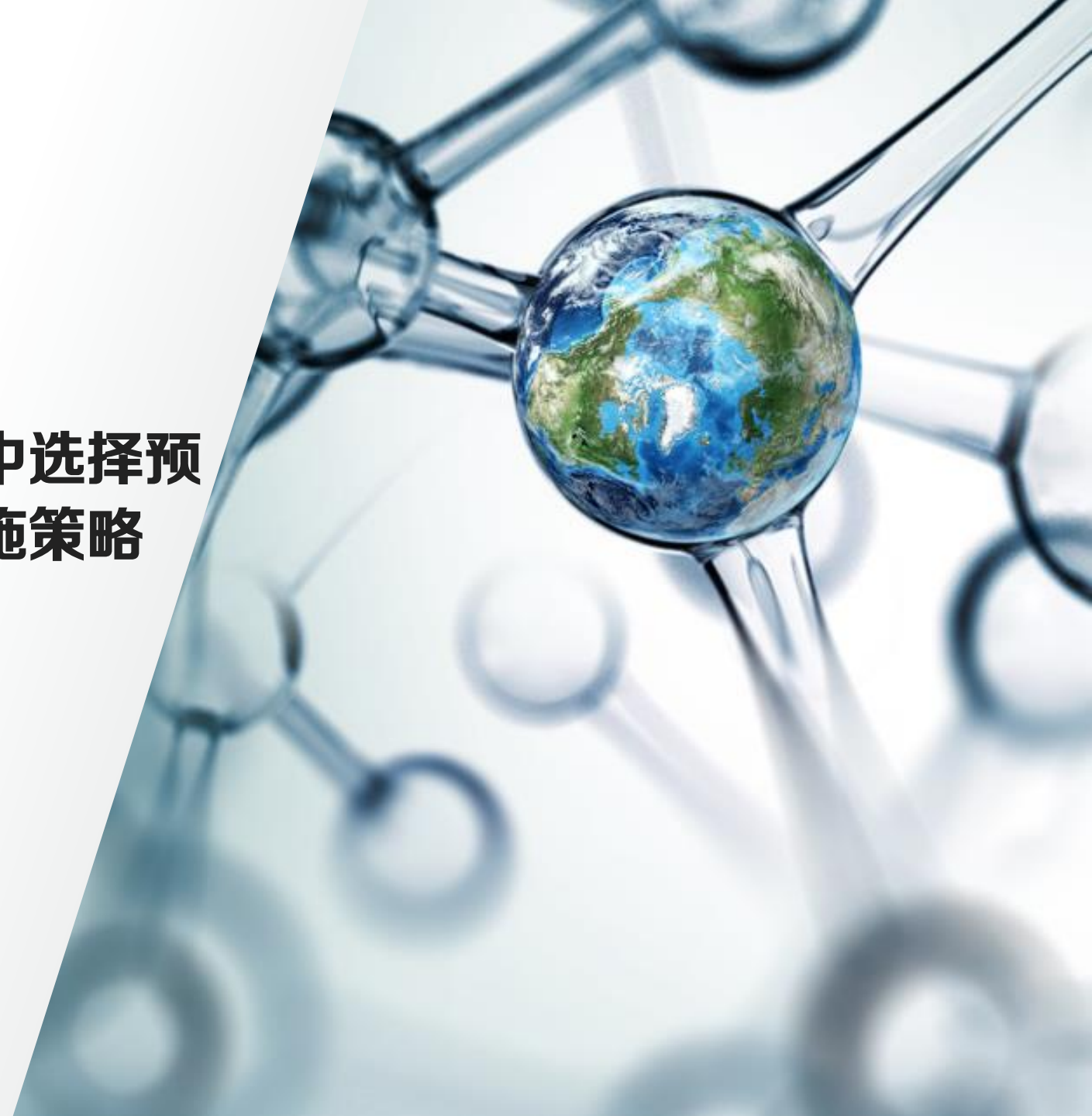


抗体类药物无菌注射剂开发过程中选择预充式注射器递送形式的挑战和实施策略

赛默飞Patheon™制药服务
全球SME
王新峰

 The world leader in serving science



Agenda

1

介绍

Introduction

2

预充式注射器的优势

Prefilled syringes: Benefits

3

如何准备进行预充式注射剂的设计

Planning for PFS introduction

4

在进行西林瓶向预充式注射器转换过程中
需要注意的要素

Criteria to Consider when switching from
vials to PFS

5

预充式注射器-一个多组件组成的装置

PFS a multicomponent device

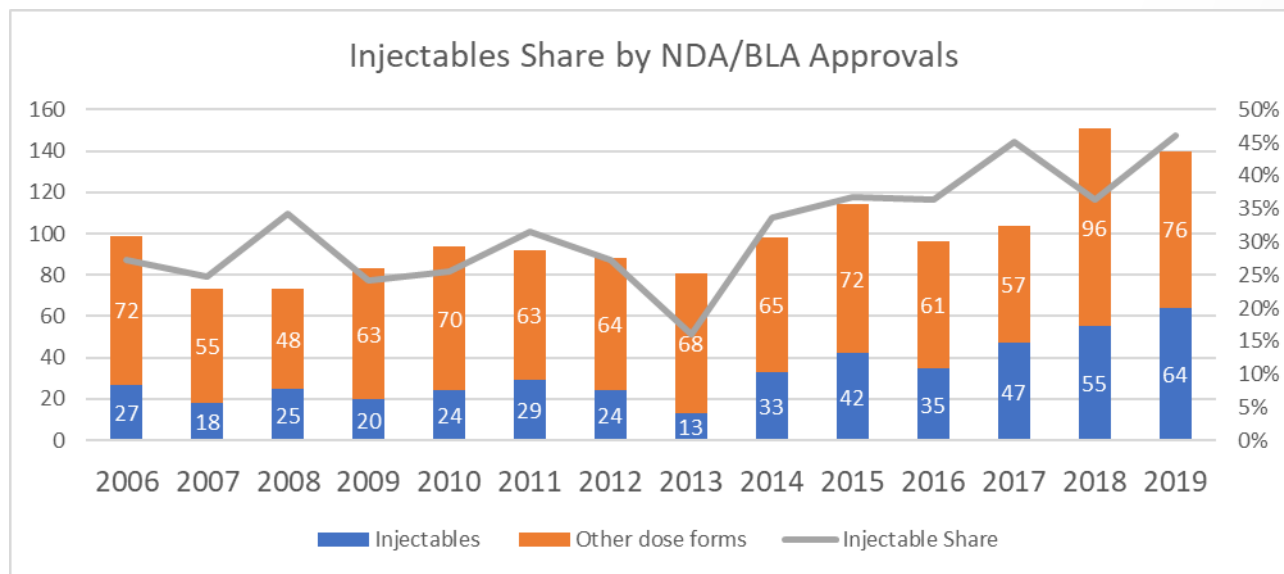
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要点和总结

Wrap-Up & Closing Remarks

注射剂在新药申请(NDA)/生物药物申请(BLA)批准中的份额

Share of injectable drugs in new drug application (NDA)/biologic drug application (BLA) approvals



液体西林瓶Liquid Vials



冻干西林瓶Lyo Vials



预充式注射器Prefilled syringes



预充式注射器市场预计到2029年将达到152.0亿美元
