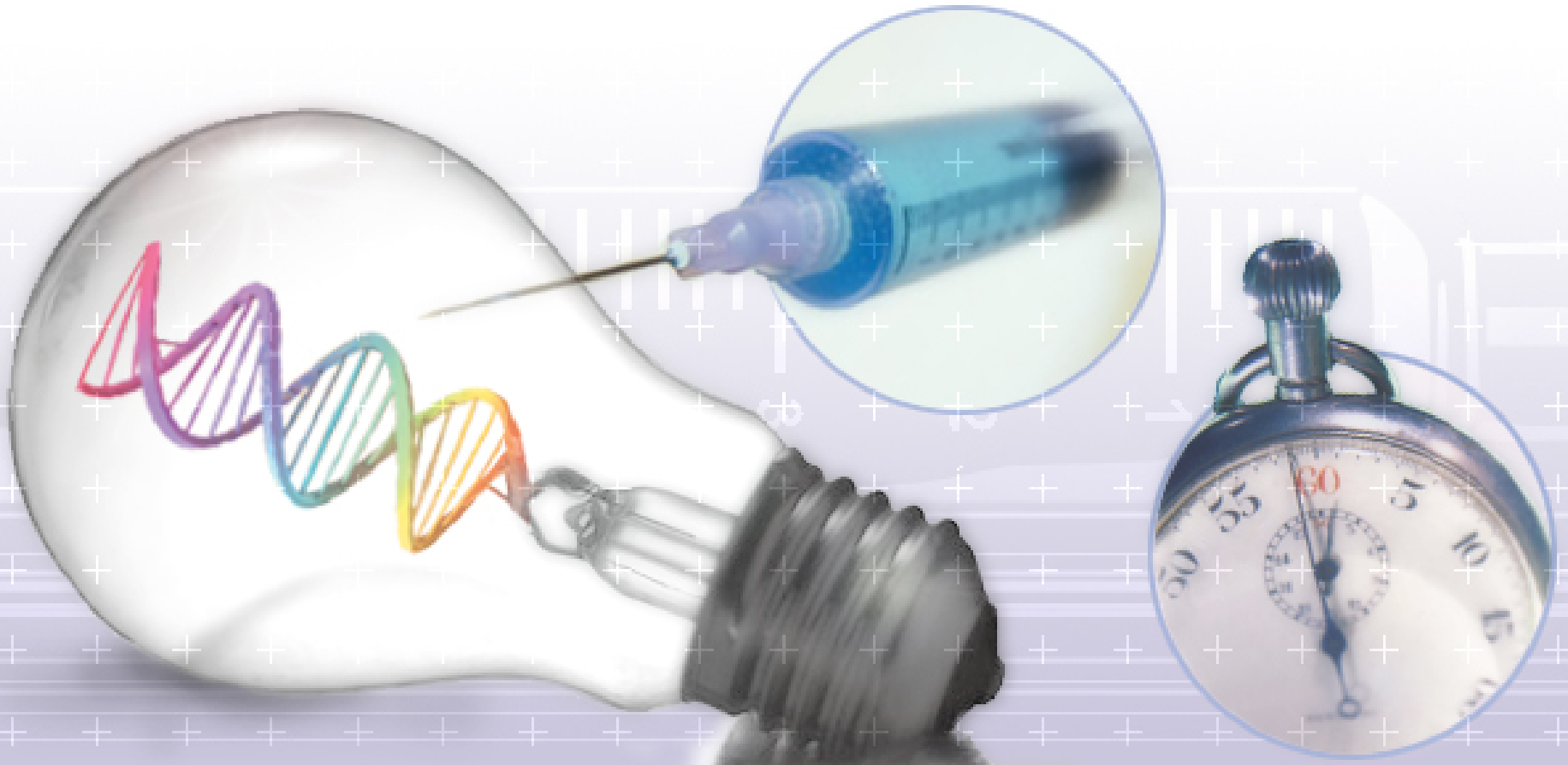


The Continuum of Events that Lead to a Successful Campaign

Lisa Cozza, Human Genome Sciences Inc
Crawford Brown, Eden Biodesign Ltd



“Much more than a contract manufacturing organisation”



