ECONOMICS OF VACCINE PRODUCTION COSTING

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Introduction

Topics covered in this presentation include:

1) Vaccine market structure
2) Outline of cost structures
3) Strategies to reduce cost drivers
4) Economic shocks
5) **Economic decision making**

**Much of the content of this presentation is based on the following sources:*

[1] Plotkin et al. 2017. *The complexity and cost of vaccine manufacturing – An overview.* **Vaccine.** 35(33): 4064-4071. Available online at:

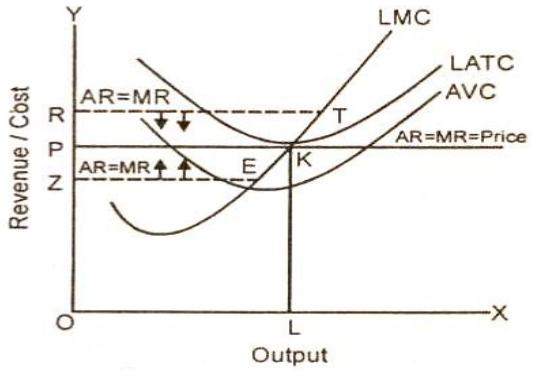
[2] Production Economics for Vaccines Handbook from the Bill & Melinda Gates Foundation. Available online at:

Vaccine Market Structure

Price taker markets (competitive, many suppliers)

Domestic markets

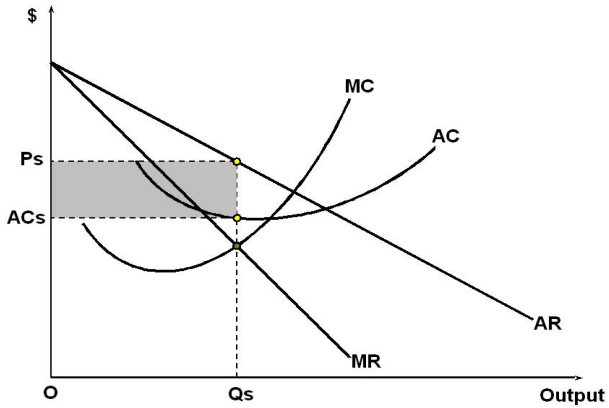
Export (procurement agencies)



https://economicsconcepts.com/long_run_equilibrium_of_the_price_taker_firm.htm

Monopoly markets (price setting, few suppliers)

Novel products



https://en.wikipedia.org/wiki/Monopolistic_competition

Price-taker vs Monopoly markets

Lower R&D cost with tech transfer	Do not influence price
Stable prices	Homogenous product
	Low barriers to entry

High prices	High R&D costs and risk
Market share	International stakeholders want to minimize supply risk
Royalties	

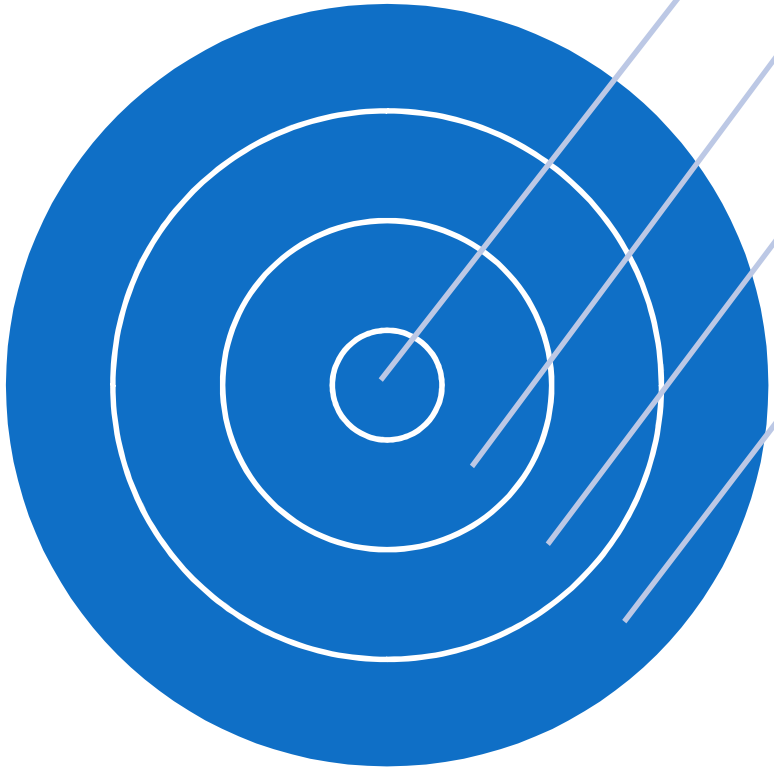
Intravacc transferring Hib conjugate vaccine technology to DCVM producers.

