1. 目的 Objective

建立质量风险管理程序，对可能影响到最终产品质量的风险因素进行确定，评估和控制，保证最终的产品 质量。指导公司规避质量事故或药害事件的发生，保护患者的切身利益。

The Quality Risk Management Procedure is established to define, evaluate and control potential risks to product quality, and to help to avoid adverse quality issues or accidents so as to assure patient benefit.

2. 范围 Scope

适用于公司质量体系内的质量风险管理。

This procedure applies to quality risk management of Gosun quality system.

3. 责任 Responsibilities

3.1 所有人员职责：按本规程执行质量风险评估，准备文件。

It is the responsibility of all personnel conducting Quality Risk Assessment and preparing the documents to adhere to this procedure.

3.2 质量风险管理组长

Team leader of quality risk management

3.2.1 负责协调跨职能和部门的质量风险管理。

Take responsibility for coordinating quality risk management across various functions and departments of the organization.

3.2.2 确保质量风险管理程序按本 SOP 规定执行，并且有充足的资源可用。

Assure that the quality risk management process as defined in this SOP is followed and that adequate resources are available.

3.3 质量受权人：负责批准《质量风险评估表 》及关闭风险管理程序。

The Qualified Person: approve < Quality risk assessment sheet > and closing of a risk management process.

3.4 QA 办：负责审核在产品生命周期内对其质量风险进行评估、控制、信息交流和回顾评审的系统化过程。

QA Office: review the systematic process of evaluation, control, communication and review of quality risks during the life circle of products.

4. 引用标准及文件 References

《药品生产质量管理规范(现行版）》

<China Good Manufacture Practice > (current)

EU GMP 指南 Volume 4

<EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use (Volume 4 ）〉

ICH Q9

5. 内容 Contents

5.1 定义 Definition

5.1.1 可测定性：发现或测定危险源存在的能力

Detectability - the ability to discover or determine the existence, presence, or fact of a hazard.

5.1.2 危害：对健康的伤害，包括产品质量缺陷或可获得性造成的伤害

Harm - damage to health, including the damage that can occur from loss of product quality or availability.

5.1.3 危险源：潜在的危害来源。

Hazard - the potential source of harm.

5.1.4 质量风险管理：一套系统的程序，用于药物产品生命周期中的风险评估、控制、信息交流以及回顾。

Quality risk management - a systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product life cycle.

5.1.5 可能性：有害事件发生的频率或可能性。

Likelihood - frequency or probability of the adverse event occurring.

5.1.6 严重性：对危险源可能造成的后果的衡量

Severity - A measure of the possible consequences of a hazard.

5.1.7 风险评估：对可能造成系统故障的原因进行仔细检查，以便做出合理可行的决策，减少或者预防故 障的发生。

Risk Assessment - A careful examination of what could cause failure of the system so that decisions can be made about what is reasonably practicable to reduce or prevent malfunctions.

5.2 质量风险管理程序的适用范围包括并不局限于以下情况：

This quality risk management procedure applies but not limited to the following issues:

5.2.1 确定洁净房间和洁净空气设施的监控位置。

Defining environmental monitoring positions of clean room and HVAC systems;

5.2.2 设定生产的标准和工艺参数。

Establishing limits and parameters of manufacturing process;

5.2.3 评估变更影响。

Evaluating effect of changes;

5.2.4 确定偏差调查和纠正措施的程度。

Determining levels of deviation investigations and correction actions;