cGMP Production
Mammalian
Microbial
Viral

HGS

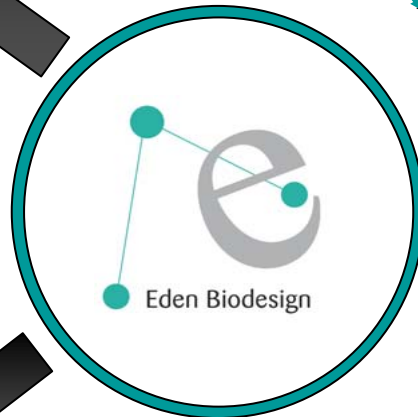
San Diego

RTP

Liverpool

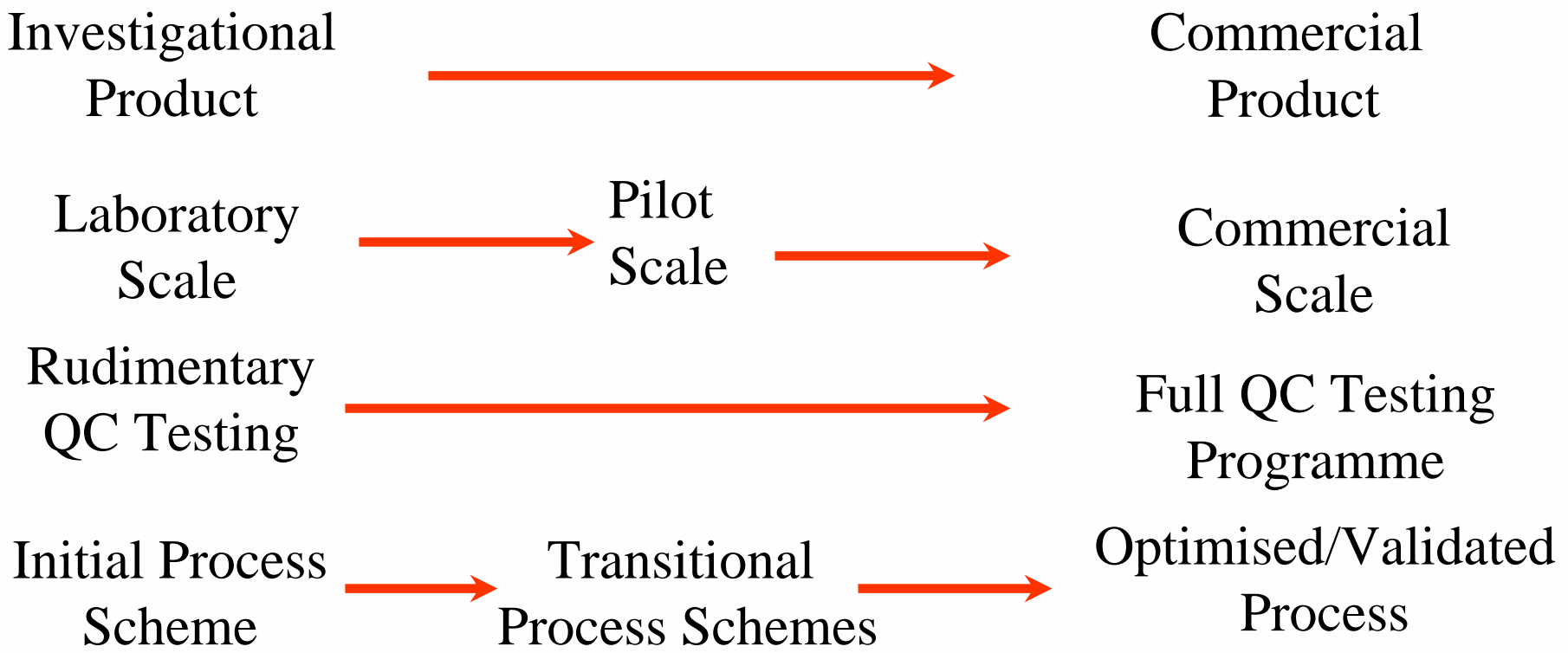
**Process & Analytical
Development**

Consultancy



- Strategic Partners**
- Eden Presence**
- Client Assignments**