The market for pre-filled syringes is expected to reach \$15.20 billion by 2029 ¹

1) Fortune Business Insight, Mar 2022.

预充式注射器的优势

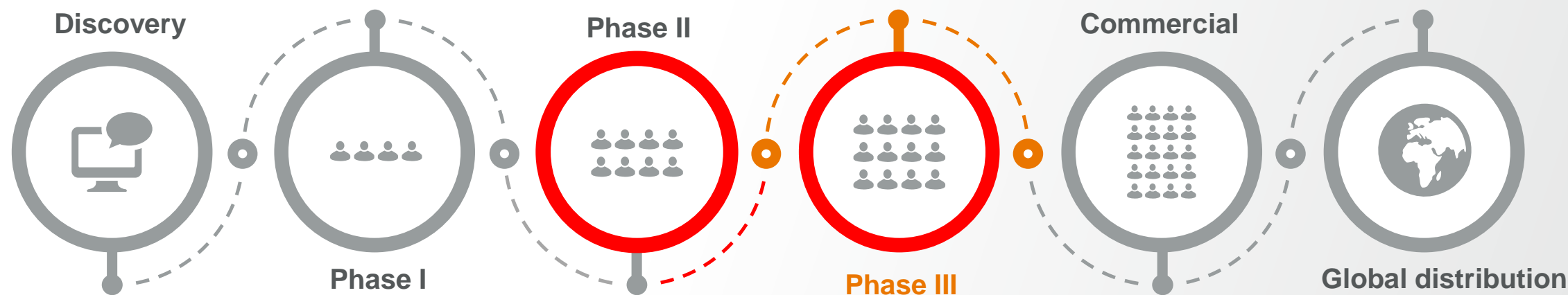
Benefits coming from prefilled syringes

- ✓ 在重症监护中，预充式注射器是进行救生治疗的快速手段 In critical care, prefilled syringes are a quick tool to administer life saving treatment.
- ✓ 能够在家自我管理，不需要住院治疗 Enables Ability to self-administration at home, without the need for hospitalization.
- ✓ 降低污染风险 Reduced risk of contamination.
- ✓ 尽量减少与医生的伤害风险，因为只需要简单的操作。 Minimized risk of injuries with physicians, as minor handling is required.
- ✓ 提高计量精度 Improved dosing accuracy.
- ✓ 降低成本 Reduced costs
- ✓ 在市场上的竞争定位 Competitive positioning on the market



在整体开发策略中，什么时候是评估预充式注射器的最佳时机

When is the right moment to evaluate prefilled syringe in your development strategy?



