PSCI PHARMACEUTICAL SUPPLY CHAIN INITIATIVE
Building responsible supply chains

细菌内毒素检测的理论与实践

Bacteria Endotoxin Testing Theory and Practice

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嘉宾介绍 Speaker Bio

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- 背景：

王晓明 MD， MS，QD 瓦格纳生物科技咨询有限公司首席顾问微生物控制、无菌保障专家

毕业于首都医科大学医学系。87年至89年，任北京红十字朝阳医院内科住院医生。

1989年至1992年，在纽约瓦格纳学院（Wagner College） 学习微生物学，获得微生物细菌学硕士学位。1990年开始，先后在美国SGS，强生公司和礼来公司从事微生物质量控制，质量管理工作。曾任美国PDA （注射药协会）的Treasure,工业微生物协会新泽西分会副会长 （VP NJSIM，）。2006年至2014年，任纽约瓦格纳学院微生物系兼职教授。教授课程包括“公共卫生及临床微生物”、“食品、工业及应用微生物”、“高级细菌生理学”以及“病毒学”等课程。

2001年起， 在礼来公司任微生物实验室经理。 2015年，被礼来公司总部派到礼来苏州制药有限公司无菌胰岛素灌装项目负责无菌保障。 2018年6月至2022年 6月，任信达生物制药公司QC微生物执行总监及MST 无菌保障专家。2022年6月至今，任QD 瓦格纳生物科技咨询有限公司首席顾问。著有《制药工业微生物控制及无菌保障》《细菌内毒素》《气流流型测试》等著作

议程 Agenda

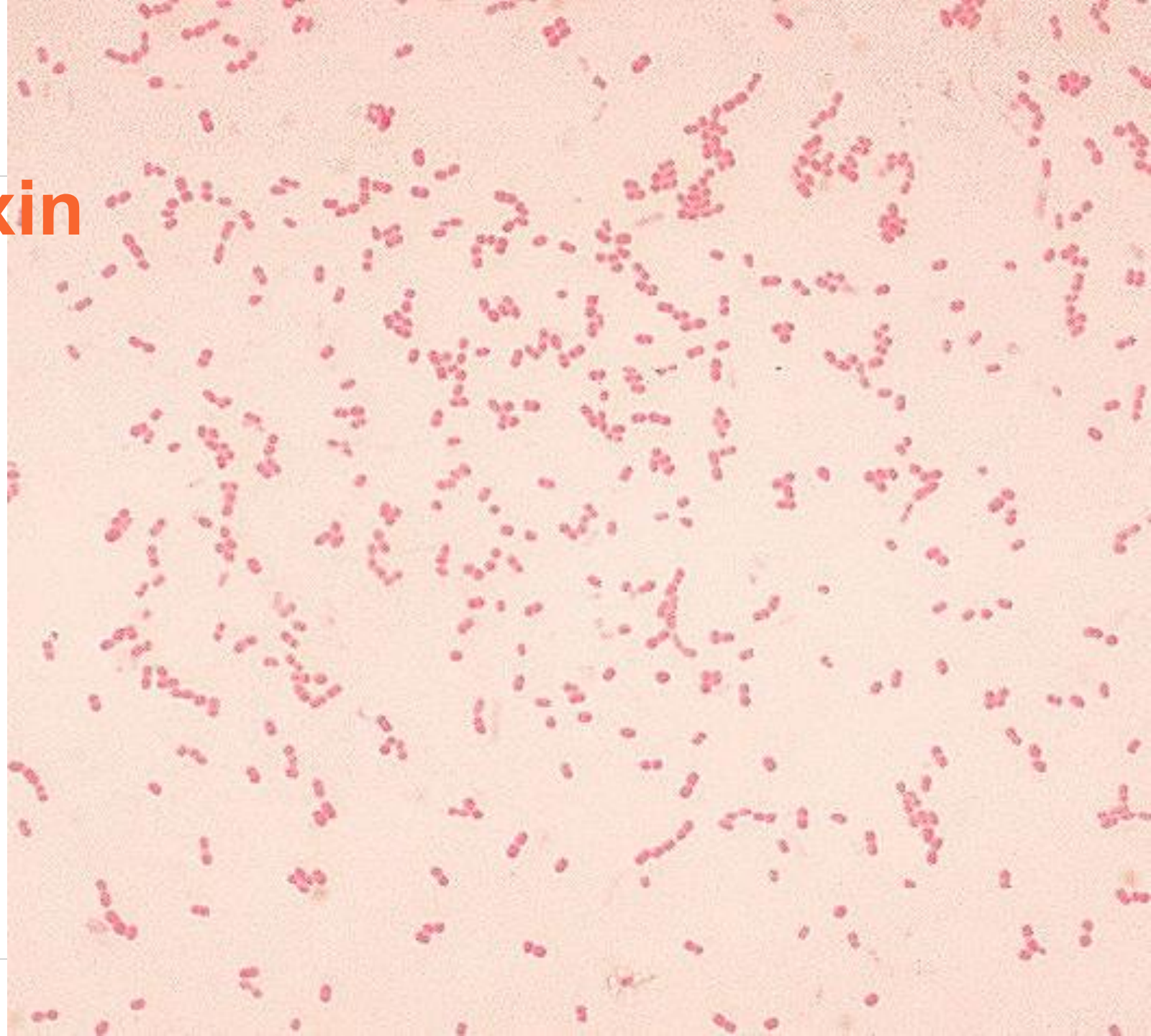
细菌内毒素检测理论及实践 Bacteria Endotoxin Testing Theory and Practice

细菌内毒素 Bacteria Endotoxin

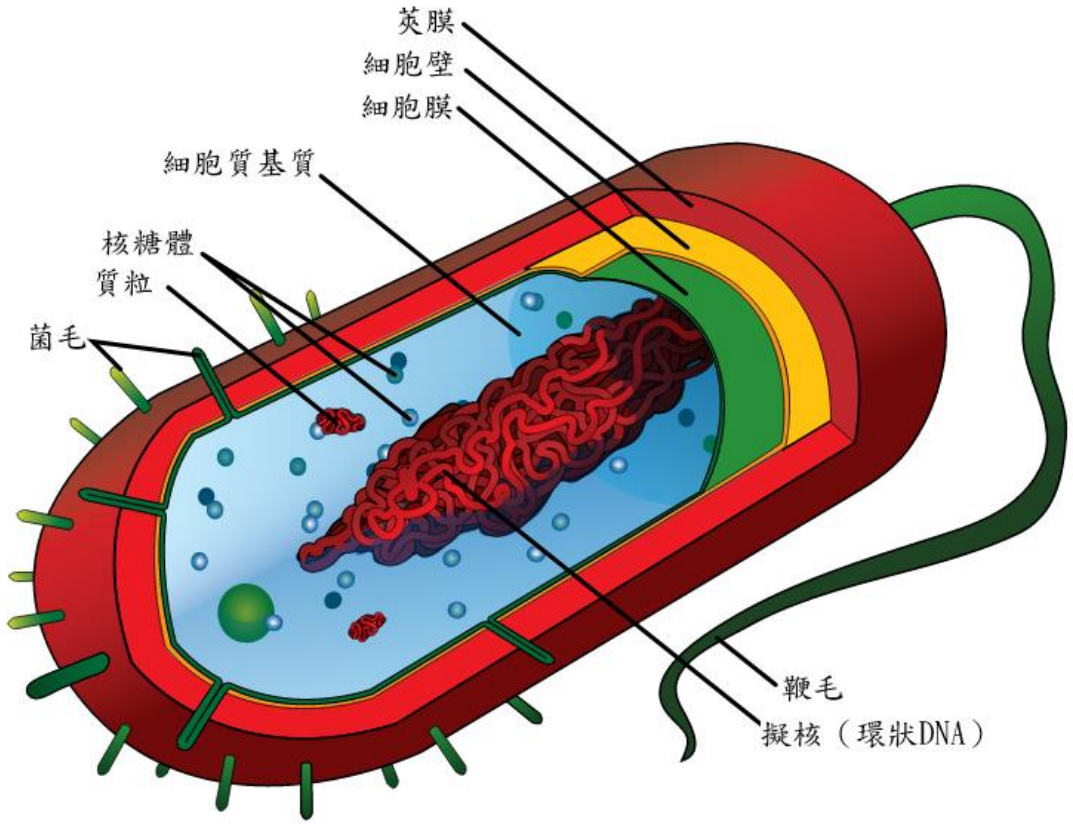
检测内毒素方法 Method for Detect endotoxin

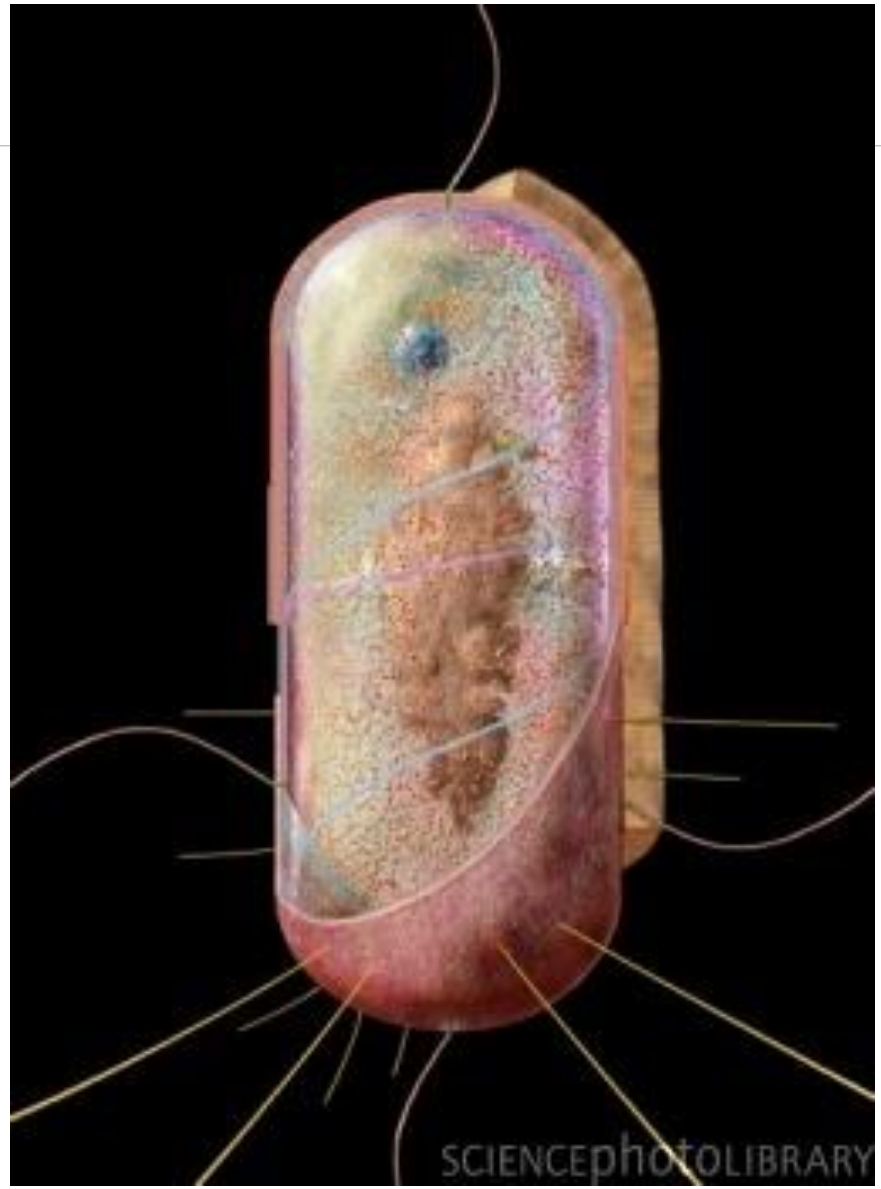
细菌内毒素检测的行业趋势 – rFC, rCR 的应用 Trend for BET –Using rCR, rFC

