

# Sustainable Practices to Reduce Waste & Environmental Impact

Kevin L. Williams, May 3rd 2023 Midwest PDA

# Your Ally in Advancing Quality

**PIONEERING DIAGNOSTICS** 

# **CURRENT SITUATION**

 Governments, regulators, standard setters (USP/EP/JP), and corporations are looking for ways to increase sustainability, supply chain resilience, improve animal welfare and reduce environmental impact.

• What is sustainability?

• Why NOW?

"Sustainable development is development that meets the needs of the present without compromising the ability of future generations to meet their own needs."

Supply chain resilience + improve animal welfare + reduce environmental impact = Sustainability

# **CURRENT SITUATION**

Industry (has no shortage of)
 issues:

- Supply Chain / pandemic recovery
- Climate change
- Animal welfare
- Prices / Inflation / Debt
- Employment disruptions



Theme for us now: Small steps can make BIG improvements toward SUSTAINABILITY...

# **CURRENT SITUATION (BET)**

- Massive need for HSC derived LAL in Pharma
- Only US compendial test ...for now
- Global demand growing faster than U.S. demand
- Sourcing Issues: the further from the source of LAL, the more likely supply chain issues are to occur
- Let's look at RECOMBINANT USAGE in general before looking at rFC more specifically





# **RECOMBINANT PRODUCTION IS VERY EFFICIENT**

UN, LID



More than 50,000 animals were needed to produce just one kilogram of insulin (enough to treat fewer than a thousand diabetic patients for just one year). Because of this, in the early 1970s, there were widespread fears about limited and uncertain supply...

1958 > 1982 NDC 0002-8215-01 100 units per mL U-100 Humulin H sulin human njection, USP combinant DNA origin SCIENTIFIC AMERICAN INDUSTRIAL MICROBIOLOGY September 1981

### **Quickly followed by:**

- 2. Human growth hormone
- 3. Blood clotting factors
- 4. Hepatitis B vaccine, an
- 5. Diagnosis of HIV infection

# **RECOMBINANT PRODUCTION IS VERY EFFICIENT**

# Precision fermentation proteins already competitive in medicine, materials, and now food!



### https://rethinkdisruption.com/the-disruption-of-insulin/

The disruption of insulin – The first product from precision fermentation, Sept. 3, 2020

# **RECOMBINANT PRODUCTION = MODERNIZATION**

### **INSULIN CREATED FROM YEAST**

Fraction of cost with far greater functionality



Long-acting Intermediate-acting Short-acting Rapid-acting Etc.

New functionality could not have been achieved using naturally harvested materials.

https://rethinkdisruption.com/the-disruption-of-insulin/

# **ANIMAL HARVESTED INSULINS RARELY USED**



- Cats and Dogs do NOT use animal insulin but use RECOMBINANT human insulin
- Recombinants are sustainable and "improvable" – manipulation of structure and associated genetic inserts for expression





rDrugs can pull the multitude of levers present on T cells, B cells, etc.

Monoclonals have been fit to block or activate dozens of these targets for cancer and autoimmune disease treatment.



# **ANOTHER EXAMPLE OF ON-GOING PARADIGM...**

**Rethink**Disruption

### Cell-based meat approved in the US for the first time ever

November 21, 2022 / By Taylor Hinds

Earlier this week it was announced that the United States Food and Drug Administration (FDA) has declared UPSIDE Foods' cultured chicken safe to eat. This approval came in

the form of a No Questions L GRAS, or Generally Regarded



\$2,472,663.14

\$10,000,000.00

\$1,000,000.00

\$100,000.00

Cell-Based Meat Costs, Historical and Projection

https://upsidefoods.com/

2031

# **ENDOLISA®**

ENDOLISA® is a new Functionality achieved with recombinant Factor C (rFC)