5.2.5 评估工艺的薄弱和高风险区。

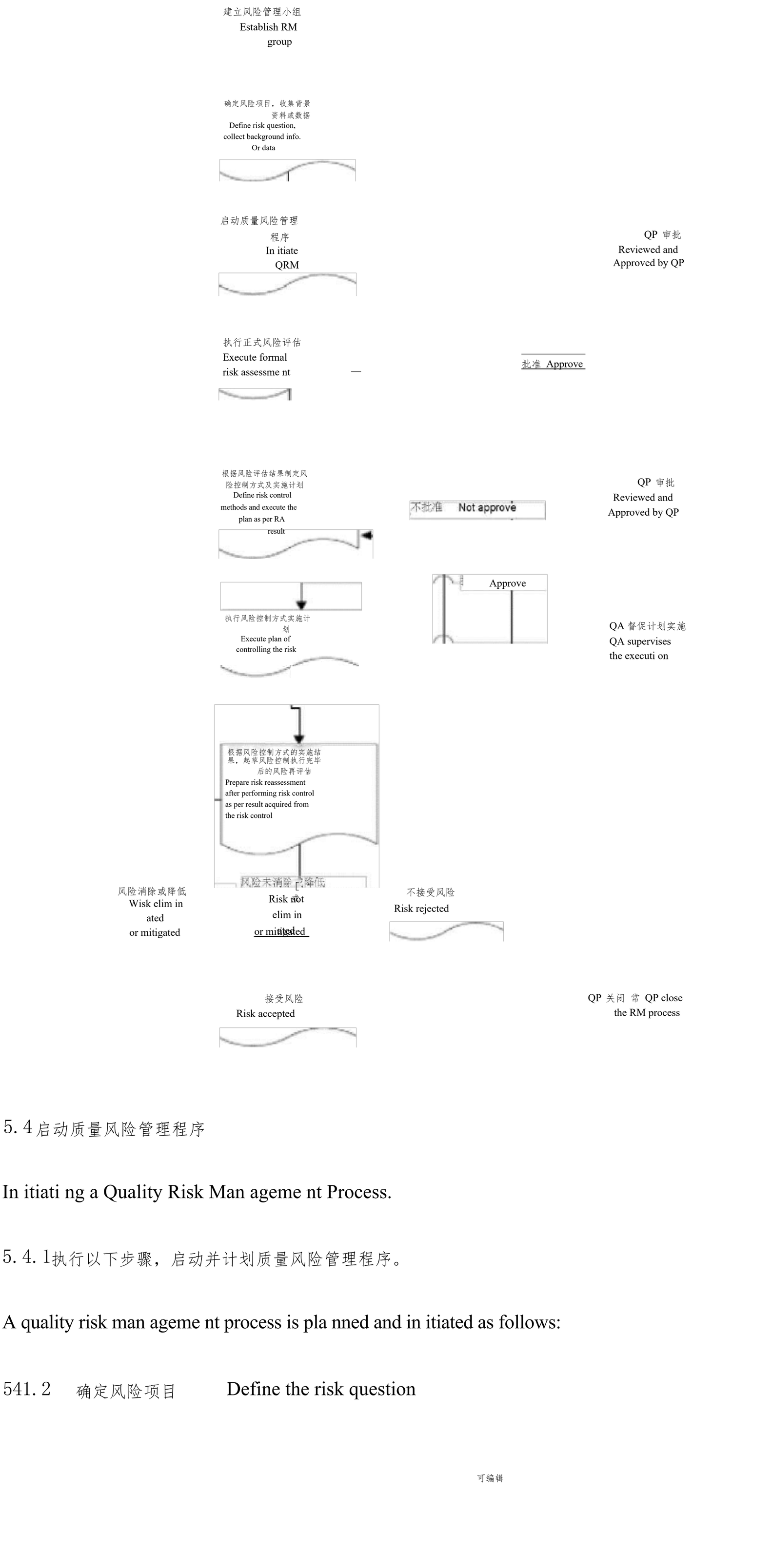
Evaluating and defining weakness and high-risk issues of manufacturing process.

5.3 质量风险管理流程

Quality Risk Management Process

质量风险管理流程图

Quality Risk Ma nageme nt Flow Chart



5.4启动质量风险管理程序

In itiati ng a Quality Risk Man ageme nt Process.

5.4.1执行以下步骤，启动并计划质量风险管理程序。

A quality risk man ageme nt process is pla nned and in itiated as follows:

541.2 确定风险项目 Define the risk question

确定难题或风险问题， 包括对相关潜在风险的设想。 质量风险评估从一个定义明确的难题或风险疑问开始。

Define the problem and/or risk question, including pertinent assumptions identifying the potential for risk. Quality risk assessments begin with a well-defined problem description or risk question.

5.4.1.3 组建质量风险管理小组 Organize a quality risk management team

由难题或风险问题部门负责人或其指定的人员担任组长，风险管理小组的成员应该至少包括该难题或风险 问题部门的成员及 QA 人员。同时根据需要，也可以邀请其他相关部门的专业成员参加。

The person in charge of or the person designated by the person in charge of the department which possesses the problem or risk question is designated as the leader of quality risk management team, and personnel engaged in the department which possesses the problem or risk question QA personnel should be involved in the quality risk management team at least. Experts of other relevant department might be involved in the team, where necessary.

5.4.1.4 风险管理小组组长，搜集潜在危险源、危害或风险评估相关的人员健康影响的背景资料或数据，并 向风险管理小组的成员讲解整个项目的情况，帮助风险管理小组成员了解整个项目。

The leader of quality risk management team assembles background information and/or data on the potential hazard, harm or human health impact relevant to the risk assessment and explains the program to team members to help them get to know this program.