Partnership for a dengue vaccine

A Butantan vaccine in final trials leads to a US$100 million agreement with a US pharma company

https://revistapesquisa.fapesp.br/en/2019/06/26/partnership-for-a-dengue-vaccine/

Cost structures



Fixed costs

Product development and facilities and equipment

Variable costs

Consumables

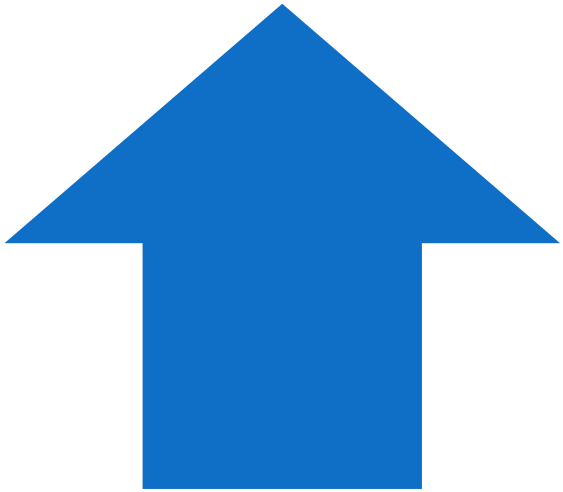
Semi-variable

Direct labor

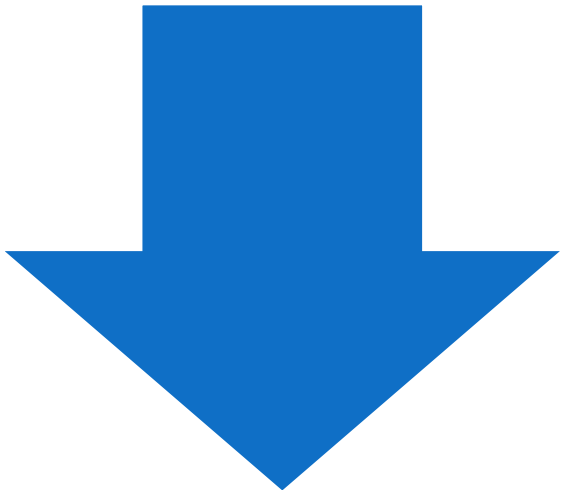
Mixed

Overhead, Licensing/Regulation and commercialization

Fixed Costs



Most significant cost facing vaccine manufacturers and cause high-entry barriers into market.

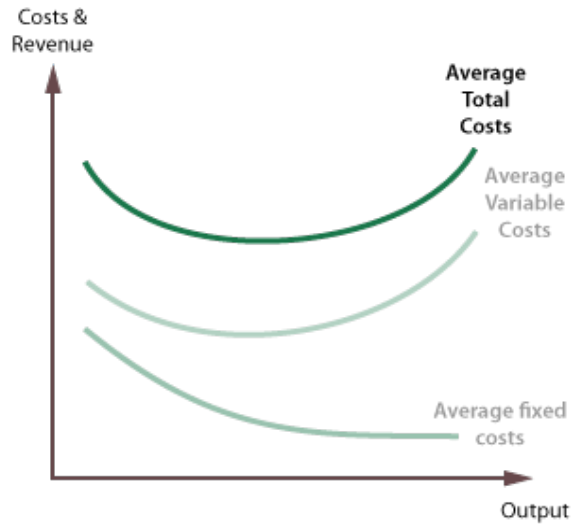


Fixed costs require large initial investment but average fixed costs will decline over time with increasing volume.

Fixed Costs

Long product-life cycle and economies of scale are crucial in achieving returns in investment on the fixed costs of vaccine production.