细菌内毒素
Bacteria Endotoxin

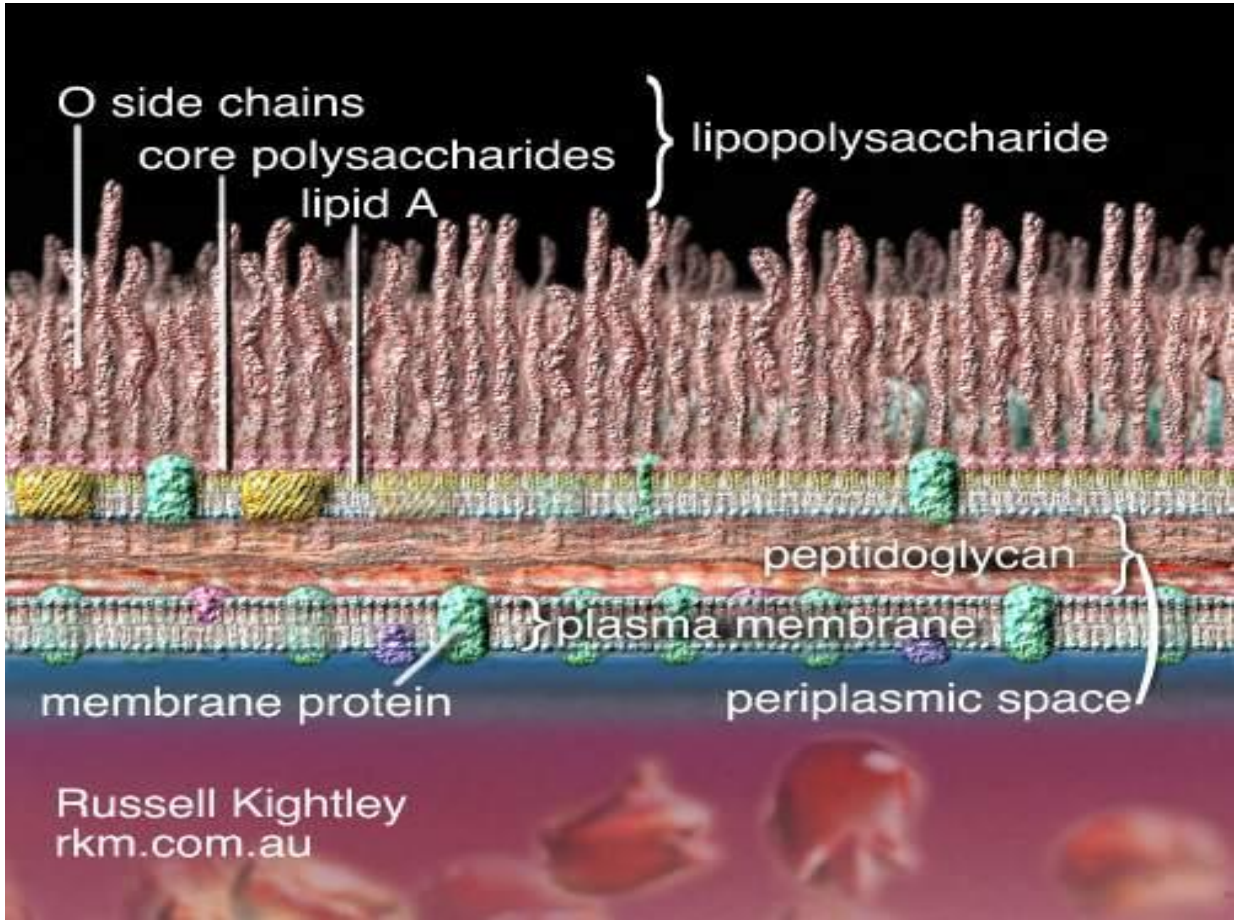


细菌内毒素
Bacteria Endotoxin

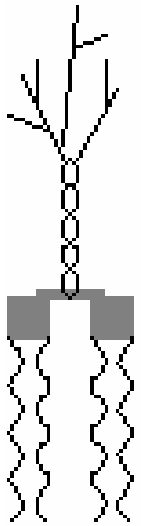




革兰氏阴性细胞壁 – 细菌内毒素



- 脂多糖 Lipopolysaccharide



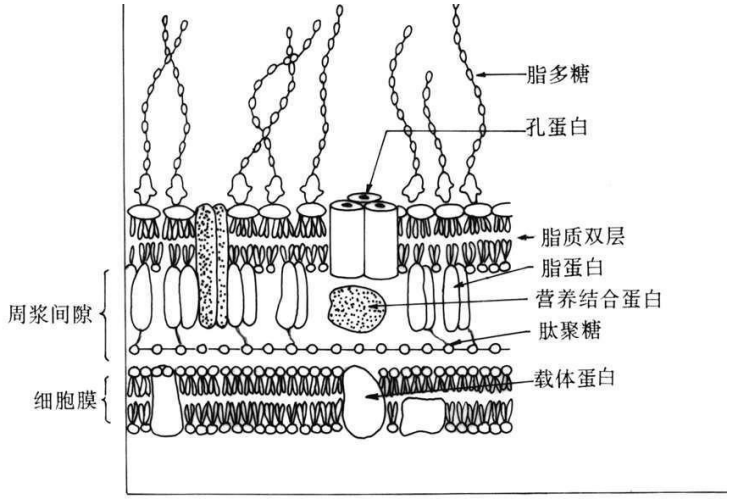
Chaînes latérales : Ag O　O抗原
(Somatiques)

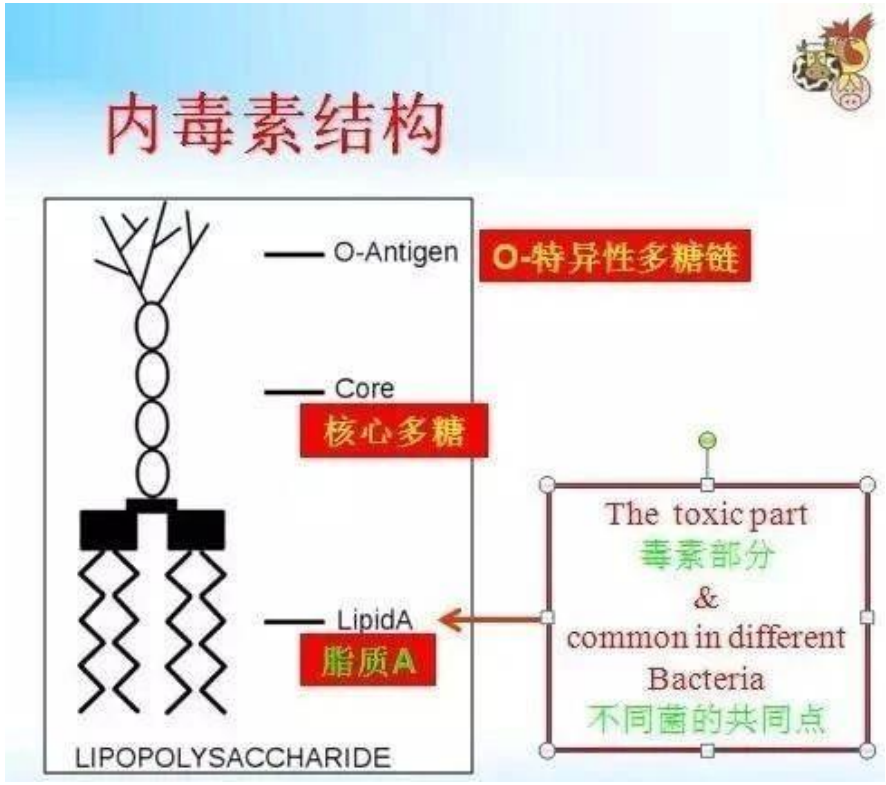
Core 多糖

Lipide A (dimère de β-1→6-glucosamine)
脂类A

细菌内毒素 Bacteria Endotoxin

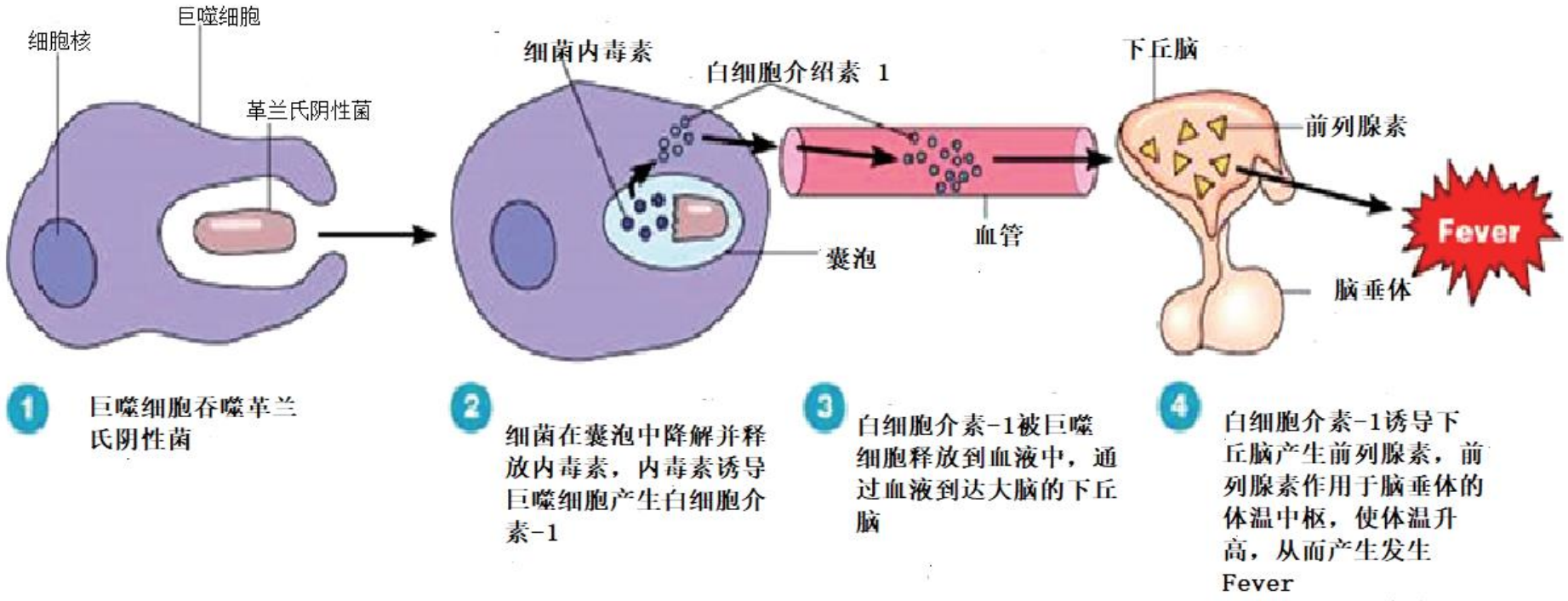
- FDA 严格限制
  - 化学成分：脂多糖
  - 脂A和多糖都是阴性菌的致病因子
  - 内毒素只有在阴性菌受伤或死亡后，才被释放出来