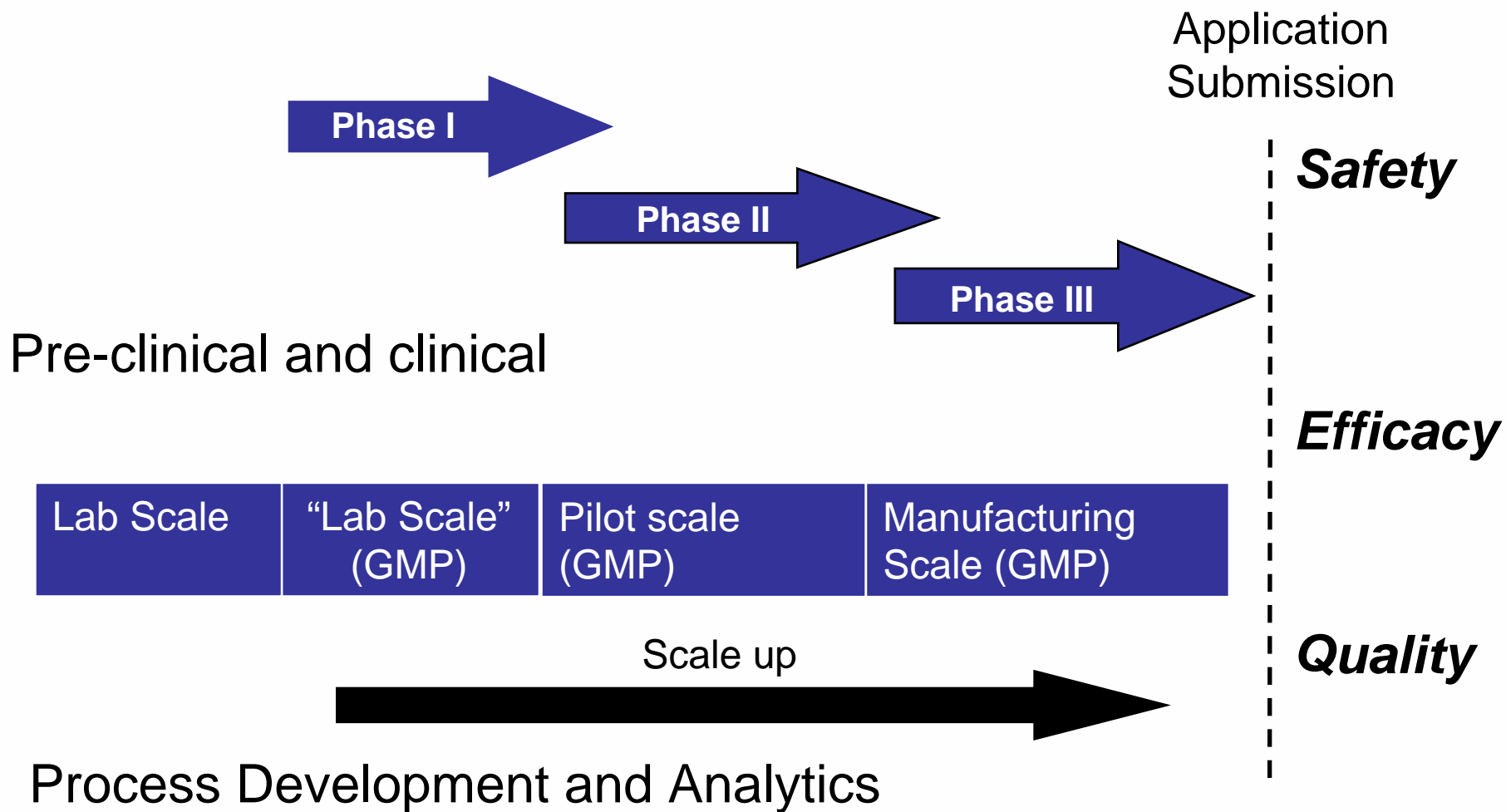
Clinical Production: A State of Flux



Change is Unavoidable

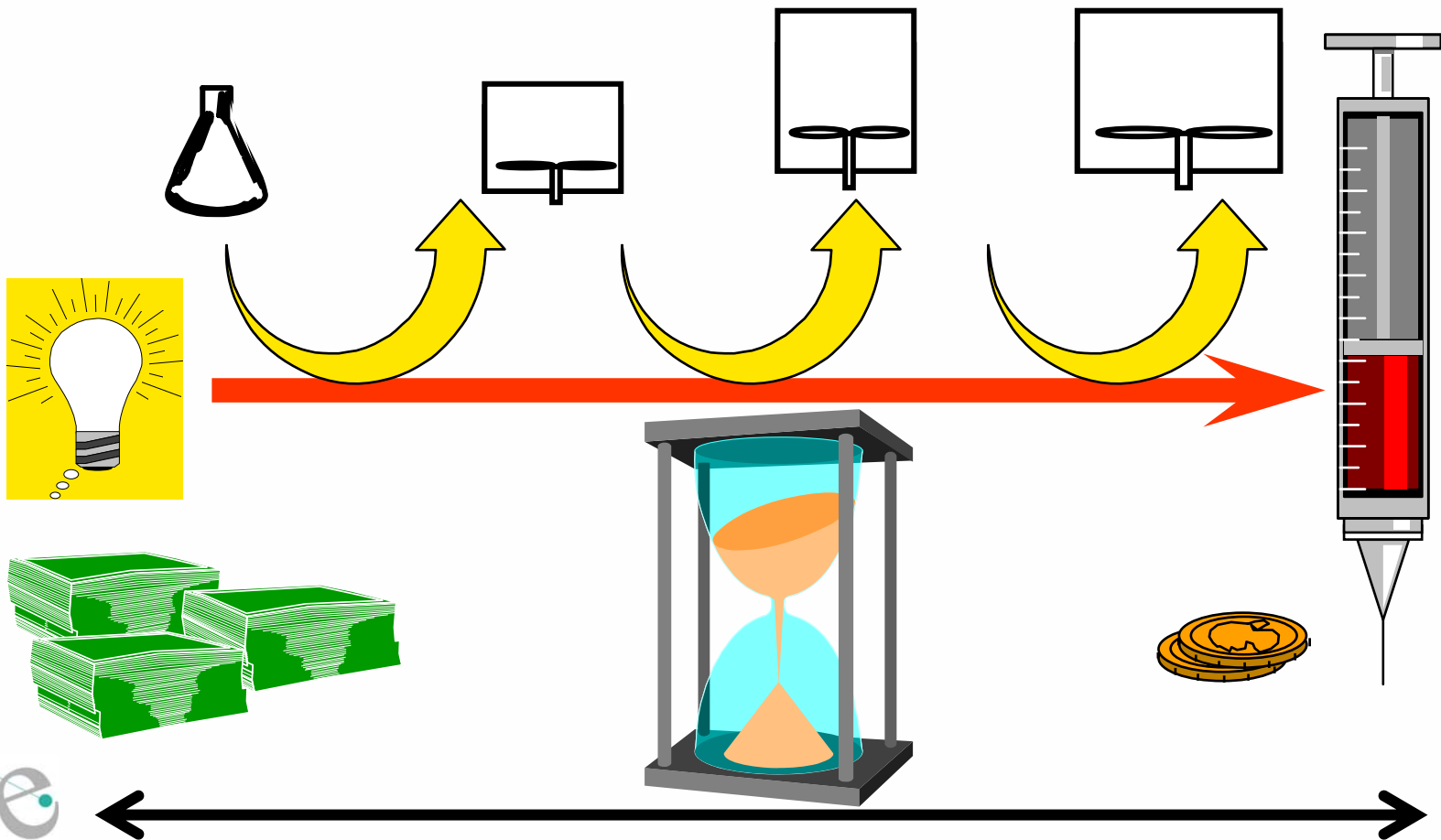


Equivalency of product at different stages of clinical development



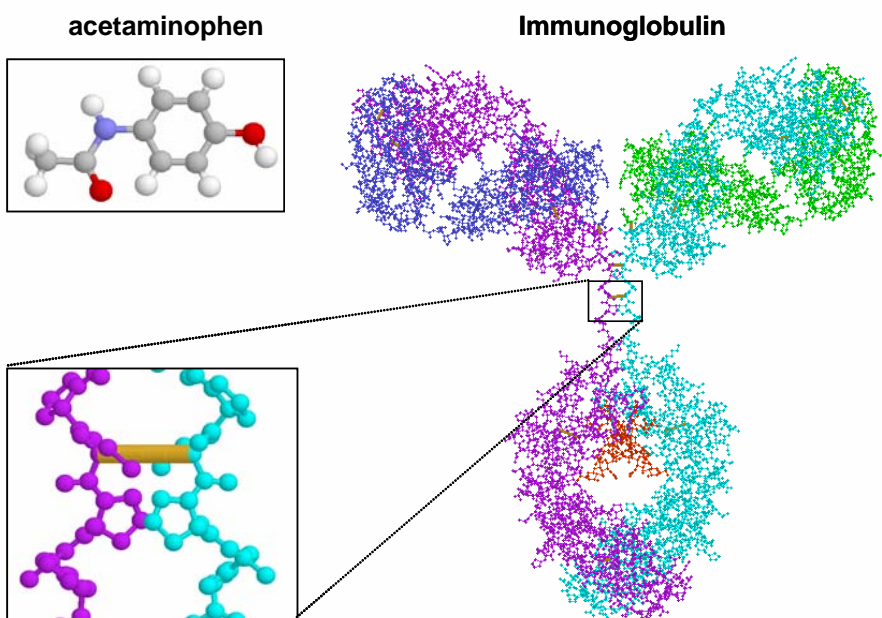
Scale Up