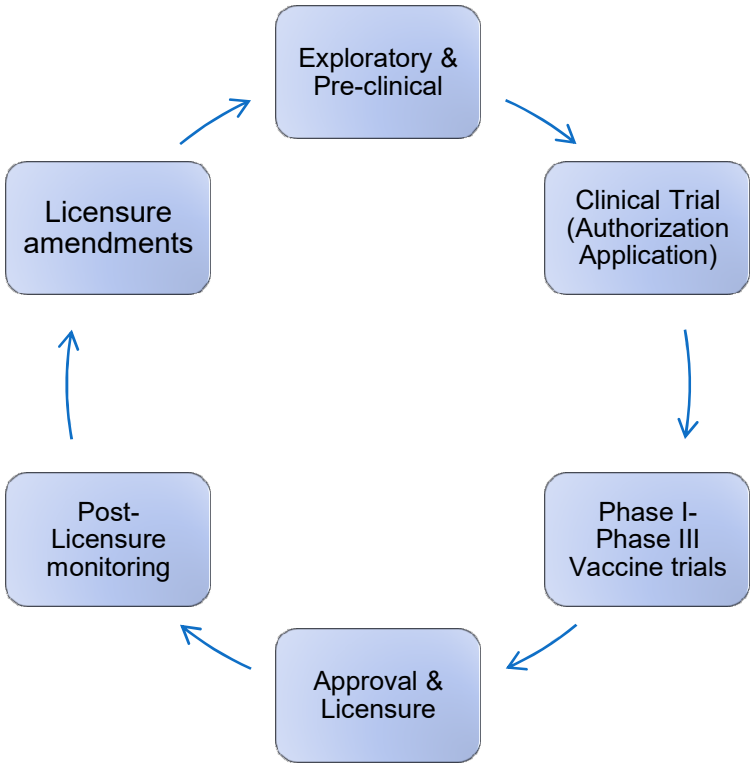
Economies of scale- cost advantages that manufacturers gain from increasing output. In other words, economies of scale will cause decreases in total costs per dose as production volume increases.