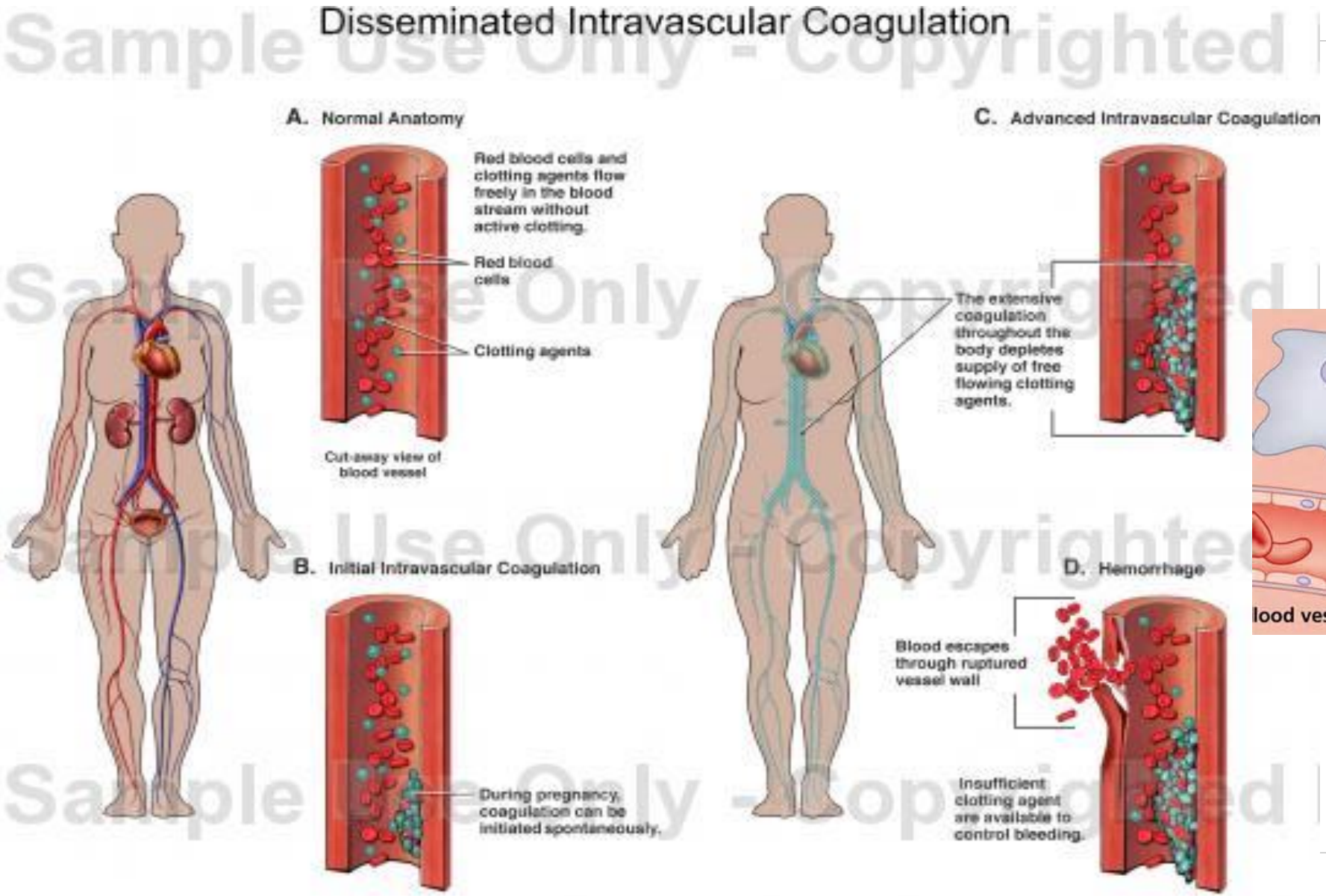


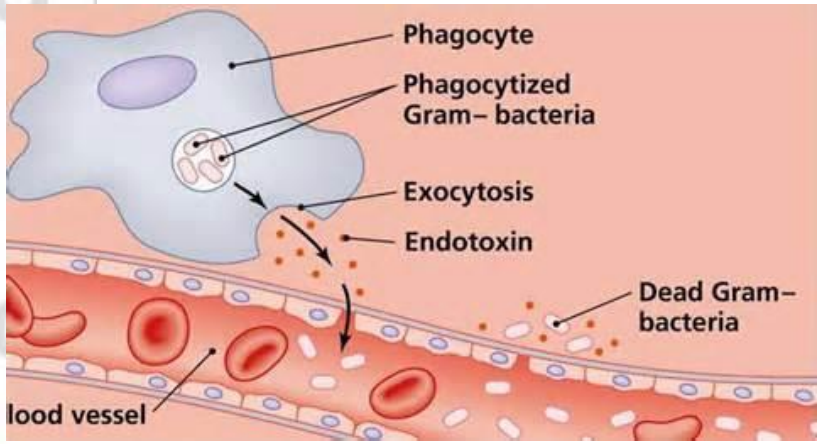
细菌内毒素的害处

- 败血症
- 弥漫性血管内凝血
- 休克，死亡



弥漫性血管内凝血 DIC





人体耐受细菌内毒素的限度

- 每公斤体重可以耐受5 内毒素国际单位
- 鞘内注射，每公斤体重可以耐受0.2 内毒素国际单位
- 非鞘内注射放射剂，每剂不超过175 内毒素国际单位
- 鞘内注射放射剂，每剂不超过14 内毒素国际单位
- 按照体表面积计算的配方药 （一般为抗癌药）： 每平方米体表面积可耐受 100 内毒素国际单位

细菌内毒素限度的设定

肠外用药类型	细菌内毒素可耐受标准（K）
人、畜用药或生物药	5EU/Kg
脊髓鞘内注射用药	0.2 EU/Kg
放射性注射用药	175 EU/最大剂量
脊髓鞘内放射性注射用药	14 EU/最大剂量
脊髓鞘内持续用药	14 EU/天
大输液剂	0.5EU/mL
注射用水	0.25EU/mL
医疗设备提取液	0.5EU/mL, ＜20EU/设备
脊髓鞘内使用的医疗设备	0.06EU/mL, ＜2.15EU/设备
眼睛前段接触的产品或设备	0.2 EU /mL，＜0.2 EU /设备
以上限度为药典建议（Compendial），[a]下面的为业界知名专家的建议。没有药典支持	
注射剂	70EU/最大剂量 [a]
辅料	3.5EU/多成分小体积辅料 [a]
新的化学实体，初步建议	1EU/mg 直到人体耐受水平的建立 [a]

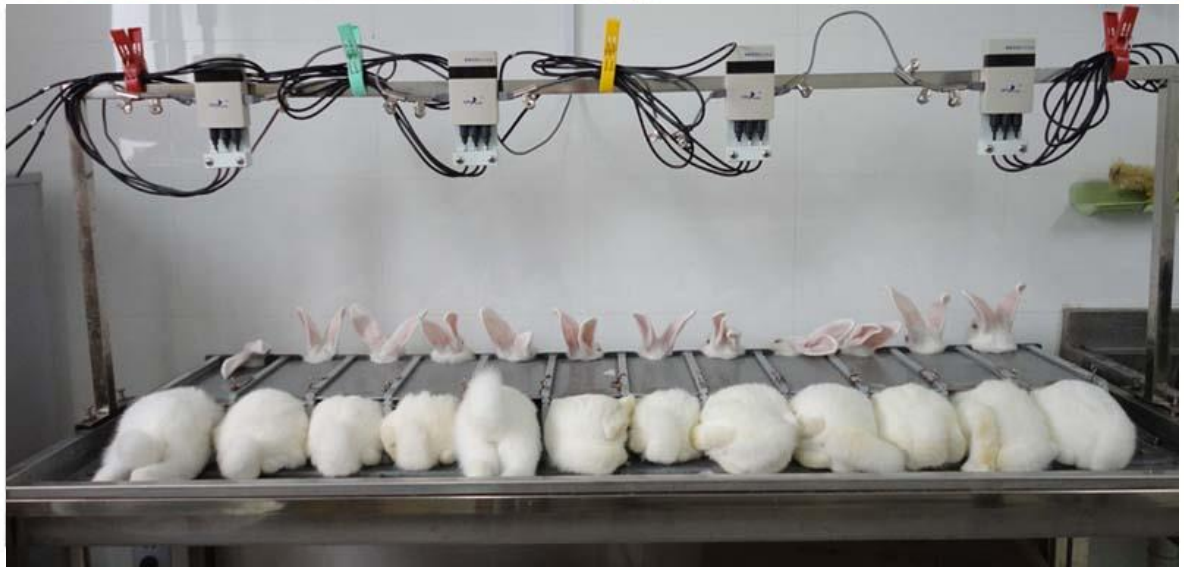
人体耐受细菌内毒素的限度

- 1996 年10月，美国疾病控制中心 （US Center for Disease Control，CDC), 对巴西一家26张病床的育婴堂内35例新生儿死亡事件进行了调查。这些新生儿是早产儿，在出生后24~72小时，死于败血症
- CDC 在检测了给这些新生儿使用的注射用水和25%葡萄糖注射液时发现，注射用水的细菌内毒素含量为0.8-5.8EU/mL (药典标准是0.25EU/mL), 25% 葡萄糖注射液的细菌内毒素含量是0.8-1.9EU/mL (药典标准是0.5EU/mL).
- 内毒素释放到循环系统引起败血症。内毒素的最小热原剂量为5EU/kg患者体重。对于一个体重70公斤的“典型病人”来说，大约需要350EU才能触发热原反应。这些新生儿的平均体重为2公斤。因此，只需要10 EU的内毒素就能引发疾病反应。只有2-3mL无菌注射用水或6-8mL葡萄糖溶液容易超过这个水平！

热源vs.细菌内毒素检测

美国药典 <151> 热原实验

- 经耳缘静脉注入10mL /Kg 38oC 产品
- 每30分钟检测肛温



为什么要用甞试剂

- 不利因素：
  - 家兔实验本身固有的特性，造成了实验结果的不稳定
    - 季节变化
    - 不同场地
    - 不同兔子的种属
  - 测试受测试样本的影响
    - 放射性药物
    - 癌症化疗药物
    - 催眠药和麻醉剂
    - 维生素、类固醇和某些抗生素
    - 许多新的药物形式，如蛋白质大分子生物制剂、基因治疗制剂、细胞制剂和其他制剂，本身可能与生物体发生反应，导致家兔发烧
    - 动物保护

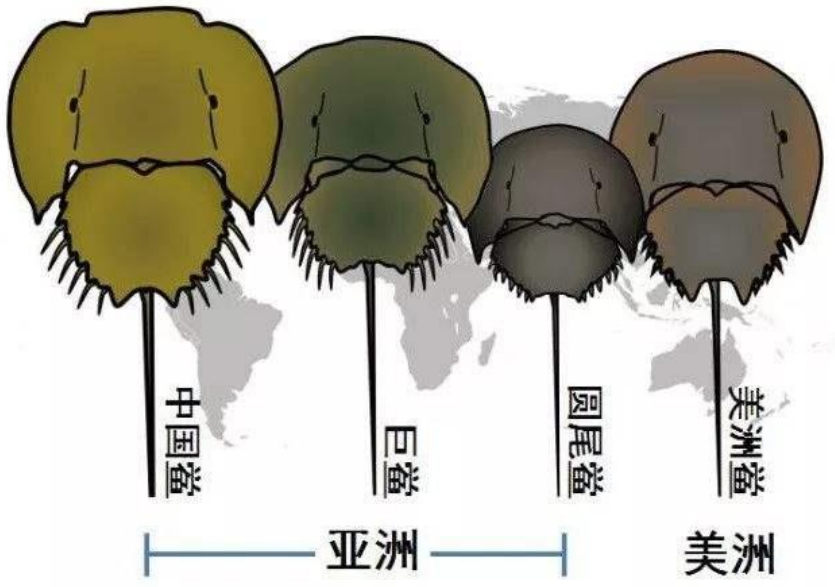
- 2024.06， 欧盟药典11.8章节，去除了家兔热原实验，并于2025.07.01开始实施。这些发展代表了动物福利向前迈出的重要一步，并将向全世界发出强烈的信息

细菌内毒素检测　Bacteria Endotoxin Testing （BET）

鲎（马蹄蟹）

Limulus amebocyte　(Horseshoe Crab)