Nature of the Challenge



Product Indication and Class

For example, mAbs are becoming 'small molecule-like'.



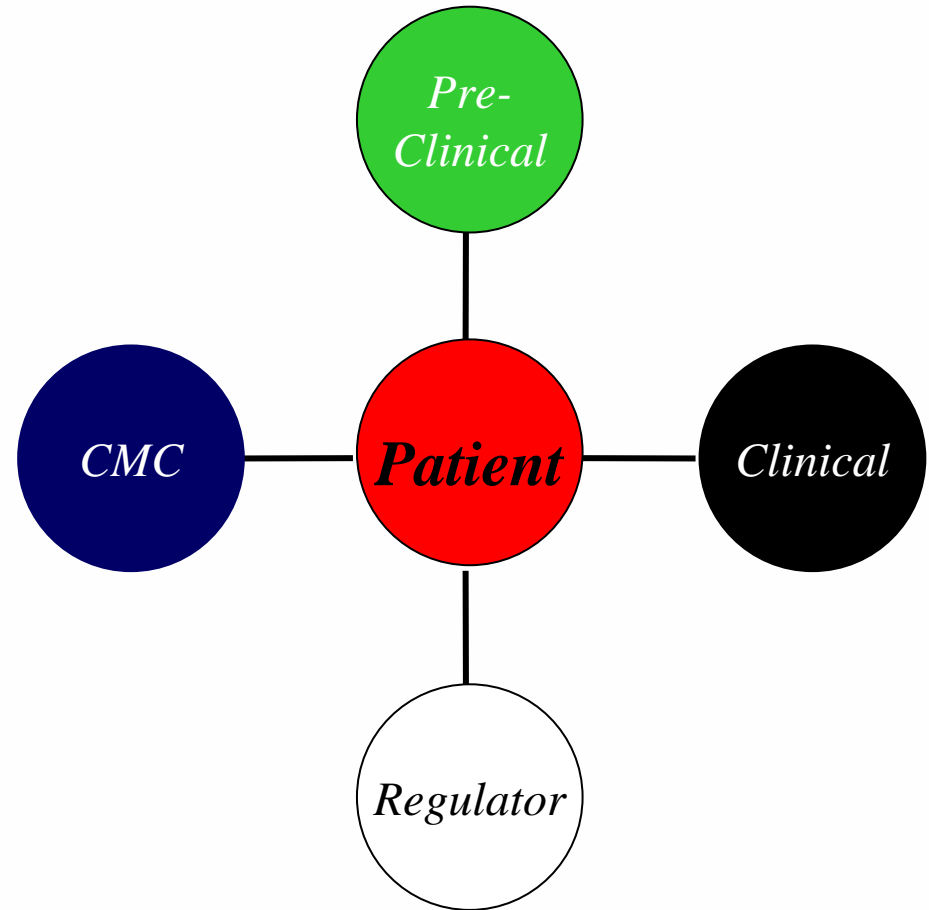
- Commercial Trends
 - Mainstream pharmaceutical product class
 - Mixed portfolio of small molecules and mAbs
- Manufacturing
 - Largely generic manufacturing design
 - Easily outsourced
 - Expanding international choice of facilities
 - Experienced scientists and engineers
- Regulatory
 - Comparability Protocols support flexibility
 - Application of PAT, QbD initiatives.
 - CDER rather than CBER oversight