临床3期阶段是否适合从西林瓶转向预充式注射器

Is Phase 3 the right moment to switch from vials to prefilled syringe?

At the initiation of Phase 3, a consistent amount of work has been done but other is still ahead

完成工作 Work Completed

- 制剂开发Formulation Development
- 工艺开发Process Development
- 动物研究Animal studies
- 安全性研究Safety Studies
- 稳定性研究Stability Studies
- 剂量递增试验Dose Escalation
- 分析方法开发Analytical Method Development
- 临床一期和二期研究Phases I and II

要做的决定 Decisions to be Made

- 剂型Presentation
- 剂量Dose
- 成分Components
- 临床试验研究设计Clinical Trial Study Design
- 商业供应策略Commercial Supply Strategy

未来工作 Work Ahead

- 临床3期研究Phase 3 Study
- 方法验证Method Validation
- 风险评估Risk assessment
- 识别关键参数Identify CPPs
- 工艺放大Scale up
- 注册Registration
- 工艺验证Process Validation
- 包装设计Packaging Design
- 法规申报Regulatory Submission

桥接策略将初始西林瓶包装形式与后期商业化预充式注射器连接起来 **Bridging strategy to link initial vial presentation to commercial prefilled syringes**

考虑 Considerations:

1

西林瓶制剂处方需要改变吗？

Does vial formulation need to be changed?

2

我们可以使用与西林瓶相同的材料制成的组件吗？ Can we use components made of the same materials used for vials?

3

你考虑过哪种注射器更适合预期的用途吗？
Have you considered which kind of syringes will fit better with the intended use?

4

预充注射器中存在的多个接触材料是怎样影响药品的稳定性？

How multiple contacts material present in prefilled syringes can affect drug product stability?

5

您所选择的预充注射器是否打算安装在自动注射器中？

Is your selected prefilled syringe intended to be assembled in an autoinjector?

内包装如何影响药品的稳定性

How primary packaging can affect drug product stability

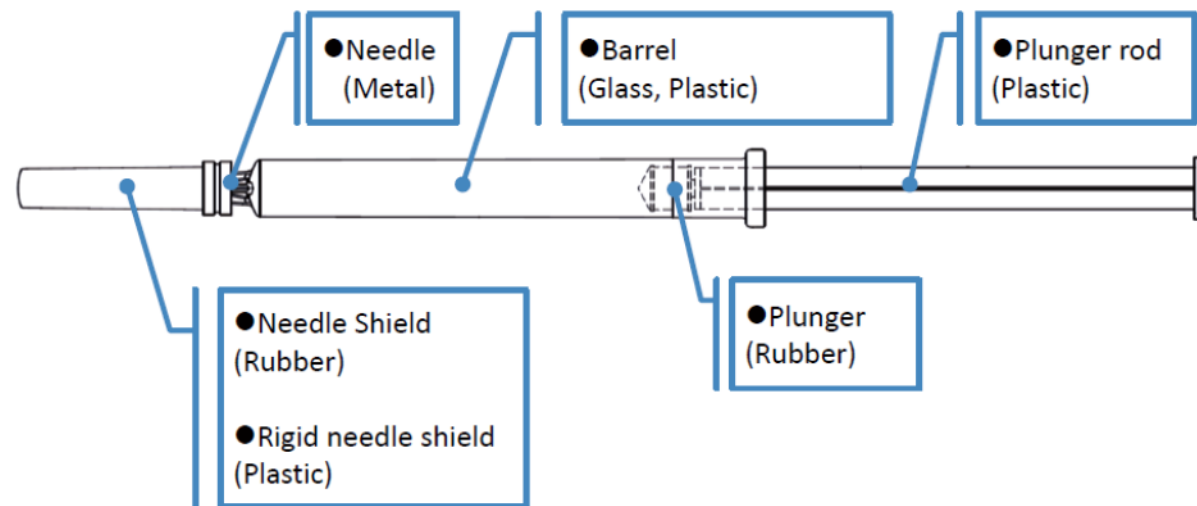
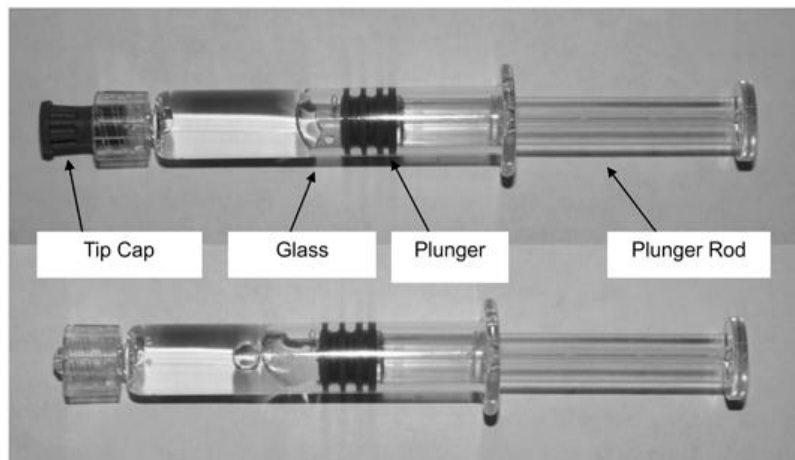
关键质量属性 Critical quality attribute	内包装的影响 Effect of primary packaging
Assay	Absorption, pH change, photostability
Uniformity of dosage	Accuracy in delivered dose
pH	pH fluctuation
Particulate matters	Presence of aggregates
Oxidation (Impurities)	Permeability of oxygen, presence of heavy metals
Particle size distribution	Induced crystallization
Extractables & Leachables	Different materials at contact