细菌内毒素检测　Bacteria Endotoxin Testing （BET）

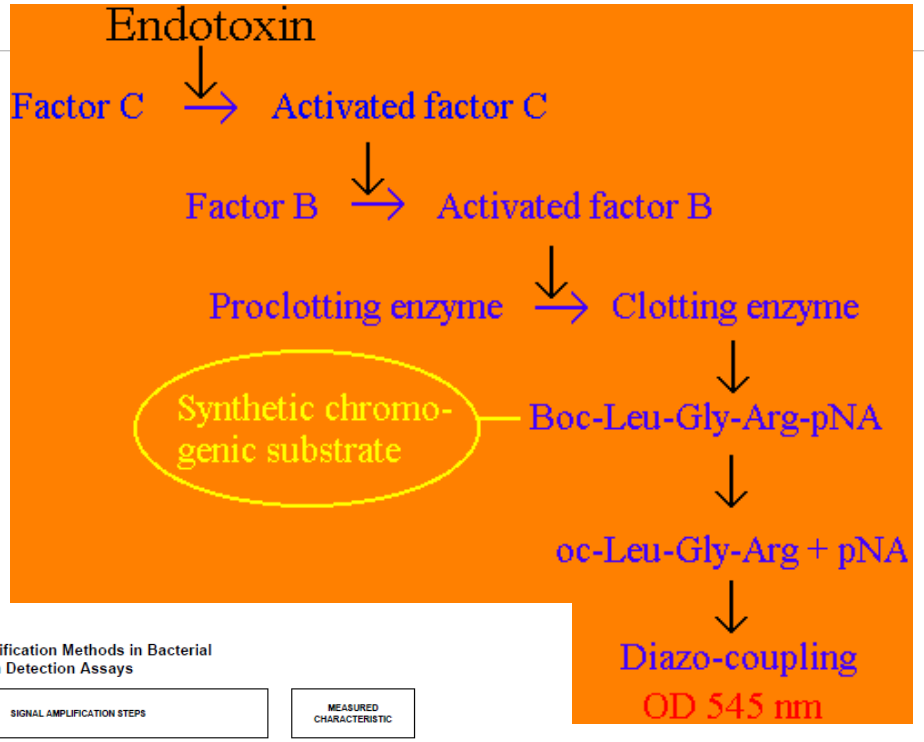


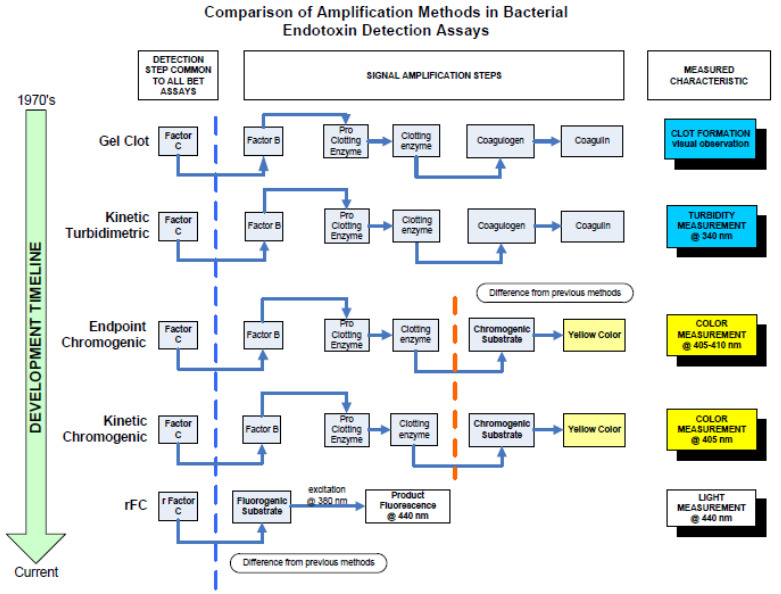
中华鲎 Tachypleus tridentatus

鲎试验 Lumilus Amebocyte Lysate （LAL）Testing

The LAL Assay

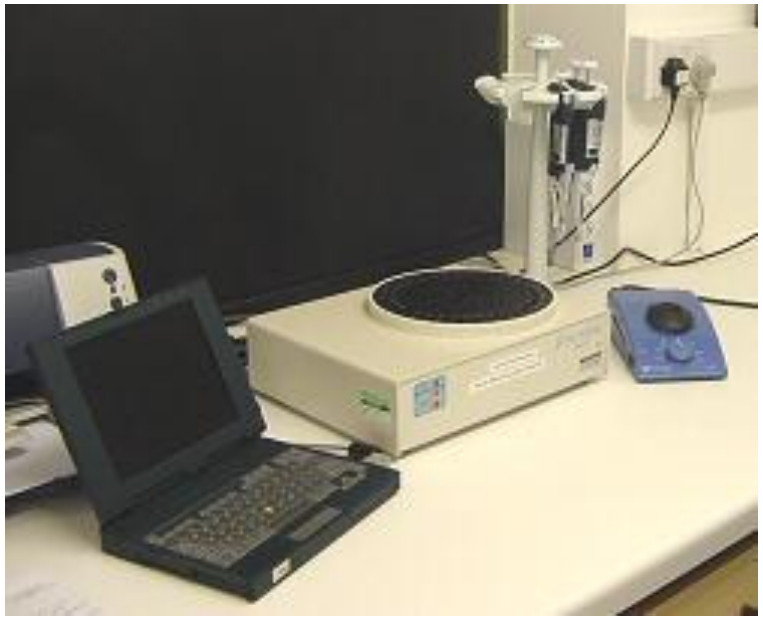
- The clotting properties of the horseshoe crab's blood were first documented by W.H. Howell of Johns Hopkins University in 1885.
- During the 1950's, the MBL scientist Fredrick Bang discovered the component of the blood that caused clotting to occur.
- Later, Dr. Bang and Dr. Jack Levin developed a method for detecting endotoxins using an extract of the white blood cells called Limulus Amebocyte Lysate (LAL).
- In the 1970's, the LAL test was recognized by the Food and Drug Administration (FDA) as an alternative to current methods of testing for endotoxins.
- Due to the efforts of Donald Hockstein, Edward Seligmann and James Cooper at FDA, the LAL test became an FDA required test for the presence of endotoxins in injectable drug products and implanted medical devices.

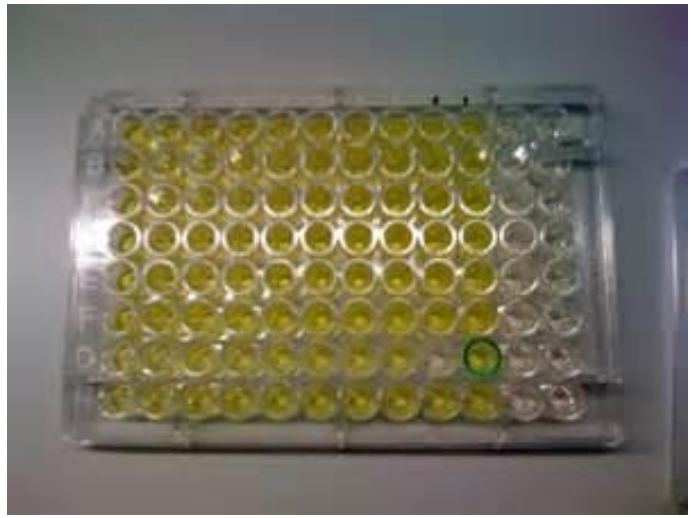




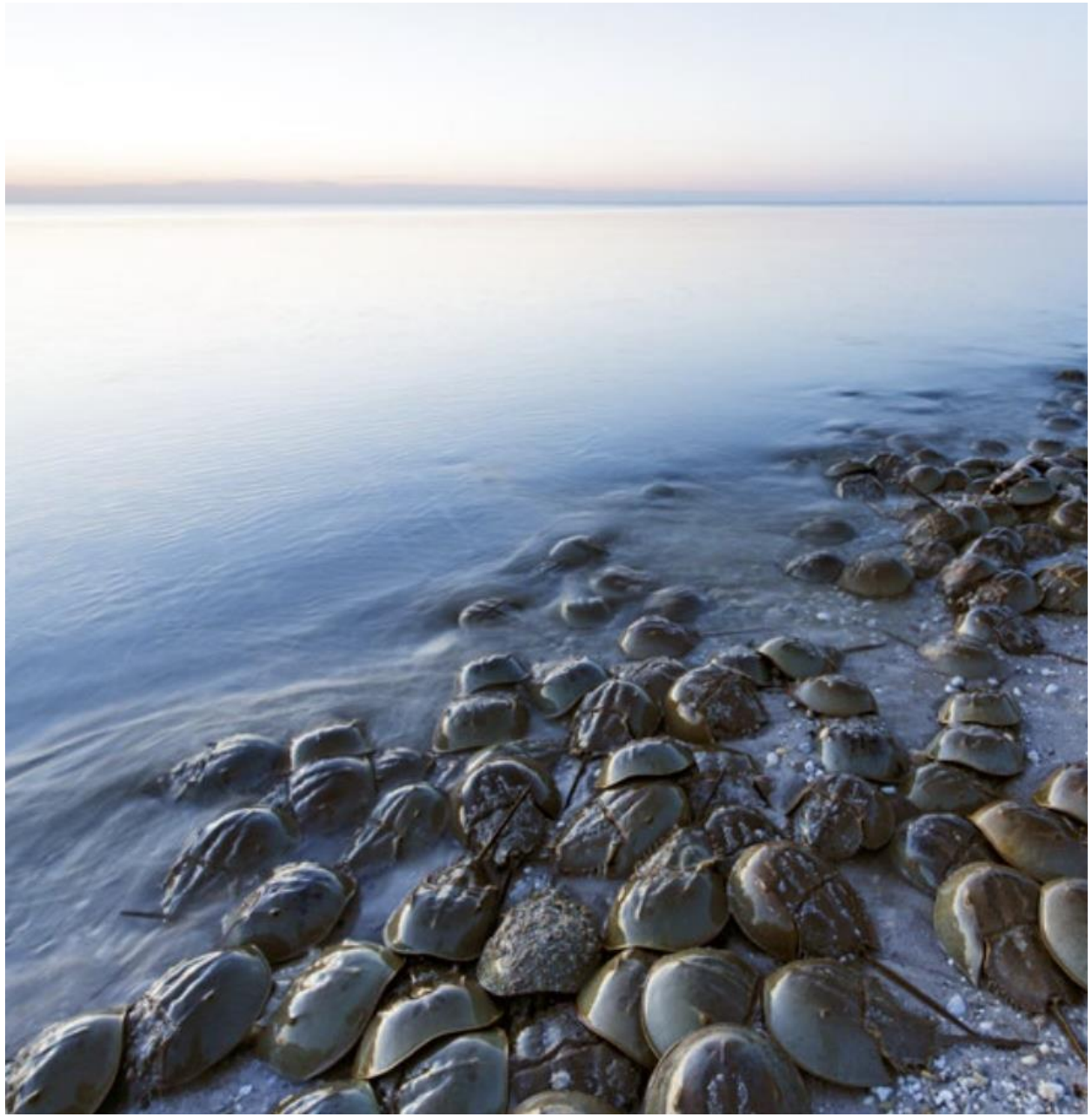
鲎试验 Lumilus Amebocyte Lysate （LAL）Testing

- 凝胶法Gel Clot
- 动态显色法KQCL
- 浊度法Turbidimetric





🦀 Horseshoe Crab



🦀 Horseshoe Crab

鲎短缺

- 疫情前，全世界每年进行7千万次鲎实验
- 由于制药行业对细菌内毒素检测的需求，马蹄蟹的数量逐年减少
- 据估计，北美每年有多达75万只马蹄蟹被采集血液。抽血后的死亡率　估计为15%，甚至可能高达30%。换句话说，每年至少有13万只马蹄蟹　因为对人类安全的检测而死亡
- 在全球范围内，美国对马蹄蟹的需求最高，2013年至2017年平均每年捕获52.5万只马蹄蟹
- 在美洲马蹄蟹数量最多的特拉华湾，马蹄蟹的数量从1990年的124万只下降到2002年的不到33.4万只

蛮短缺

- 福建省平潭河蟹的数量从1954年的1000对/天减少到2002年的4对/天
- 香港水域潮间带的幼虫数量在2002年至2009年的七年间减少了90%
- 在过去的15年里，大西洋马蹄蟹的数量减少了90%，该物种现在被列入世界自然保护联盟濒危物种红色名录
- 亚洲马蹄蟹的数量也受到了类似的影响，现在被认为是濒危物种
- 这种经历了四五次大灭绝的活化石，很可能在我们这一代消失