HGS-Eden Approach

Beginning with the *end* in mind



It's where we prefer to start

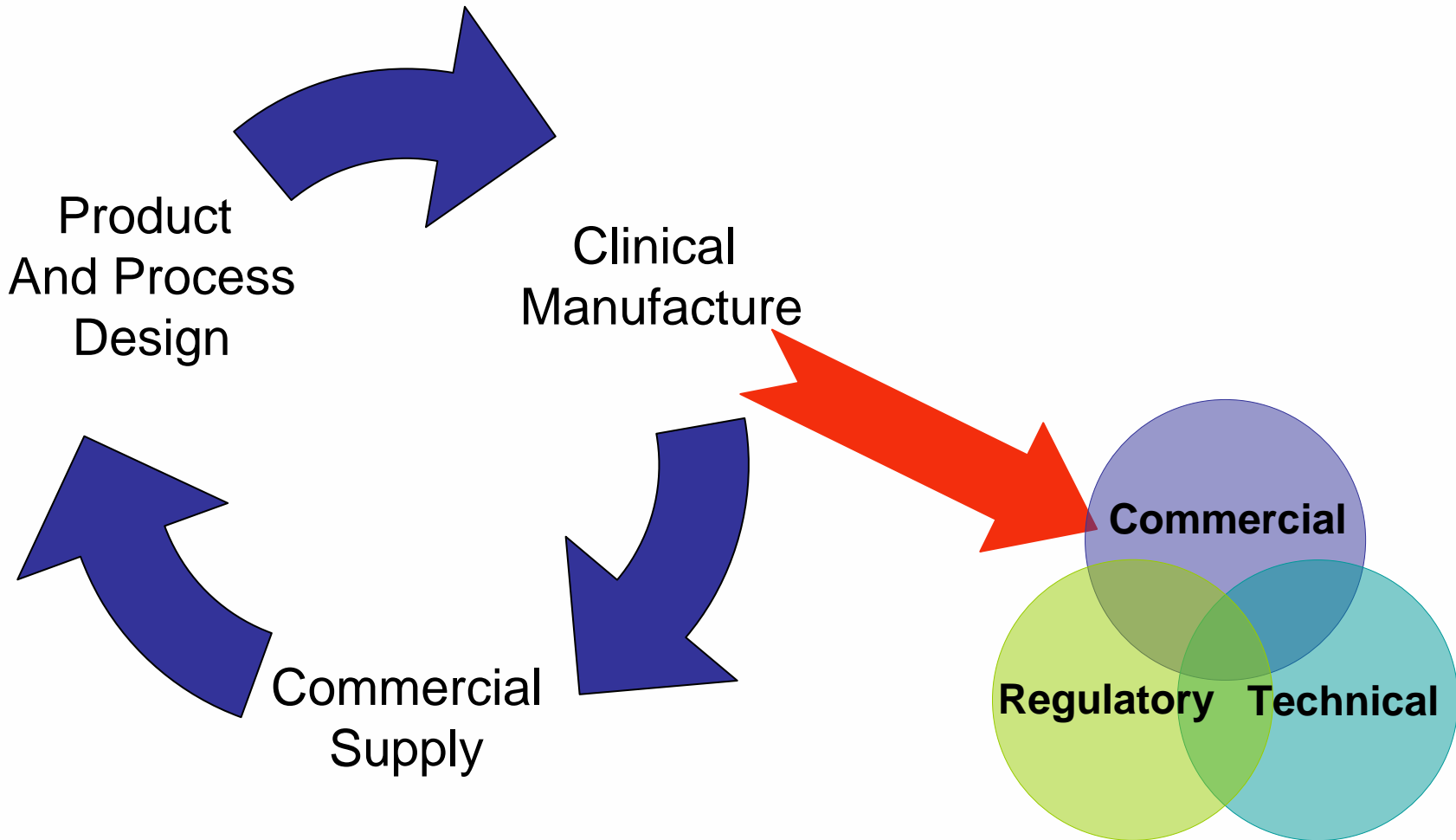


Human Genome Sciences

- Founded in 1992
- Located in Rockville, Maryland
- 900 employees
- Publicly traded on NASDAQ
- cGMP Production
 - 20,000 Liter
 - 5,000 Liter
 - 1,600 Liter
- Partners with GSK, Novartis and Hospira
- Pipeline of products in mid-late stage clinical development
- HGS will provide cell line development, analytical, formulation, stability, liquid and/or lyo fill finish development

HGS will provide a one stop shop for your large scale mammalian cell culture needs

HGS and Eden Alliance Jointly Designed Tech Transfer Procedure



Same Equipment, Same Vendor. But.....

- ❑ Territorial compliance may differ e.g. disposable containers irradiation and assembly QA compliance differences
- ❑ Same vendor different software; especially analytical and small process equipment.
- ❑ Same large scale unit operation but spares different, e.g. elastomers in fermenters and filter units, all product contact parts

You say tom~~a~~to I say tomato. Same words
But.....

- ❑ Client assay validated in HGS-Eden terms really means qualified
- ❑ Internal reference standard in HGS-Eden terms really a research standard without provenance