	Substance	Solvent	EndoLISA	LAL assay
Buffer/pH	Acetate (pH 4.0)	100 mM NaCl	50 mM	12.5 mM
	Acetate (pH 5.0)	100 mM NaCl	100 mM <sup>a</sup>	12.5 mM
	MES (pH 6.0)	100 mM NaCl	100 mM <sup>a</sup>	5 mM
	Potassium phosphate	100 mM NaCl	100 mM <sup>a</sup>	50 mM
	(pH 7.2)			
	Imidazole (pH 7.4)	Water	500 mM	40 mM
	HEPES (pH 7.5)	100 mM NaCl	100 mM <sup>a</sup>	100 mM <sup>a</sup>
	Sodium borate (pH 9.0)	100 mM NaCl	100 mM <sup>a</sup>	50 mM
Salt	NaCl	Water	1 M	0.5 M
	KCL	Water	1 M	0.25 M
Chaotropic agent	Urea	Water	6 M	0.5 M
	Guanidinium chloride	Water	1 M	0.05 M
Organic solvent	Methanol	Water	20% <sup>a</sup>	5%
	Ethanol	Water	30% 60	X 0.5%
	2-Propanol	Water	20%	0.2%
	DMSO	Water	10%	2%
Detergent	SDS	Water	0.05%	0.001%
	СТАВ	Water	0.004%	0.0001%
	Zwittergent 3-14	Water	0.02%	0.005%
	Tween 20	Water	2%	0.1%
	Triton X-100	Water	0.02%	0.005%
Chelator	EDTA (pH 8.0)	Water	0.4 mM	0.4 mM
	Citrate (pH 7.5)	Water	10 mM	10 mM
Protease inhibitor	Benzamidine	Water	100 mM <sup>a</sup> 🖌 100	0.1 mM
	PMSF	2-Propanol	5 mM	<0.05 mM
Antibiotic	Rifampicin	Methanol	3.5 mg/ml	0.04 mg/ml
	Chloramphenicol	Ethanol	3.5 mg/ml	0.1 mg/ml

EndoLISA®: a novel and reliable method for endotoxin detection. NATURE METHODS | OCTOBER 2011

### https://sdgs.un.org/goals

# **U.N. SUSTAINABILITY DEVELOPMENT GOALS**



https://sdgs.un.org/goals

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https://sdgs.un.org/goals

# **U.N. SUSTAINABILITY DEV. GOALS CITED BY PHARMA**

# Drug Manufacturers are developing strategies to meet sustainability goals, and in many cases adopting the guidelines provided in the United Nations (UN) Sustainable Development Goals (SDG).

### Goal 3: Good Health and Wellbeing

### Goal 12: Responsible Consumption & Production

### Goal 14: Life Below Water

This goal is focused on promoting healthy lives and well-being for all people and is essential for sustainable development. The test for bacterial endotoxins forms a critical part of assurance of the quality of injectable medicines. Sustainable consumption and production is about doing more and better with less. These fundamental principles not only support a healthy planet, but also facilitate good business practice. This goal relates to everything we do in the laboratory environment. Whilst considerations for this goal also capture elements of food waste, more broadly speaking, waste leads to environmental degradation. Without the oceans, the Earth would not be habitable for humankind; ultimately without the oceans, we would not be here. There has been a deterioration of coastal waters over the period of industrialisation and this must change. There are multiple factors that put pressure on our coastal habitats, including the pressures on marine biodiversity. As this is so fundamentally critical to the health of the planet, marine protected areas must be established and effectively managed; resource, infrastructure and regulations must be in place to reduce overfishing, marine pollution, acidification and also habitat deterioration and loss. It is clear that the Life Below Water goal directly links to considerations for the Horseshoe Crab populations and thus, bacterial endotoxin testing.

### Goal 15: Life On Land

Many animal and plant species are threatened with extinction; life below water does not stand alone; the balance is intricately connected to life on land. Providing habitat protection and reducing the risk of biodiversity loss, has a subsequent impact on the biodiversity and Life On Land. Humans continue to encroach on fragile ecosystems in many different ways. Therefore, to provide mitigations to protect against species loss, the interconnections must be key consideration.

- Life Below Water goal is directly linked to the HSC populations and the BET. Aim is to reduce pressure on Marine Biodiversity
- Life On Land: Interconnection is key to also protect Life On Land

### TAKEAWAY: REPLACING LAL WITH RECOMBINANT REAGENTS...

- LAL has been a life-saver for several decades and HSC protections have been facilitated by LAL manufacturers, but now...
- Life on Land > shorebirds are endangered by lack of HSC eggs they need to feed on during migratory journey.



- Life below water > HSC is a keystone species with rippling effects if HSCs are further threatened.
- One easy tool to help alleviate the pressure on the HSC population = rFC

# **RECOMBINANT REVOLUTION IS A MOVE FROM...**

- Scarcity -----> Abundance
- Animal sourcing -----> Bioreactor grown (synthetic)
- Empirical /approximate -----> Exact science / specific = Modernization
- Local (LAL. Atlantic seaboard) -----> Global production
- Farm / shore -----> Lab
- Fixed production -----> Fully scalable
- Unsustainable -----> Sustainable production

# WHAT SPECIFICALLY CAN WE DO?



Move to animal-free products Reduce reagent Waste

(micro & chemistry)

Reduce plastic waste (or at least do not increase)



Recycle plastic <u>if</u> <u>possible -</u> difficult when drugs are added to it

# **WASTE REDUCTION = COST REDUCTION**

- We can look at non-animal derived test reagents
  - rFC production follows the paradigm of biologic drug production
  - · Waste less by using exactly what you need



The image demonstrates how 4 columns of sample or 32 total wells required approximately 3.2 mL. The lowest amount of LAL that met this volume would require reconstitution of a 5.2 mL vial (or two 2.6 mL vials) and therefore would have wasted 2 mL of LAL for the test. This is a significant amount when considered on a cumulative, annual basis.