https://www.economicsonline.co.uk/Business_economics/Costs.html

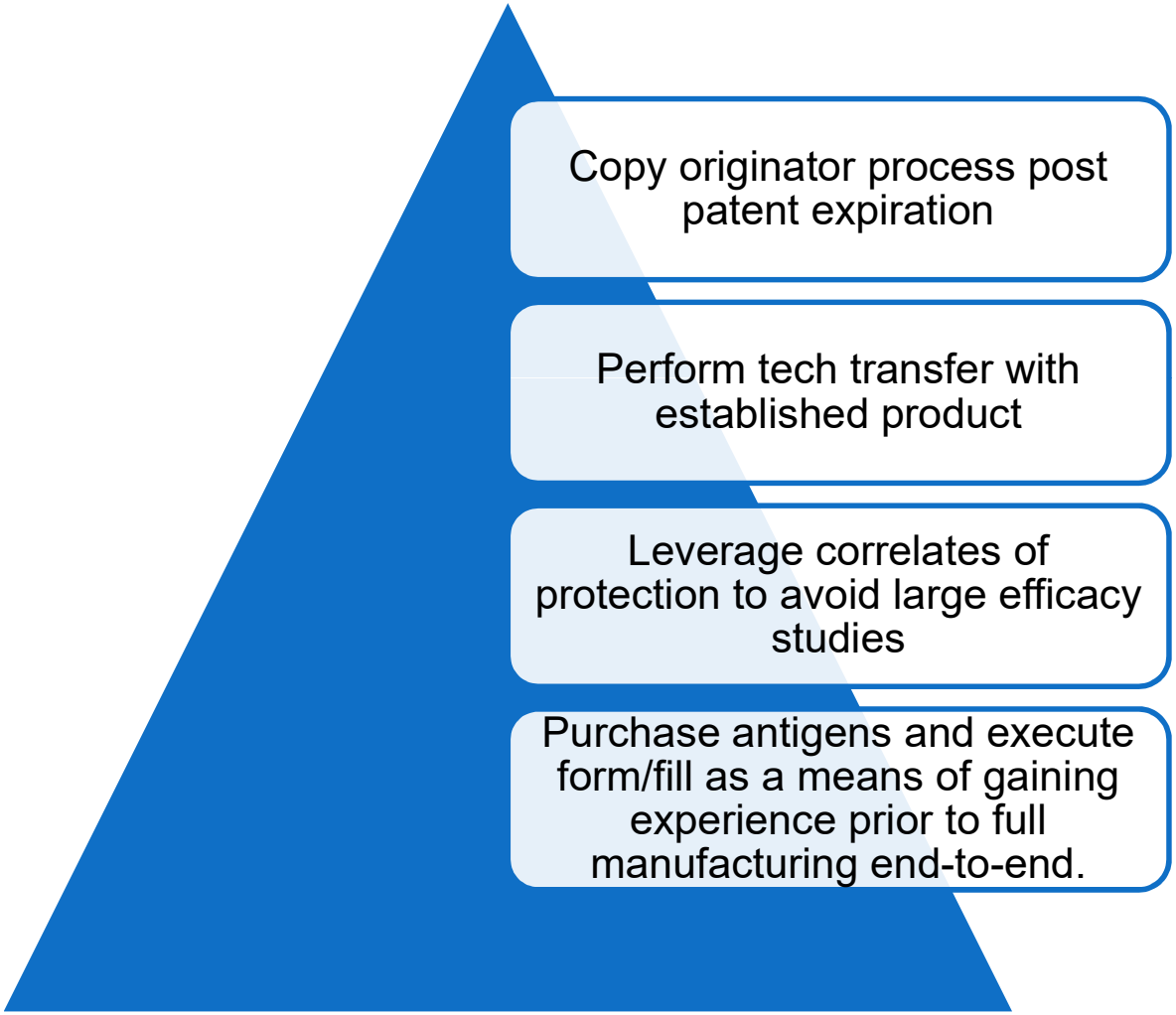
Product development

Vaccine product development a complex multistep process requiring significant time and financial investment:



Entire process takes 15 years or more and estimated to cost between 200 and 500 million dollars

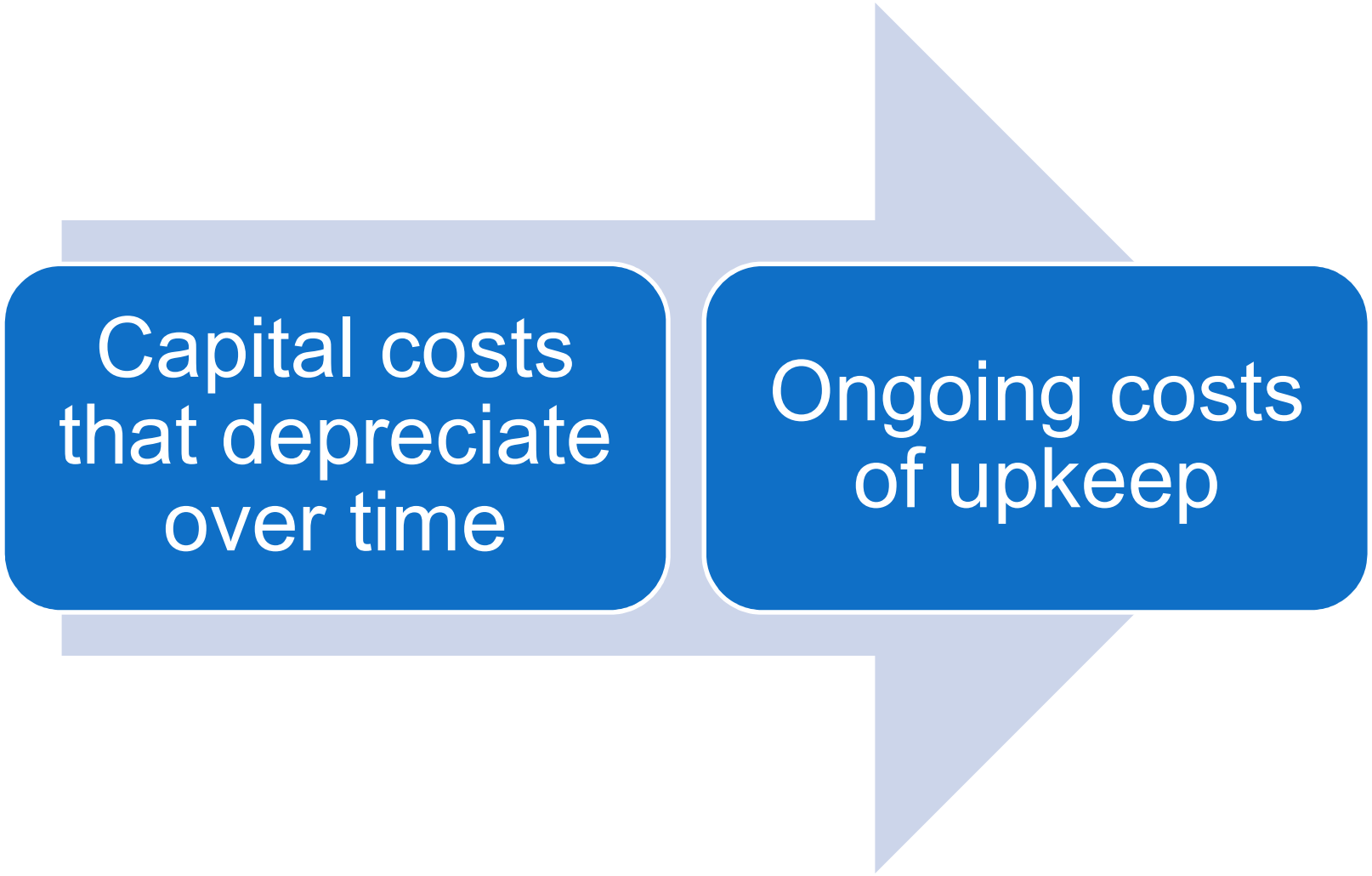
Ways to reduce production costs of product development