當短缺

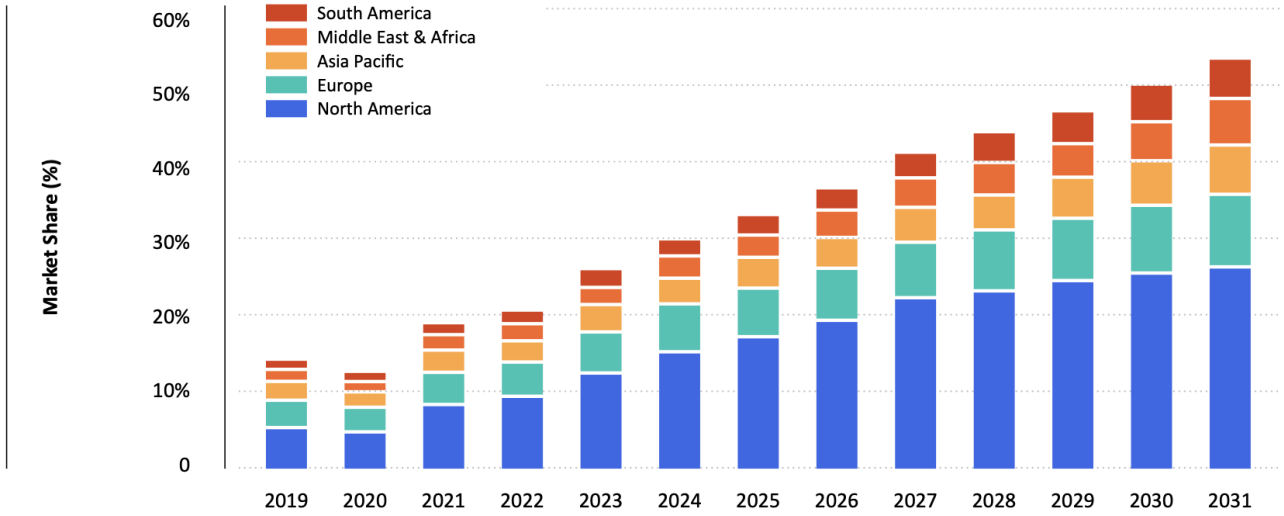
复眼
Compound eye
棘
INSIDE
THE CRAB
1 Head 头
2 Abdomen 腹
3 Tail 尾
壳
Carapace (shell)
食道
Gullet
卵
Eggs (female)
Stomach 胃
Brain 脑
步足
Walking legs
Gills 书腮

内毒素检测市场数据与背景

随着生物医学的发展，对内毒素检测的需求正在增加，预计将继续这样做，对鲎产生直接影响。

Endotoxin Testing Market Share (%) by Region (2019 - 2031)

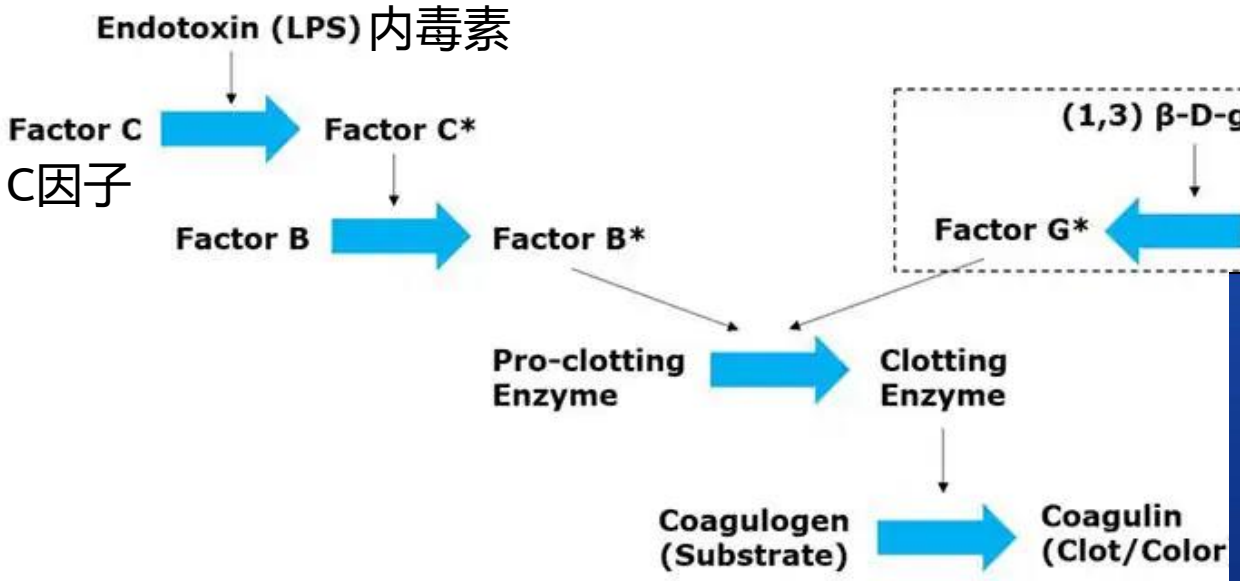
Chart from 'Endotoxin Testing Market Report 2025', Cognitive Market Research

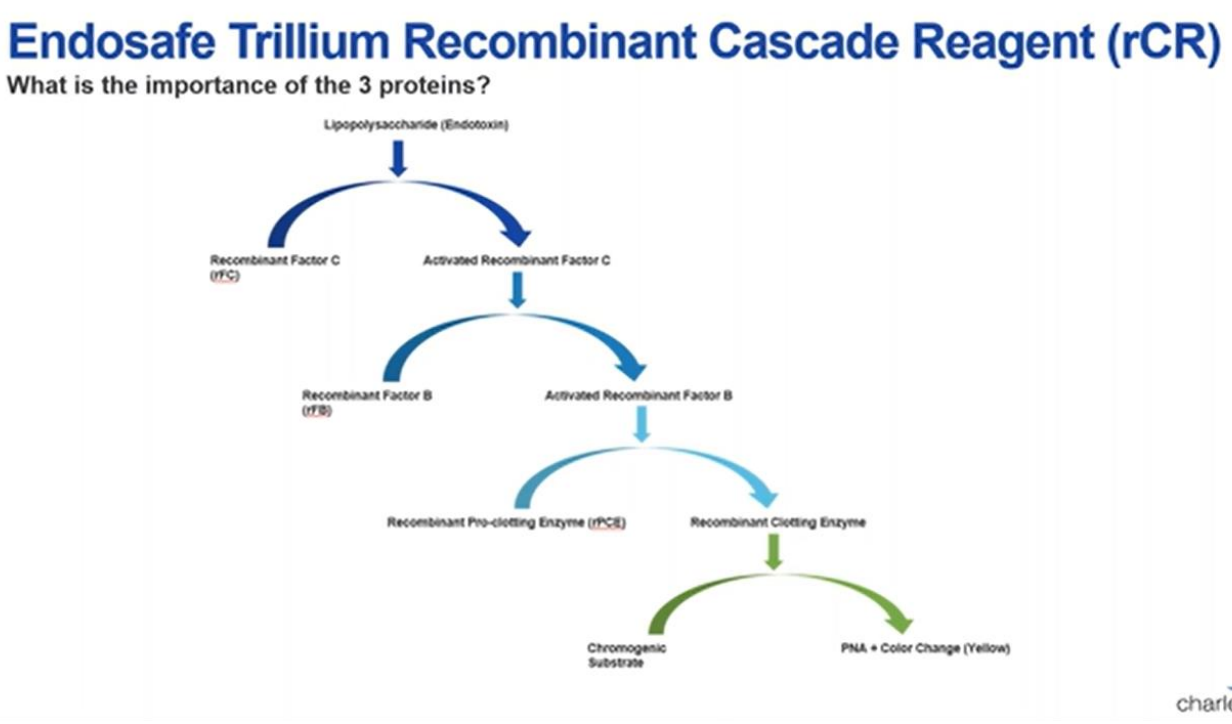


目前，每年大约有9千万到1亿剂细菌内毒素检测试剂出售，其市场包括:

- 注射用水
- 药品
- 透析产品
- 细胞、基于治疗产品
- 动物健康产品
- 医疗器械

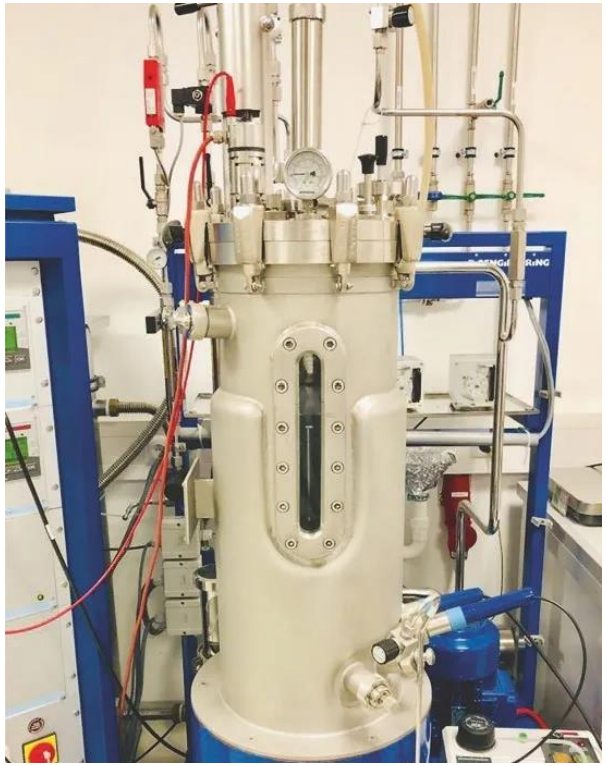
细菌内毒素检测的行业趋势 – rFC, rCR 的应用





细菌内毒素检测的行业趋势 – rFC, rCR 的应用

- 更高的可用性: 一个30L的生物反应器产生的rCR可以替代至少6000只马蹄蟹的血，不仅拯救了一个日益濒危的物种，还节省了时间和金钱



PSCI 会员

- **PSCI 会员代表着1.2 （一千两百亿美元）tn 的产值，70~80% 的市场份额**

From the Biggest*:

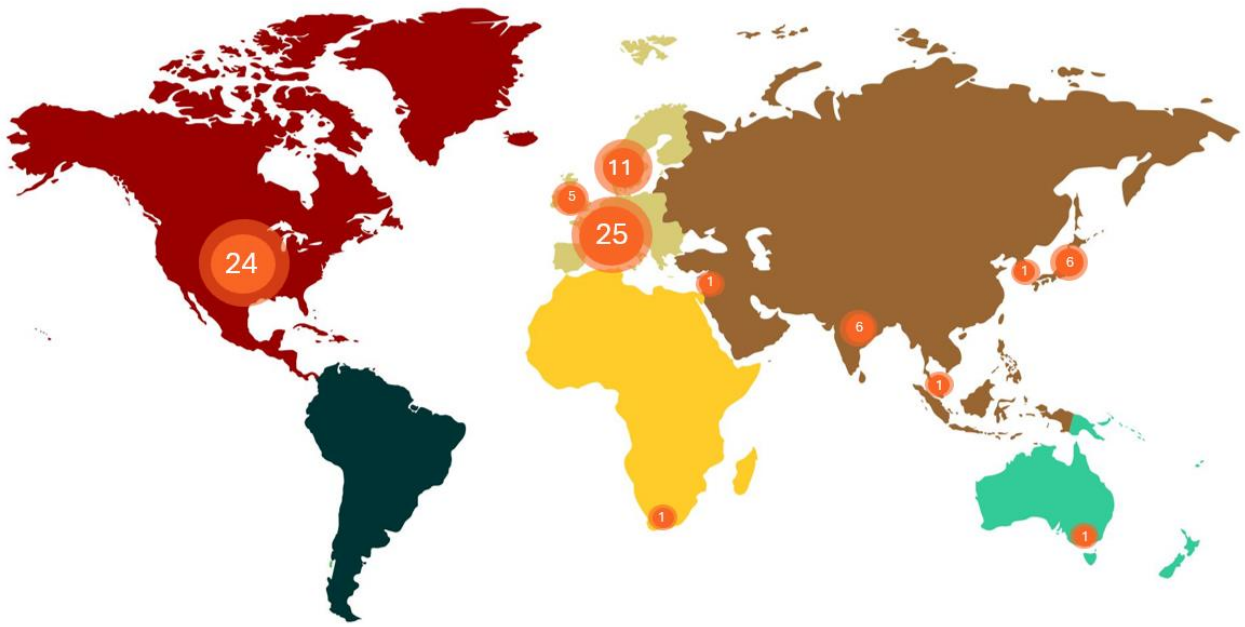
Johnson&Johnson, BASF We create chemistry, Roche, MERCK, Pfizer, abbvie, BAYER, sanofi, NOVARTIS, AstraZeneca, Bristol Myers Squibb, Abbott, gsk, Lilly, novo nordisk, Takeda, AMGEN, Boehringer Ingelheim, GILEAD, MERCK

To the Smallest*:

acino, ten 23, TIEFENBACHER GROUP, hameln, EVOLAN.