5.4.1.5 风险管理小组成员依据自己的专业， 使用 5.6 中介绍的质量风险管理方法， 找到该项目中可能存在 的影响到产品质量的危险源，并对这些危险源进行分析讨论，确认各类危险源对最终产品质量影响的严重性， 风险管理小组组长根据最后的风险分析的结果， 起草《质量风险评估表》 （编号： G04.016- R $_1$）第一部分内容， 《质量风险评估表》第一部分的内容应包括但不限于：风险项目名称、存在的危险源、风险发生后的危害、目 前的控制方式等。

According to their expertise, quality risk management team members employ the quality risk management tools listed in article 5.6 to identify and analyze potential risk sources that may affect

product quality and define the severity; the team leader prepare the first part of Quality Risk assessment Sheet （No.: G04.016- R $_1$） based on the conclusion of risk analysis. The content of Quality Risk assessment Sheet includes but is not limited to name of the risk question, existing hazard resources, possible consequences and current controls, etc.

5.4.1.6 明确风险评估的计划开始时间和完成时间 Specify the timeline of risk management process.

5.4.2 质量风险分析报告交相关部门会审， QP 批准质量风险评估的启动。

After being finished, the quality analysis report is reviewed by relevant departments and approved by Qualified Person before the quality risk assessment program is initiated.

5.4.3 从质量管理部文件 QA 处取得质量风险评估编号，按以下方式编号： QRA yy-mm-dd ，yy 为两位年 号，mm 为两位月号，dd 为两位月度流水号。 文件 QA 发放编号的同时登记 《质量风险管理台帐》（编号：G04.016-R $_3$）。

The QA personnel in charge of documentation assigns a number to quality risk assessment in the form of “QRA yy-mm-dd ”, where “ yy” is the last two figures of the year, “mm ” is the two figures indicating the month, and “dd ” is the two sequential numbers which are renewed monthly.

The assigned number is recorded in Quality Risk Management Log （No.: G04.016-R $_3$） by the QA personnel in charge of documentation.

5.5 执行正式风险评估 Deploy a risk assessment

5.5.1 按以下步骤执行风险评估 The risk assessment is deployed as follows:

5.5.1.1 质量风险评估启动后，由风险管理小组组长组织小组成员，或邀请其它相关部门的专业成员， 填写《质量风险评估表》 （编号： G04.016- R $_1$）第二部分内容—执行正式风险评估，第二部分的内容应包括但不限于：数据评估（总结数据的充分性，有效性及其他相关方面） 、风险识别、风险分析及评估、拟定采用的控制 方式，风险控制实施的标准等。

After a risk assessment is initiated, members of the quality risk management team and/or experts

of relevant departments, organized by the team leader, fill out the second part of Quality Risk assessment Sheet (No.: G04.016- R $_1$) with (including but not limited to) data assessment (adequacy, effectiveness and other related aspects of the data), risk identification, risk analysis and evaluation, proposed risk control methods, acceptance criteria of execution of risk control, etc.

5.5.1.1.1 由风险管理小组组长组织小组成员， 或邀请其它相关部门的专业成员， 收集相关数据（历史数据、 理论分析、已知的见解或相关利益者的关注点），并总结数据的充分性、有效性及其他相关方面。填入《质量 风险评估表》（编号： G04.016- R $_1$)的“数据评估”中。

Members of the quality risk management team and/or experts of relevant departments, organized by the team leader, assemble relevant data (historical data, theoretical analysis, informed opinions or concerns of stakeholders), summarize adequacy, effectiveness and other relevant aspects and fill out the “ Data Evaluation ” item of the Quality Risk assessment Sheet (No.: G04.016- R $_1$).

5.5.1.1.2 风险管理小组成员依据自己的专业，根据风险提问(什么可能出错？)和问题描述，系统地利用 “数据评估”中的信息来确定该项目中可能存在的影响到产品质量的危险源，并填入《质量风险评估表》（编 号： G04.016- R $_1$)的“风险识别”中。

According to their expertise, quality risk management team members use fundamental question “what might go wrong ” and information listed in “ Data Evaluation ” mentioned above to identify hazards referring to the risk question or problem description and fill out the “ Risk Identification ” item of the Quality Risk assessment Sheet (No.: G04.016- R $_1$).

5.5.1.1.3 风险分析及评估： 风险管理小组对这些危险源进行分析讨论，确认各类危险源对最终产品质量 影响的严重性以及风险发生的可能性。如若可能，可应用风险管理工具分析和评价风险。风险管理工具的适用 性由危险源的特点和可能造成的严重性确定。

Risk analysis and evaluation: the risk management team estimate hazard resources, define the

severity of harms and likelihood of occurrence. Analyze and evaluate risk using risk management tools if appropriate. The appropriateness of the tool will be justified by the nature and probable severity of the hazard.

