：

1. 数据真实性，完整性，批记录可追踪，有备份功能，且都要有审计追踪功能
2. 打印功能：每批可打印记录
3. 数据存储：要有数据上传存储功能，导出的数据不能更改
4. 授权：具有权限设置，特别是可设置的参数之处，只有 QA 人员才能进行数据更改。
5. 防污染，防交叉污染
6. 防人为差错
7. 原材料，工艺过程，厂房设施，工艺设备，等都有文件支持及固定程序, 如工艺设备的

IQ/OQ/PQ 等文件。

工艺设备中的离心机在疫苗生产中可用到哪个环节？

对于疫苗企业生产环节中使用离心机（高速及超速）进行样品分离纯化的方法已被广泛使用，比如流感疫苗、狂犬疫苗、脊髓灰质炎疫苗、脑膜炎、Hib 肺炎、百日咳、流行性乙型脑炎、乙型肝炎等多种疫苗的纯化。Koki Holdings 公司（前身为 Hitachi Koki 日立工机公司）的 himac 系列离心机自 1955 年至今已有 60 多年的制造历史，其超速及高速离心机已被国内外众多疫苗企业所使用，用在样品前处理中样品的收集及除杂质，病毒样品的浓缩，及最终的纯化等过程中。

himac 离心机在数据管理方面如何满足 GMP 要求？

himac 离心机主机本身具有密码锁功能，设有三级管理权限。其 Log Manager 软件可进行实时的数据管理；记录间隔可从 10 秒到 5 分钟不等。该软件符合 U.S. FDA 21 CFR Part II，具有数字签名；审计跟踪；数据文件加密等功能，保证全过程所有数据真实、完整、可追溯，符合 GMP 的要求。himac 超速离心机主机本身也具有 USB 及 LAN 接口，作为数据通

讯使用.另外，该网络版 Log Manager 软件可同时管理多达 16 台 himac 超离或高离，进行实时数据管理，实现了远程数据管理。

himac 离心机在灭菌及防污染方面能提供哪些保障？

新版 GMP 特别强调防污染，生物安全是所有疫苗生产首要考虑的事情。himac 离心机可加装 HEPA，部分转头可高压灭菌，也有生物安全转头及特殊密封型转头可选，为生物安全提供了保障，保证了疫苗的品质。

如果是大规模生产用的离心机，可以做到 SIP（在线蒸汽灭菌）吗？

对于大规模生产的需求，用户可以选择 himac 的大容量连续流超速离心机 CC40NX，进行大量样品的提纯。该 CC40NX 满足 GMP 的要求， 且在消毒灭菌方面，除了常规的 CIP，还有独有的 SIP（在线蒸汽灭菌）功能，能更好的保障消毒灭菌及疫苗的品质。

FAQ in GMP regarding Vaccine Production

What is GMP?

GMP, the abbreviation of Good Manufacturing Practices, are the practices required in order to conform to the guidelines that control the authorization and licensing of the manufacturers of pharmaceuticals and food and etc. GMP request these manufacturers to implement policy, process control, quality assurance and testing to assure the products are consistently high quality and meeting regulation.

Who established the GMP?

WHO (World Health Organization) has established detailed guidelines for good manufacturing practice. Many countries have formulated their own requirements for GMP based on WHO GMP. Others have harmonized their requirements, for example in the Association of South-East Asian Nations (ASEAN), in the European Union and through the Pharmaceutical Inspection Convention.

When did the GMP begin?

The first WHO draft text on good manufacturing practices (GMP) was prepared in 1967 by a group of consultants at the request of the Twentieth World Health Assembly (resolution WHA20.34). It was subsequently submitted to the Twenty-first World Health Assembly under the title Draft requirements for good manufacturing practice in the manufacture and quality control of medicines and pharmaceutical specialties and was accepted.

What is the correct concept to implement GMP?

Making poor quality products does not save money. In the long run, it is more expensive finding mistakes after they have been made than preventing them in the first place. GMP is designed to ensure that mistakes do not occur. Implementation of GMP is an investment in good quality medicines. This will improve the health of the individual patient and the community, as well as benefiting the pharmaceutical industry and health professionals. Making and distributing poor quality medicines leads to loss of credibility for everyone: both public and private health care and the manufacturer.

What is the current version of the GMP?

The current document is a revision of WHO Good manufacturing practices for pharmaceutical products: main principles, previously published in WHO Technical Report Series, No. 961, 2011, Annex 3.

What are the main requirements of the current version of GMP?

The current version GMP emphasize on:

1. Data authenticity, integrity, batch record traceability, backup and audit trail functions
2. Print function: printable records per batch
3. Data storage: To have data upload storage function and the exported data cannot be changed.
4. Authorization: With permission settings, especially where parameters can be set and only QA personnel can make any changes.
5. Prevent contamination nor cross-contamination
6. Avoid human mistakes nor errors
7. Raw materials, processes, plant facilities, process equipment, etc. have document support and fixed procedures, such as IQ/OQ/PQ for process equipment.

Which part of the process equipment is used in vaccine production?

High speed and ultra-speed centrifuges have been widely used for separating and purifying samples in the production process of vaccine production, such as influenza vaccine, rabies vaccine, polio vaccine, meningitis, Hib pneumonia, whooping cough, epidemic encephalitis, hepatitis B and other vaccines. The himac series of centrifuges from Koki Holdings (formerly Hitachi Koki Hitachi Machinery Co., Ltd.) have been manufacturing for more than 60 years since 1955. Its ultra-speed and high-speed centrifuges have been used by many world famous vaccine companies for sample collection, treatment, removal of impurities, concentration of the virus sample, and final purification.

How does the himac centrifuge help users to meet GMP requirements in data management?

The himac centrifuges come with password access function with three access levels. Its Log Manager software provides real-time data management that can record intervals range from 10 seconds to 5 minutes. The software complies with U.S. FDA 21 CFR Part 11, with electronic signature, audit trail, data file encryption and other functions that can ensure that all data in the whole process is true, complete, traceable and in line with GMP requirements. The himac ultracentrifuge also has built-in USB and LAN port for data communication. In addition, the network version of Log Manager Software allows managing up to 16 himac ultra and high speed centrifuges and performing real-time data management and realizing remote data management.

What protection does the himac centrifuge offer in terms of sterilization and contamination prevention?

The current version of GMP put emphasis on contamination prevention. Biosafety is the primary consideration for all vaccine production. The himac centrifuge can be equipped with HEPA. Some of the rotors can be autoclaved. There are also bio-safe rotors or bio-sealed rotors, which provide bio-safety and ensure the quality of the vaccine.

If the centrifuge is used for large-scale production, can SIP (Sterilization In Place) be done?

SIP

For large-scale production needs, users can choose Himac's large-capacity continuous flow ultracentrifuge CC40NX for a large number of sample purification. The CC40NX meets the requirements of GMP. In addition to the conventional CIP, CC40NX has the unique SIP (Sterilization In Place) function for disinfection and sterilization which can enhance the efficiency of sterilization and thus the quality of vaccine is guaranteed.