Risk/Reward tradeoffs in Product development

- Development costs vary greatly between vaccine types: Phase I development costs can vary from 2 million USD for translational products to 60 million USD for novel vaccines.
- Benefits of R&D in novel vaccine – first to market (monopoly prices), royalties from transfers , BUT high costs of R&D also risks in development failures i.e. efficacy to low.
- Manufacturers may choose to obtain technology from MNCs or biotechs to reduce the cost and time inherent to R&D. Low-risk strategy – prices subject to the market, lower revenue.

Facilities and equipment



Vaccine manufacturing facilities

Identify optimal capacity and forecast specific market need

Careful assessment of market opportunities required to determine optimal capacity and utilization.

Outcomes

- Underutilized facilities result in additional fixed cost burden increasing the per-unit dose cost
- Capacity not large enough to meet market need can lead to greater opportunity costs

Ways to reduce production costs of facilities and equipment

Plan for high facility utilization (make the most of existing resources):

- Force fit new processes into established platforms
- Increase utilization of existing facilities
- Use multi-dose vials

For example:

Share filling lines across multiple vaccines when applicable

Shift production volumes to multi-dose vials to reduce filling costs

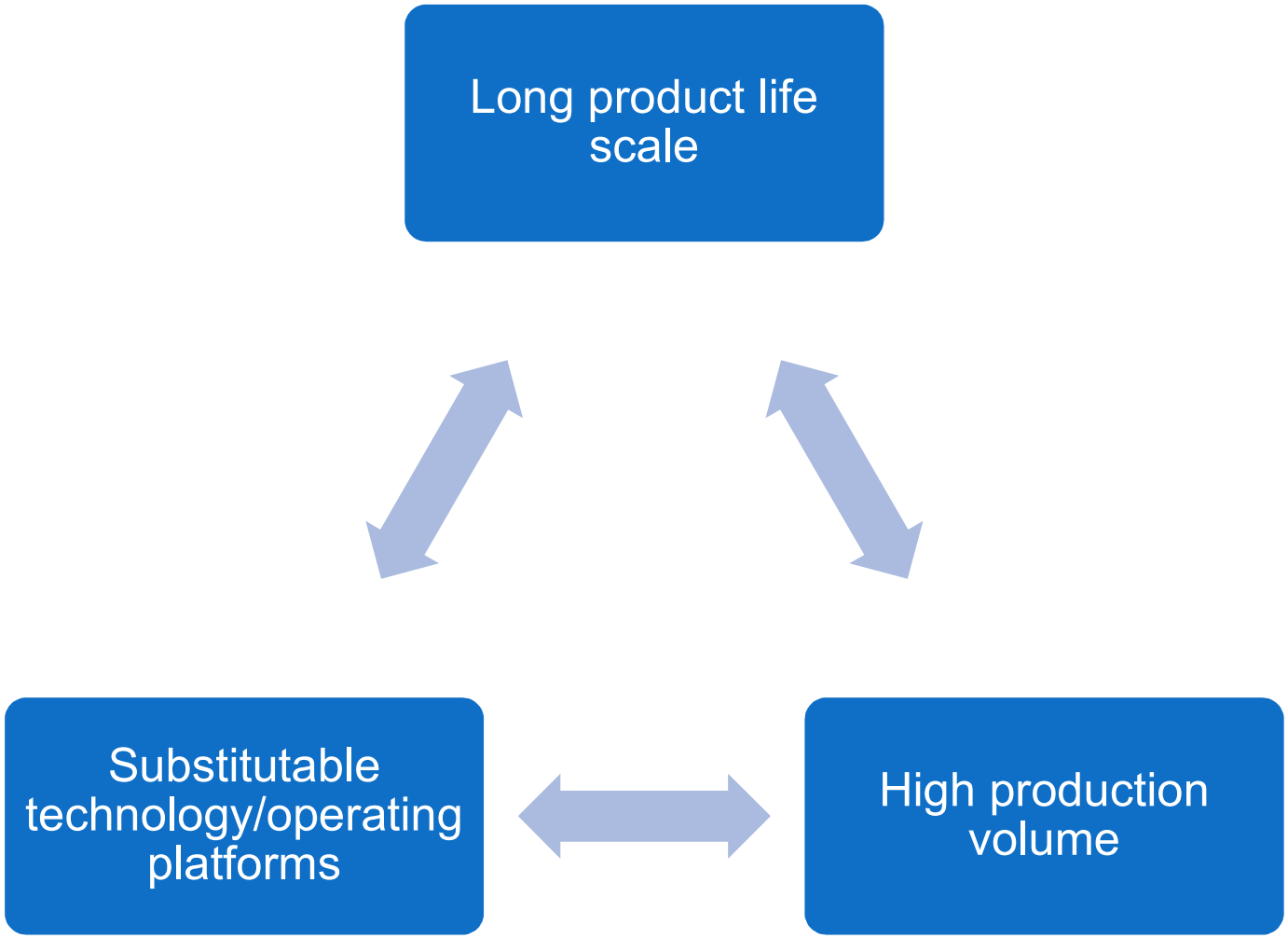
Ways to reduce production costs of facilities and equipment