□ 风险控制的目的是为了减少或降低风险使其达到可接受水平。某种情况下，风险是可接受的。当风险超过可接受水平时，必须采取相关措施以降低或避免质量风险。

The purpose of risk control is to reduce the risk to an acceptable level. In some instances, it is appropriate to accept the risk. When risk exceeds an acceptable level then measures must be proposed for mitigation or avoidance of quality risk.

□ 风险减少一般包括危害的严重性和可能性的降低。

Risk reduction will generally include actions taken to mitigate the severity and probability of harm.

□ 提高危害的可测定性的步骤和引起的质量风险也可作为风险控制策略的一部分。

Processes that improve the detectability of hazards and quality risks may also be used as part of a risk control strategy.

□风险控制方式与风险的严重性相呼应。

The ways of the quality risk management process should be commensurate with the level of risk.

□ 评估降低风险影响的措施，这些措施可能造成新的风险或增加早前风险的严重性。

Evaluate the impact of risk reduction measures that may introduce new risk or increase the significance of early risk.

5.5.1.2 风险管理小组组长依据风险控制方式制定风险控制方式实施计划， 实施计划中应该包括， 但不局限 于以下内容：风险控制方式、控制方式的开始时间、控制方式的完成时间、控制方式的负责部门及负责人等。

According to the risk control measures the leader of risk management team prepare a risk control

plan, which includes but is not limited to risk control measures, starting time and closing time of risk control measures, responsible person and responsible department for implementation of risk control measures, etc.

5.5.1.3 质量风险分析报告交相关部门会审， QP 批准质量风险分析结果。

Quality risk analysis reports are reviewed by relevant departments and the conclusions of quality risk analysis are approved by the Qualified Person.

5.6 质量风险管理记录 Documentation of quality risk management

QA 在《质量风险管理记录》（编号： G04.016-R $_2$）中记录所有的质量风险控制实施情况。

Implementation of quality risk controls is recorded in Quality Risk Management Record (No.: G04.016-R $_2$) by QA.

5.7 质量风险分析的方法 Quality risk analysis methodology

在风险分析及评估过程中，如若可能，应用风险管理工具分析和评估风险。风险评估工具的适用性由危险 源的特点和可能造成的严重性确定。

Analyze and evaluate risk using risk management tools if appropriate. The appropriateness of the tool will be justified by the nature and probable severity of the hazard.

基本风险管理工具有：

Basic risk management tools include:

a) 简易化工具(流程图、检查表、头脑风暴等等)

Facilitation devices (flow charts, check sheets, brainstorming, etc)

b) 失败模式效果分析（ FMEA ）

Failure Mode Effects Analysis (FMEA)

c) 危害分析及关键控制点（ HACCP ）

d) 鱼骨图分析 Fishbone Analysis

Supporting statistical tools

－某些质量风险管理工具检测危险的能力（可测定性）被认为是对风险的评估。

- In some risk management tools, the ability to detect the harm （detectability ） is considered in the estimation of risk.

－风险评估的结果要么是对风险的定量评估，要么是对风险范围的定性描述。当风险被定性描述为 “高”“中”“低”时，尽量要对其进行详细描述。

- The output of a risk assessment will either be a quantitative estimate of risk or a qualitative description of a range of risk. When risk is expressed using qualitative descriptors, such as “ medium ” , or “ low ” , these must be defined in as much detail as possible.

5.8 风险评估的关闭 Closing of risk assessment

5.8.1 风险控制方式实施结束后，风险管理小组组长根据风险控制实施计划实施的结果，填写《质量风险 评估表》（编号：G04.016-R_i）第三部分内容：风险控制执行完毕后的风险再评估，对控制后的风险项目按 5.5 项重新进行风险评估，以确定风险是否消除或降低风险至可接受的程度。

At the end of execution of risk control protocol, according to the outputs of risk control, leader of risk the management team fills out the third part of Quality Risk Assessment Sheet （No,: G04.016- R_1）, Risk Reassessment, to reassess the risk as specified in article 5.5 and to determine if the risk is eliminated or reduced to an acceptable level.

5.8.2 风险控制执行完毕后的风险再评估内容应包括但不限于以下内容：控制方式实施后的风险结果、实 施风险控制方式前后的风险对比、实施结论等。

Risk reassessment includes but is not limited to outputs of risk controls, comparison between the risk before and after execution of risk controls, conclusion, etc.