- ❑ Easily available media in USA, not produced in Europe despite being an international vendor



Freezing the Bulk Drug Substance in liquid nitrogen seems quick, cheap and easy, right?

- Try freezing 60 liters of BDS
- Process “validation” not possible
- No stability data at -40
- Could cause Phase 3 risk or delay to program



HGS-Eden Risk Mitigation Approach

- ❑ Scale down models of the Large Scale
- ❑ Staff transfer to and from USA and UK
- ❑ Shared scale up philosophy
- ❑ Understands cost drivers at large scale
- ❑ Support the process from concept to kilogram
- ❑ Standardised systems for tech transfer



Eden/HGS Tech Transfer Protocol

Basic Process Fit

Detailed Process Fit
 • Fit Model
 • PFD schematic

EDEN/ CRO Development
 • Process Development
 • Assay Development

HGS Demo Run(s)

Analytical TT to HGS

gBOM

dBOM

Detailed PFD

Sample Plan

BOD

Batch Records (+ SOPs)

Training

Facility/ Equipment Prep

Change Over

Eng Run

HGS Tech Transfer

RFP Response

Contract Discussions

Process Development

HGS Process Demo



Standardized Tech Transfer

Schedule		Duration	Start	Finish	February				March					
					E	B	M	T	E	B	M	T		
		0 days	Thu 9/22/05	Thu 9/22/05										
		21 days	Thu 9/22/05	Sat 10/22/05										
		20 days	Thu 9/22/05	Wed 10/12/05										