Excess LAL can be frozen, but some have seen performance degradation.

# LIMIT PLASTIC WASTE

- Single sample test cartridges are 4-5 times more plastic than a 96-well plate (by weight)
- 20-21 cartridges needed to = one 96 well plate





# **ENDOZYME® II GO – GOPLATE™ OR STRIPS**

### We can save analyst time and money



Pre-spiked PPCs, Just add samples

• /

- Add water to reconstitute standard curve
- No CSE
  reconstitution
- It's in the wells
- No dilution stds
- No vortexing stds
- Just add water
- Just add samples

# **CURRENT BIG PHARMA ACTIVITIES**

**3 CASE STUDIES** 

# CURRENT BIG PHARMA ACTIVITIES CASE 1

A Strategic Approach to Optimisations of Testing Bacterial Endotoxins – by AstraZeneca

Authors: Dennis Wong, Karen Capper, Miriam Guest, Phil Duncanson – AstraZeneca AstraZeneca's focus on sustainability is fundamental to its company strategy - part of the mission to meet UN SDG goals.

### **Stated Goals**

Strategy for testing endotoxin solutions:

- Reduce the burden on the horseshoe crab
- Reduce waste
- Increase efficiencies
- Minimal change burden



AstraZeneca



-	Short-term strategy Employed cartridge testing to reduce LAL use	Long-term strategy is to employ recombinant reagent testing to eliminate LAL use
-	Short-term benefits Total volume of LAL used reduced by > 60%	Long-term benefits - validate non-animal derived synthetic alternative reagents
	,	

# CURRENT BIG PHARMA ACTIVITIES CASE 2

Eli Lilly - Development of rFC as alternative method for endotoxin testing that helps protect wildlife and coastal, marine and watershed environments

Terrestrial and Aquatic Biodiversity Conservation Expenditures that improve protection of coastal, marine and watershed environments. Example projects may include, but are not limited to:

Development of an alternative method for endotoxin testing that helps protect wildlife and coastal, marine and watershed environments Life below water

È

land

The terrestrial and aquatic biodiversity conservation goal for Eli Lilly & Company.

Eli Lilly allocated €9M to its ecologically sound endotoxin testing method initiative

### **<u>SI</u>** Terrestrial and Aquatic Biodiversity Conservation

Lilly worked to validate an alternative method of endotoxin testing – a necessary step for our medicines – that does not require sourcing horseshoe crabs. Several species of crabs are under threat or endangered from habitat loss and overharvesting, which negatively affects the ecosystems and other species inhabited by horseshoe crabs. This industry-leading effort helped influence changes in the European pharmacopoeia in 2020 and may help facilitate broader industry adoption and conversion to endotoxin testing alternatives that do not require the use of horseshoe crabs or other live animals. Impact Metrics: Five Lilly medicines were developed

using the alternative endotoxin testing method, including three

COVID-19 antibodies, and were authorized for use

Ecologically Sound Endotoxin Testing Method €9 million

Proceeds Allocated:



### Sustainability Bond Allocation and Impact Report

# CURRENT BIG PHARMA ACTIVITIES CASE 3

## Validation Strategy for New Recombinant Factor C Users

Authors: Evelyn Der, Carmen Marin, Vivian Grunert de Fonseca

### Importance of a Sustainable Alternative Method at Roche

### **Stated Goals**

- **3Rs Incentive Awareness** awareness for animal welfare: refine, reduce & replace
  - Supports Roche's Mission: Replace non-sustainable animal dependent analytical methods with alternative methods
- **39,000** water samples annually for endotoxins
  - Alternative methods => significant impact on ANIMAL PROTECTION



# **USP PHARMACOPEIAL DISCUSSION GROUP (PDG)**

# USP project to evaluate rFC as Sustainable Solution

Encourage smaller volumes:

•Utilizing and/or reusing lower toxicity solvents

•Revisions to Chapter <31> and <41> (volumetric & balances measurements)

Other ongoing projects

usp

Evaluation of endotoxin recombinant factor C (rFC) for absence of pyrogen assurance

- Phasing out calomel electrodes (mercury [II] chloride)
- Replacing outdated wet chemistry methods using hazardous reagents
- Eliminating odor/taste aka "organoleptic" tests
- Continuing elimination of toxic solvents
- Analytical quality by design (AQbD) concepts to include reduction in waste generation

# Question & Answer

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### PIONEERING DIAGNOSTICS