*2023 revenues

Geographic spread of membership:



PSCI 会员

PSCI 的立场

- ✓ **保护：** 所有的濒危物种，不再捕捞鲎
- ✓ **减少：** 使用天然资源的检测方法
- ✓ **理解：** 动物福利和动物保护立场

The PSCI's Position

Against this backdrop, the PSCI – representing 74 of the world's largest pharmaceutical companies and their suppliers – is pleased to affirm the following elements of good practice, and to encourage their adoption by all members:

Protect all endangered species – no further collection of TAL. The PSCI's members will end commercial pressure on the populations of *Tachypleus gigas* and *Tachypleus tridentatus*, by committing to no further collections from these species. PSCI members and first tier suppliers will no longer use TAL after existing supplies have been exhausted.

Minimize the requirements for naturally derived testing materials. The PSCI recognizes that members will potentially require a range of endotoxin testing techniques, and the availability of rFC, other recombinant reagents, and microfluidics offers members a route to dramatically reduce the demand for LAL. Members are encouraged to explore and adopt alternatives, setting themselves internal goals to minimize the volume of LAL used in their own operations and first tier suppliers.

Understand the animal welfare and conservation position. For the residual use of LAL, members are encouraged to take an active and intentional approach to sourcing, to understand where the material derives from and the animal welfare and biodiversity considerations that may result. Members are encouraged to co-operate and share data on traceability, populations and conservation status of *Limulus polyphemus*.

Governance and monitoring

This is a PSCI position paper, but it is not a formal membership requirement of PSCI; the organization believes it to be good practice and a progressive approach to be widely adopted.

Members are encouraged to adopt positions as set out in this paper and to promote their adoption throughout the supply chain.

PSCI in turn commits to:

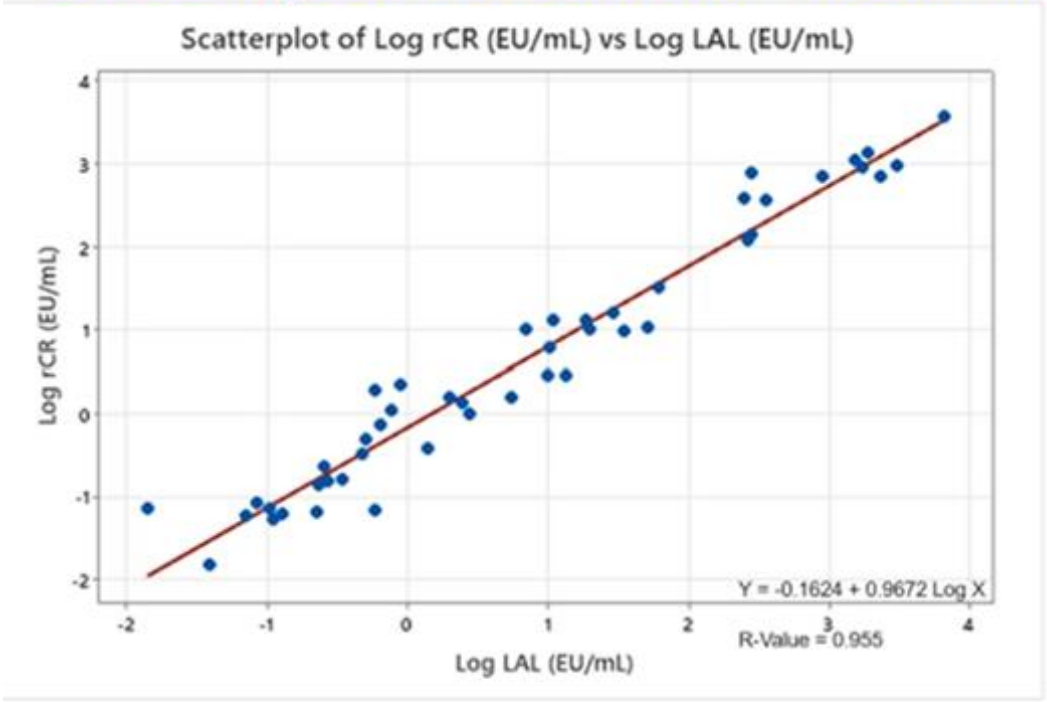
- monitor and review our members' approach on this and report it on an anonymized basis
- engage with others to learn and develop particularly on the US conservation position
- prepare guidance, materials and support to members and suppliers to implement the good practice elements of this statement.

***重要:** 这份文件不是成员的资格要求，而表明一个引领行业进步的姿态*

细菌内毒素检测的行业趋势 – rFC, rCR 的应用

- LAL的来源是区域性的，在全球一些地区，尤其是亚洲，不太广泛
- rCR可以在世界任何地方的生物反应器中持续生产，使全球供应能够跟上内毒素检测的需求

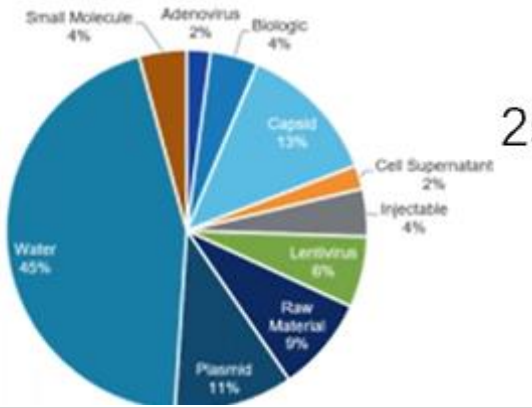
Beta Samples With Endotoxin Present in Both Data Sets



Statistical Analysis for the ratio of rCR Endotoxin Value (EU/mL) to LAL Endotoxin Value (EU/mL).

N = 47
Mean = 89.3%
StDev = 92.4
95% CI = 62.2%, 116.4%

The 95% CI range falls within the expected range of the test (50 – 200%) indicates that the rCR data is equivalent to LAL.



25% has endotoxin

细菌内毒素检测的行业趋势 – rFC, rCR 的应用

- 许多研究比较了rCR和LAL内毒素测试的性能，结果一致表明，市售的rCR测试至少与LAL测试一样好，甚至更好

Interference Patterns

Sample Composition: Small Molecule

Category	Dilution / Concentration	LAL EU/unit	LAL %Recovery	rCR EU/unit	rCR %Recovery
Small Molecule	1 mg/mL	<0.005	90	<0.005	107
Small Molecule	1:2000	<100	87	<100	72
Small Molecule	1 U/mL	<0.005	74	<0.005	63
Small Molecule	3.333 mg/mL	<0.0015	147	<0.0015	116
Small Molecule	1.667 mg/mL	<0.003	79	<0.003	86
Small Molecule	5 mg/mL	<0.001	138	<0.001	113
Small Molecule	2.5 mg/mL	<0.02	97	<0.02	83
Small Molecule	5 mg/mL	<0.001	82	<0.001	77
Small Molecule	5 mg/mL	<0.001	88	<0.001	69
Small Molecule	10 mg/mL	<0.005	67	<0.005	60
Small Molecule	5 mg/mL	<0.001	167	<0.001	88
Small Molecule	0.833 mg/mL	<0.006	93	<0.006	109
Small Molecule	0.667 mg/mL	<0.0075	72	<0.0075	108
Small Molecule	1:1	<0.005	75	<0.005	88
Small Molecule	1:1	<0.005	114	<0.005	90
Small Molecule	0.1 g/mL	<0.05	61	<0.05	79
Small Molecule	1 mg/mL	<0.005	133	<0.005	149
Small Molecule	1:1	<0.005	107	<0.005	99
Small Molecule	1:1	<0.005	70	<0.005	64
Small Molecule	1:1	<0.005	83	<0.005	78
Small Molecule	1:10	<0.05	86	<0.05	85
Small Molecule*	1:1	<0.005	N/A**	<0.005	70
Small Molecule*	1:10	<0.05	84	<0.05	99

* These are the same sample at two different dilutions

** Spike recovery not returned at 1:1, sample repeated at 1:10

Interference Patterns

Sample Composition: Capsids and Plasmids

Category	Dilution	LAL (EU/mL)	LAL % Recovery	rCR (EU/mL)	rCR % Recovery
Capsid	1:10	0.0509	106	<0.05	106
Capsid	1:10	<0.05	120	<0.05	123
Capsid	1:10	<0.05	127	0.0711	115
Capsid	1:10	<0.05	119	<0.05	94
Plasmid	1:10	0.0667	127	<0.05	108
Plasmid	1:10	0.053	114	<0.05	89
Plasmid	1:10	0.0506	126	<0.05	107
Plasmid	1:10	<0.05	107	<0.05	89
Plasmid	1:10	<0.05	110	<0.05	83
Plasmid	1:10	0.0523	128	<0.05	108
Plasmid	1:10	0.0637	131	<0.05	103
Plasmid	1:10	0.0576	131	<0.05	100
Plasmid	1:10	<0.05	131	<0.05	110

Interference Patterns

Sample Composition: Large Molecules

Category	Dilution / Concentration	LAL EU/unit	LAL % Recovery	rCR EU/unit	rCR % Recovery
Large Molecule	1:10	<0.05	129	<0.05	172
Large Molecule	1:10	<0.05	129	<0.05	189
Large Molecule	1:10	<0.05	143	<0.05	110
Large Molecule	1:10	<0.05	133	<0.05	129
Large Molecule	0.05 U/mL	<0.100	86	<0.100	111
Large Molecule	0.025 U/mL	<0.200	76	<0.200	140

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Table 1. Assessment of PyroSmart NextGen® Analytical Performance Compared to Pyrochrome® According to USP <1225> and the ICH Q2 Guideline

Analytical Performance Characteristics		PyroSmart NextGen® Results	Pyrochrome® Results	Acceptance Criteria
1. Linearity (absolute value, correlation coefficient)	**0.01-10 EU/mL**	Minimum: 0.998 Maximum: 1.000	Minimum: 0.998 Maximum: 1.000	|r| ≥0.980
2. Accuracy (recovery)	**Standard Curve**	**Min-Max (%)**	**Min-Max (%)**	
	0.01 EU/mL	85-98	88-100	
	0.1 EU/mL	99-121	98-116	
	1.0 EU/mL	109-122	105-116	
	10 EU/mL	85-95	87-98	50-200%
	USP-RSE	**Min-Max (%)**	**Min-Max (%)**	
	0.05 EU/mL	109-118	95-115	
	0.5 EU/mL	116-131	107-127	
	5.0 EU/mL	116-134	130-153	
3. Precision				
3-1 Repeatability (CV)	**Standard Curve**	**Min-Max (%)**	**Min-Max (%)**	
	0.01 EU/mL	3-21	2-21	
	0.1 EU/mL	5-11	7-13	
	1.0 EU/mL	8-18	7-17	
	10 EU/mL	12-17	13-18	CV ≤30%
	USP-RSE	**Min-Max (%)**	**Min-Max (%)**	
	0.05 EU/mL	6-16	6-19	
	0.5 EU/mL	5-15	4-17	
	5.0 EU/mL	6-12	4-11	
3-2 Intermediate Precision (95% CI for CV)	**Standard Curve**	**Min-Max (%)**	**Min-Max (%)**	
	0.01 EU/mL	11-19	9-15	
	0.1 EU/mL	7-13	7-13	
	1.0 EU/mL	10-17	9-16	
	10 EU/mL	10-17	11-20	CV ≤30%
	USP-RSE	**Min-Max (%)**	**Min-Max (%)**	
	0.05 EU/mL	8-14	9-16	
	0.5 EU/mL	7-13	8-15	
	5.0 EU/mL	7-12	7-13	
4. Range		**0.01-10 EU/mL**	**0.01-10 EU/mL**	Precision, accuracy, and linearity at suitable level
5. Quantitation Limit		**At 0.01 EU/mL** Accuracy: 85-98% Repeatability: 3-21%	**At 0.01 EU/mL** Accuracy: 88-100% Repeatability: 2-21%	The lowest concentration of endotoxin that can be quantitatively determined with suitable precision and accuracy
6. Specificity		**Lot 1 Samples** Sample Concentration: <5.56 - <1.11 EU/mL Repeatability: 0-8% PPC Recovery: 96-134%	**Lot 1 Samples** Sample Concentration: <5.56 - <1.11 EU/mL Repeatability: 0-11% PPC Recovery: 88-121%	For a sample matrix that does not contain endotoxin, the endotoxin concentration is determined as undetected with suitable precision and accuracy (PPC recovery)