Bill of Materials		M Upstream through Recovery												
(Batch Record Name)	Batch Record #	Part #	Description/Duration	Quantity/ Yield per Run	UOM	Kanban (Y/N)	Yield							
Set-up of Bioreactor Controls														

PFD

DOWNSTREAM PROCESS FLOW DIAGRAM (BELWARD, 1600 L)

STAGE 8: HIC PURIFICATION

Sample Plan		BP-51091												
Process Step	Sample Description	QLIMS ID	Assays	Test Window	No. of Samples	Manufacturing pulls		Sample required			Container	Storage Temp. [°C]	Delivery Location	Testing Group
						Sample Volume [mL]	No. of Samples	Sample Vol. required [mL]	Total Sample Vol. required [mL]					
Buffer Preparation	Equil./Wash 1		pH Cond	STAT STAT	*	*		2	25	50	PP			

- Standard deliverables
- Centralized group
- Standard approach

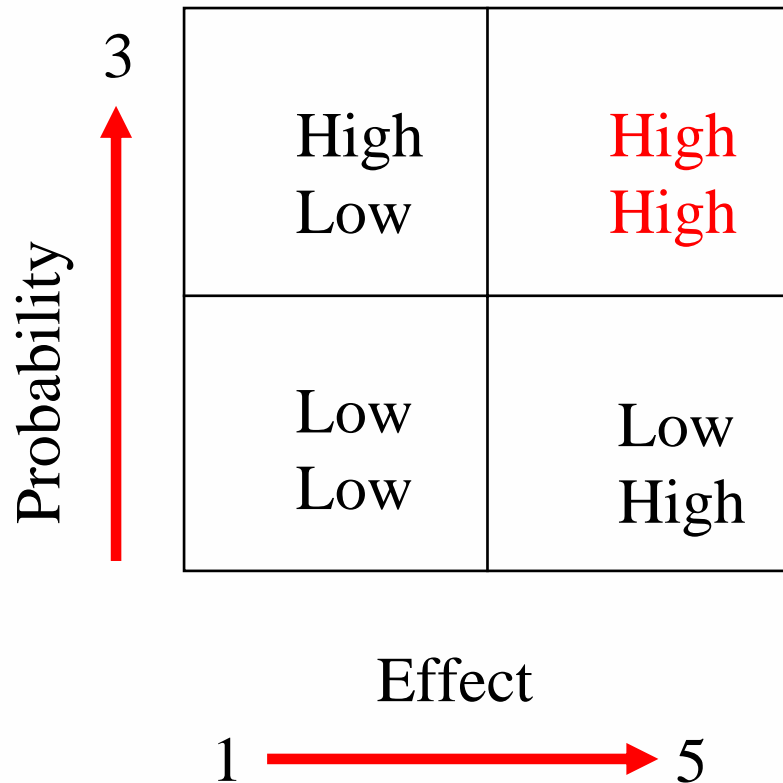
Process Step	Sample Description	Cond	STAT	No. of Samples	Sample Volume [mL]	No. of Samples	Sample Vol. required [mL]	Total Sample Vol. required [mL]	Container	Storage Temp. [°C]	Delivery Location	Testing Group
ProSep vA Ultra Pool	Endotoxin	24 hours	*	*	*	3	10	30	PETG	2-8	3A, Rm 2700	QC Micro
	A280	STAT	*	*	*	1	25	25	PETG	2-8		

Projec 10ma
Date: Wed 5/11/05

HGS10XX
211

PROJ
STAC

Actively Manage the High Risks



- Fit Feasibility
- Release Assay Transfer
- Raw material supply
- Assumptions vs reality
- cGMP filling contractor
- Seamless Program Management

Never underestimate the value of good programme management

- ❑ Change is the norm
- ❑ Communication the critical success factor or most common reason for failure



Success by Doing: *Technology Transfer*

- ❑ Multi-faceted

Equipment	Facility
Data	People

- ❑ Should be seamless
- ❑ Designed to mitigate risk
- ❑ Already started at negotiation
- ❑ Begin with the end in Mind