例子:潜在相互作用来源于接触的材料

Example of potential interactions depending from materials at contact

相互作用Nature of interaction	影响的因素Causing factor	相关联的物质Related material
Physical	Aggregation by silicon oil	Due to silicon needed to allow plunger gliding
	Aggregation by tungsten	For glass stacked needle
	Interaction with glue	For glass stacked needle
Chemical	Alkali elution	Glass PFS
	Gas permeability	Plastic PFS
	Residual Radicals	Dependent from sterilization process
Other	Delamination	Glass PFS

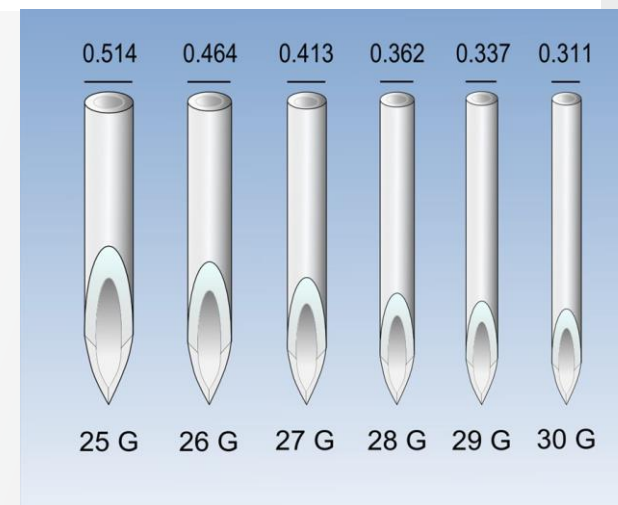
Luer Lock 鲁尔锁or 带针头一体式 Stacked needles?



皮内Intradermal: 25 – 27G

皮下Subcutaneous: 23 – 30G

肌肉Intramuscular: 18 – 25G



玻璃材质带针头一体式预充式注射器的常规的生产工艺过程

Typical manufacturing process for glass stacked needle syringe

- ✓ 注射器针筒是由有高温灼烧制的玻管成型制成 Syringes are formed using glass tubes molded by flames.
- ✓ 用钨钉定型的小孔将针头固定在针尖上，然后用UV固化的胶水粘合。The needle is applied to the tip with a tungsten pin and then bonded with a UV cured glue.
- ✓ 注射器针筒清洗，内表面硅化 Syringes are washed and the barrel is siliconized.
- ✓ 采用柔软或坚硬的针护套 A soft or rigid needle shield is applied.
- ✓ 注射器是嵌在蜂巢盒子中，保护管，用袋子包裹，然后灭菌(通常通过环氧乙烷处理)。The syringe is nested, tubbed, bagged, and then sterilized (usually through ethylene oxide treatment).



Key Takeaways 关键知识点



- Leverage product and process knowledge 平衡产品和工艺的知识
- Adopt scientific and risk-based approach 采取科学和风险导向的方法
- Identify TPP and CQAs 识别产品目标属性和关键质量特性
- Utilize early development data for developing commercial SKU 利用早期开发数据开发商业SKU



- Align with expectations and regulatory requirements 符合期望和监管要求
- Complete all required stage gates before moving on to Phase III 在进入临床三期之前完成所有的相关卡
- Risk-based process evaluation, data driven improvements 基于风险的过程评估，数据驱动的改进



- Plan and execute 计划和实施
- Define requirements at each project phase 明确项目每个阶段的需求
- Implement proper documentation throughout development and clinical phase work 在整个开发和临床阶段的工作中实施所需要的合适的文档
- Finalize Production & Marketing strategy 制定生产和营销策略

Thank you