Data from: A Demonstration of the Validation Process for Alternative Endotoxin Testing Methods Using PyroSmart NextGen rCR

细菌内毒素检测的行业趋势 – rFC, rCR 的应用

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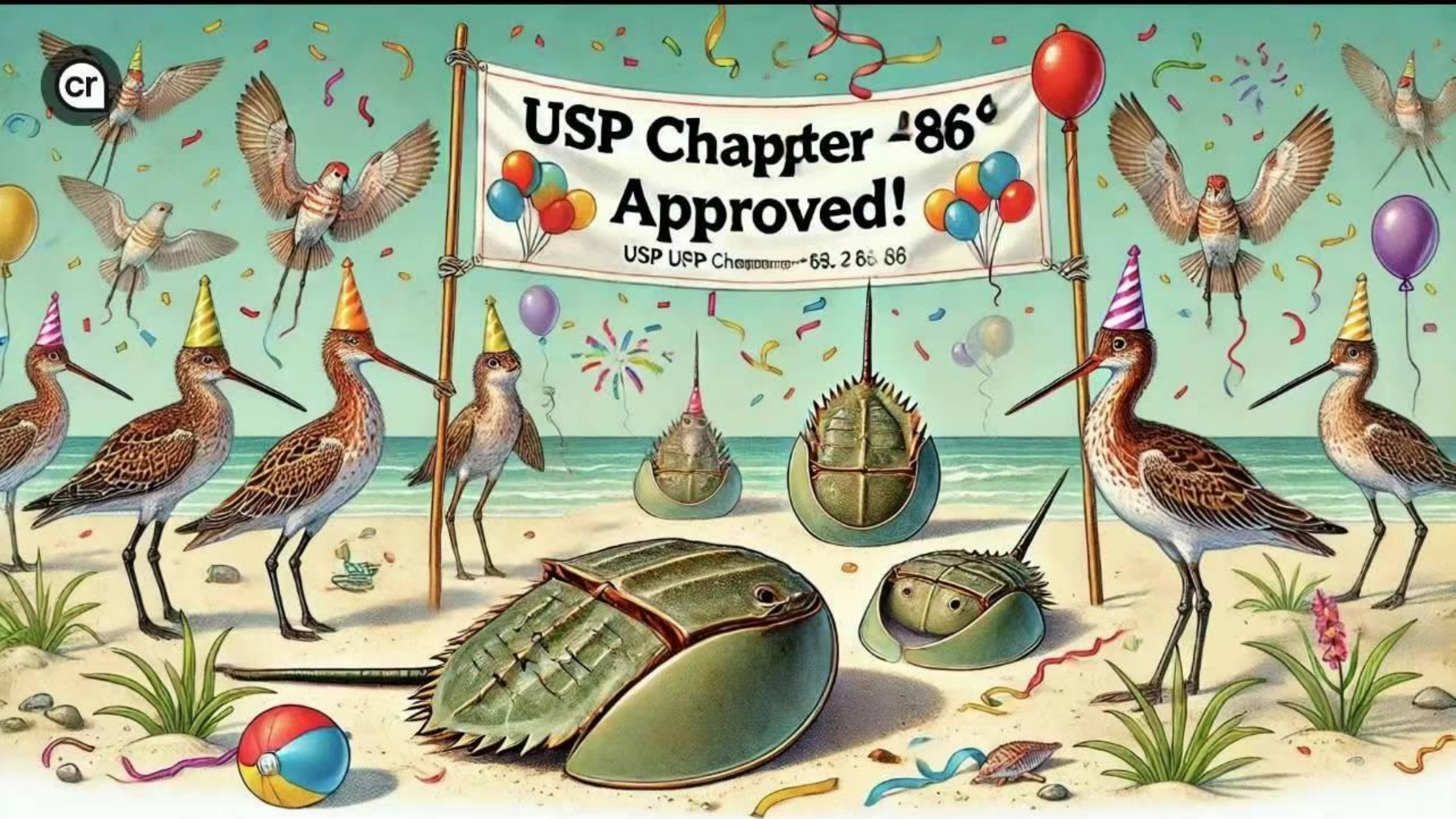
Table 2. Assessment of PyroSmart NextGen® Analytical Performance Compared to Pyrotell®-T According to USP <1225> and the ICH Q2 Guideline

Analytical Performance Characteristics		PyroSmart NextGen® Results	Pyrotell®-T Results	Acceptance Criteria
1. Linearity (absolute value, correlation coefficient)	**0.001-1.0 EU/mL**	Minimum: 0.996 Maximum: 0.998	Minimum: 0.987 Maximum: 0.993	$\|r\| \geq 0.980$
2. Accuracy (recovery)	**Standard Curve**	**Min-Max (%)**	**Min-Max (%)**	
	0.001 EU/mL	83-87	63-75	
	0.01 EU/mL	110-117	134-171	
	0.1 EU/mL	121-132	136-146	
	1.0 EU/mL	79-84	67-74	50-200%
	USP-RSE	**Min-Max (%)**	**Min-Max (%)**	
	0.003 EU/mL	80-120	76-124	
	0.03 EU/mL	112-139	118-173	
	0.3 EU/mL	102-128	93-116	
3. Precision				
3-1 Repeatability (CV)	**Standard Curve**	**Min-Max (%)**	**Min-Max (%)**	
	0.001 EU/mL	3-12	3-20	
	0.01 EU/mL	3-9	3-9	
	0.1 EU/mL	1-4	2-12	
	1.0 EU/mL	1-10	2-9	CV ≤35% 0.001 EU/mL CV ≤30% 0.01-1.0 EU/mL
	USP-RSE	**Min-Max (%)**	**Min-Max (%)**	
	0.003 EU/mL	1-7	3-29	
	0.03 EU/mL	3-10	2-15	
	0.3 EU/mL	2-6	3-12	
3-2 Intermediate Precision (95% CI for CV)	**Standard Curve**	**Min-Max (%)**	**Min-Max (%)**	
	0.001 EU/mL	7-12	11-20	
	0.01 EU/mL	5-9	7-13	
	0.1 EU/mL	3-5	5-9	
	1.0 EU/mL	4-7	5-9	CV ≤35% 0.001 EU/mL CV ≤30% 0.01-1.0 EU/mL
	USP-RSE	**Min-Max (%)**	**Min-Max (%)**	
	0.003 EU/mL	12-22	17-30	
	0.03 EU/mL	8-15	14-25	
	0.3 EU/mL	7-12	8-15	
4. Range		**0.001-1.0 EU/mL**	**0.001-1.0 EU/mL**	Precision, accuracy, and linearity at suitable level
5. Quantitation Limit		**At 0.001 EU/mL** Accuracy: 83-87% Repeatability: 3-12%	**At 0.001 EU/mL** Accuracy: 63-75% Repeatability: 3-20%	The lowest concentration of endotoxin that can be quantitatively determined with suitable precision and accuracy
6. Specificity		**Lot 1 Samples** Sample Concentration: <5.56 - <1.11 EU/mL Repeatability: 0-9% RRC Recovery: 116-140%	**Lot 1 Samples** Sample Concentration: <5.56 - <1.11 EU/mL Repeatability: 0-19% RRC Recovery: 121-167%	For a sample matrix that does not contain endotoxin, the endotoxin concentration is determined as undetected with suitable precision and accuracy (RRC recovery)

Data from: A Demonstration of the Validation Process for Alternative Endotoxin Testing Methods Using PyroSmart NextGen rCR

药典微生物检测及药典方法 Compendial Microbial Testing

2024年7月26日，马里兰州罗克维尔——美国药典委员会微生物学专家委员会已批准将第<86>章《使用重组试剂的细菌内毒素检测》纳入《美国药典–国家处方集》（USP–NF）。该章节允许在细菌内毒素检测中使用非动物源性试剂。该章节的最终文本将于2024年11月发布，并将于2025年5月正式生效。


USP Chapter <86>
Approved!

药典微生物检测及药典方法 Compendial Microbial Testing

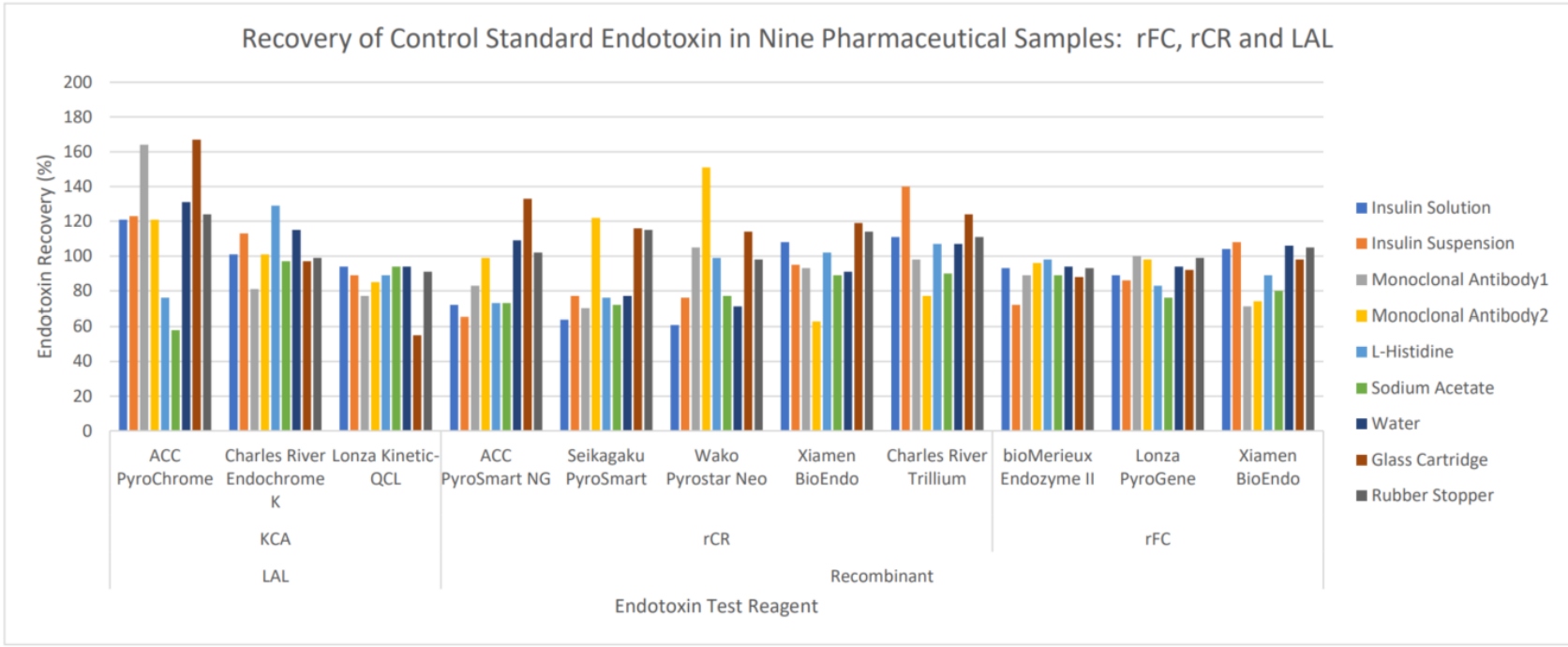
KEY RESULTS

Table 1: Recombinant reagents are more specific for endotoxin in the presence of beta glucans (yeastolate

Reagent	Reagent Type	Calculated Result (EU/mg)	%PPC
Lonza Kinetic-QCL	LAL - KCA	0.0687	133
ACC PyroChrome	LAL - KCA	>4.00	NA
Charles River Endochrome K	LAL - KCA	0.0639	123
ACC PyroSmart NG	rCR	<0.0400	100
Seikagaku PyroSmart	rCR	<0.0400	87
Wako Pyrostar Neo	rCR	<0.0400	56
Xiamen BioEndo	rCR	<0.0400	76
Charles River Trillium	rCR	<0.0200	107
bioMerieux Endozyme II	rFC	<0.0400	79
Lonza PyroGene	rFC	<0.0400	71
Xiamen BioEndo	rFC	<0.0400	91

KEY RESULTS

Figure 1: Recombinant Reagents Recover Endotoxin Comparable to Naturally-Derived Reagents



- Compendial recovery criteria is 50-200%; product dilutions were based on equivalent LOQs, not necessarily optimized for PPC recovery
- Theoretical recovery target is 90.9% based on a 10 µL “hot spike” into 100 µL sample

改变基本原理

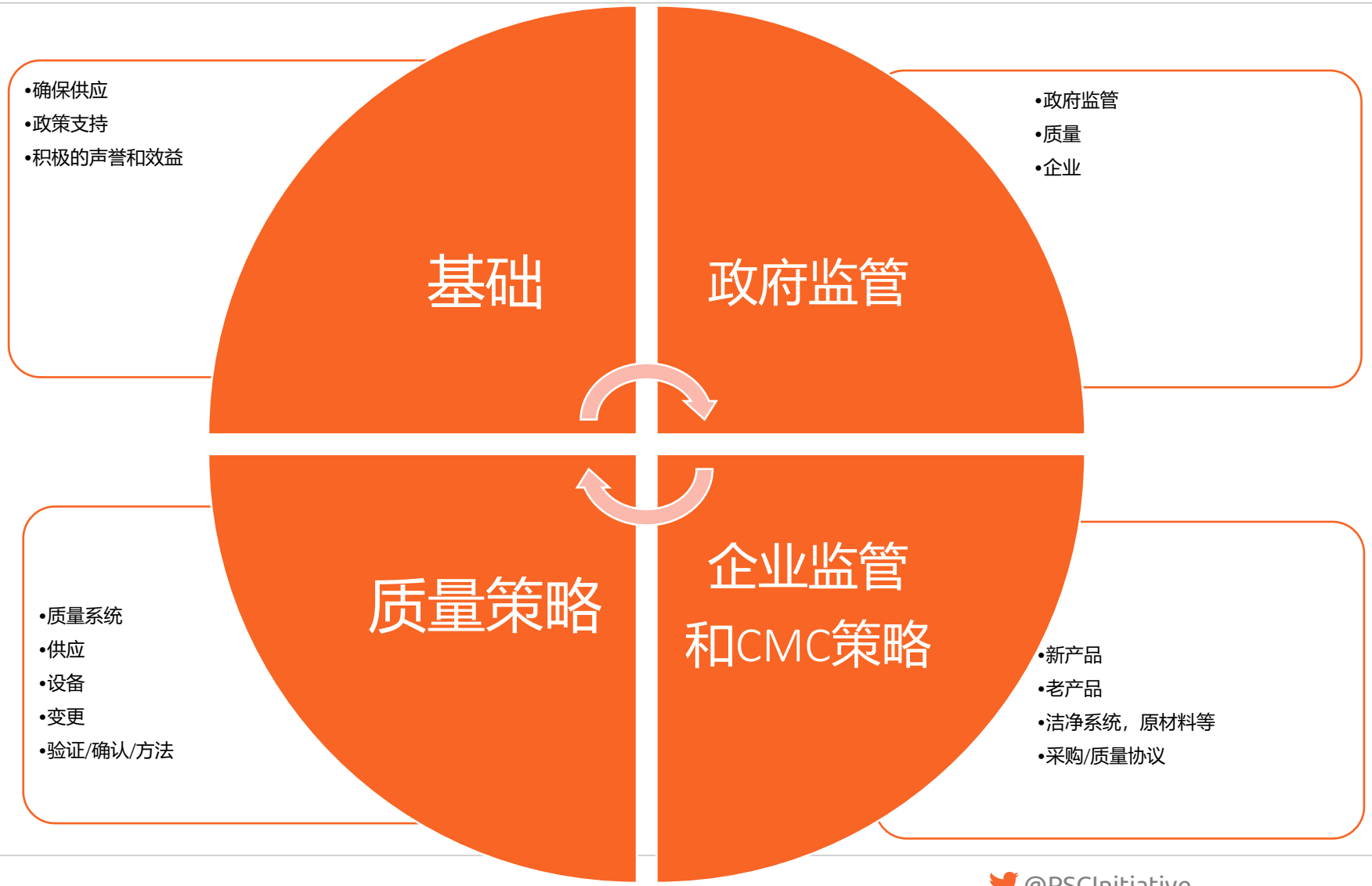
质量

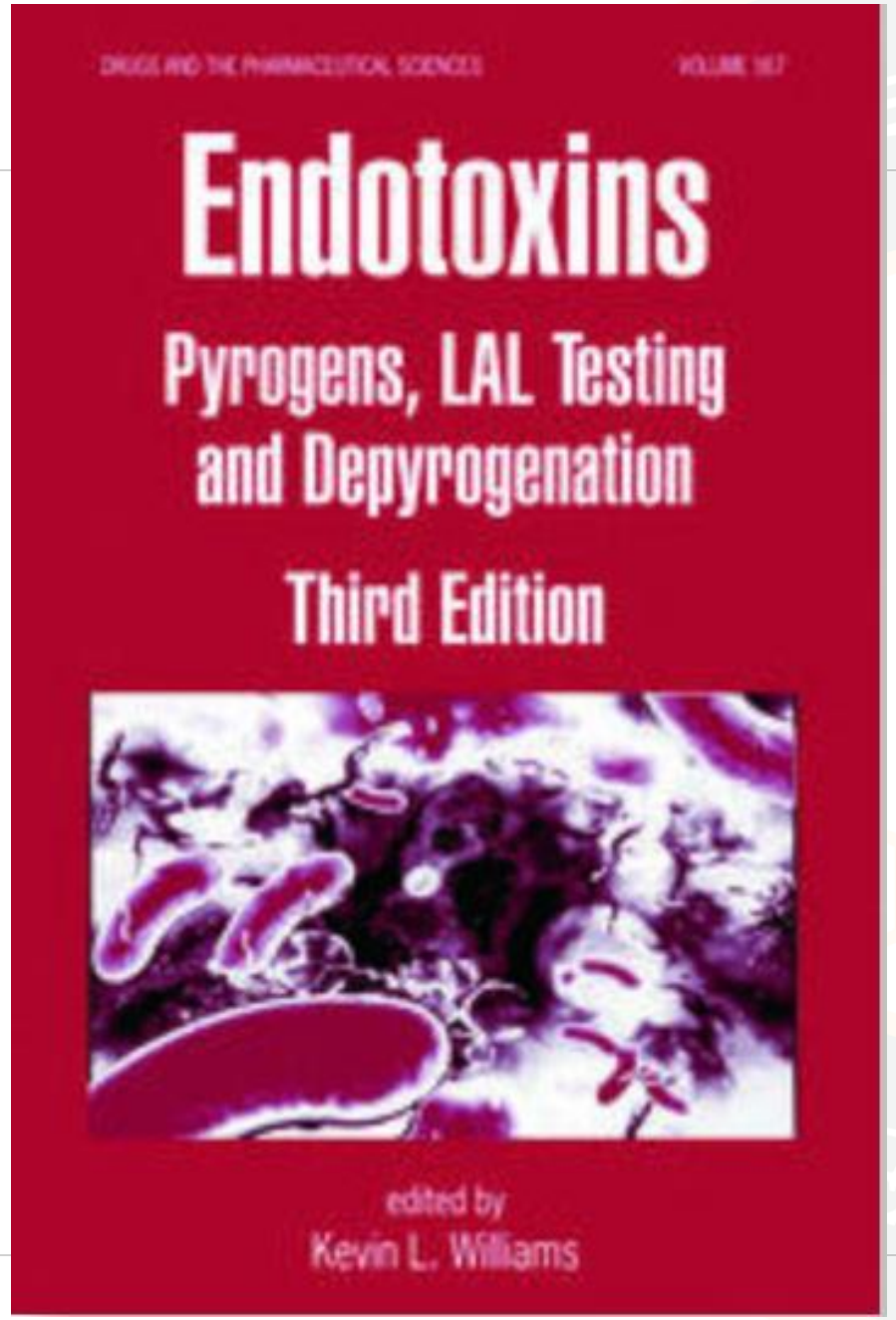
供应链

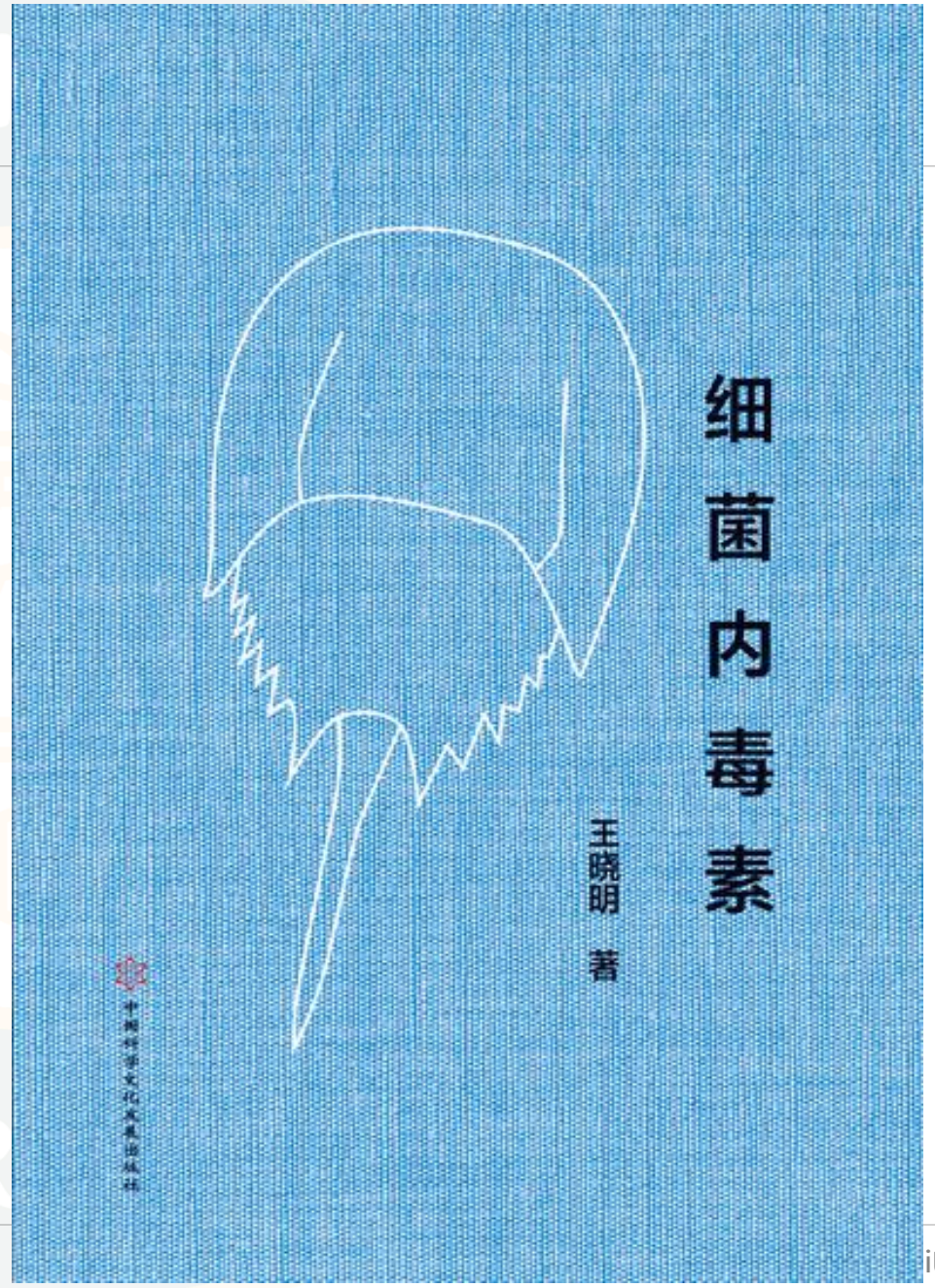
道德

资源

改变计划


•确保供应
•政策支持
•积极的声誉和效益
基础
政府监管
•政府监管
•质量
•企业
质量策略
企业监管
和CMC策略
•质量系统
•供应
•设备
•变更
•验证/确认/方法
•新产品
•老产品
•洁净系统，原材料等
•采购/质量协议


Endotoxins
Pyrogens, LAL Testing and Depyrogenation
Third Edition
edited by
Kevin L. Williams


细菌内毒素
王晓明 著

提问环节 Q&A

感谢