Smaller impact strategies to reduce COGS:

- Use singe-use disposable systems to reduce capital cost
- Minimize classified production space with closed systems and Restricted Access Barrier Systems (RABs)
- Leverage blow-fill-seal (BFS) filling technology to shrink clean room footprint and reduce final product component costs, and reduce labor
- Utilize Contract Manufacturing Organizations (CMO) for low volume products or until demand supports facility construction e.g. Seasonal influenza vaccines often produced at a CMO.

For example a management decision to reduce capital cost in (1) would increase operating consumable costs.

Long-term fixed cost reduction

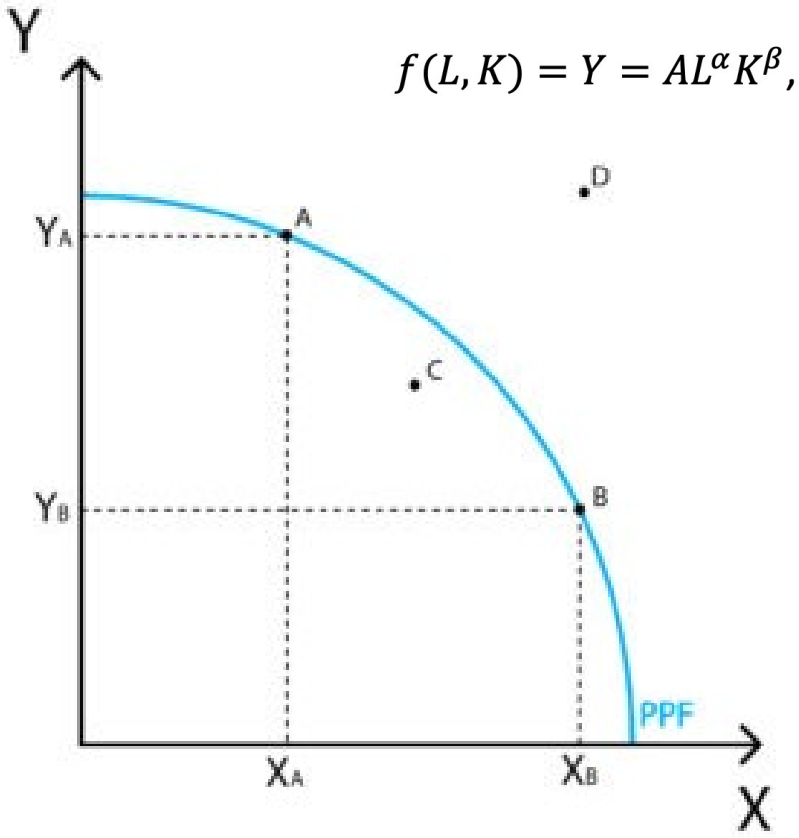


Production capacity

Marginal rate of transformation (MRT):

How much of one product do you have to give up to produce one more unit of another product.

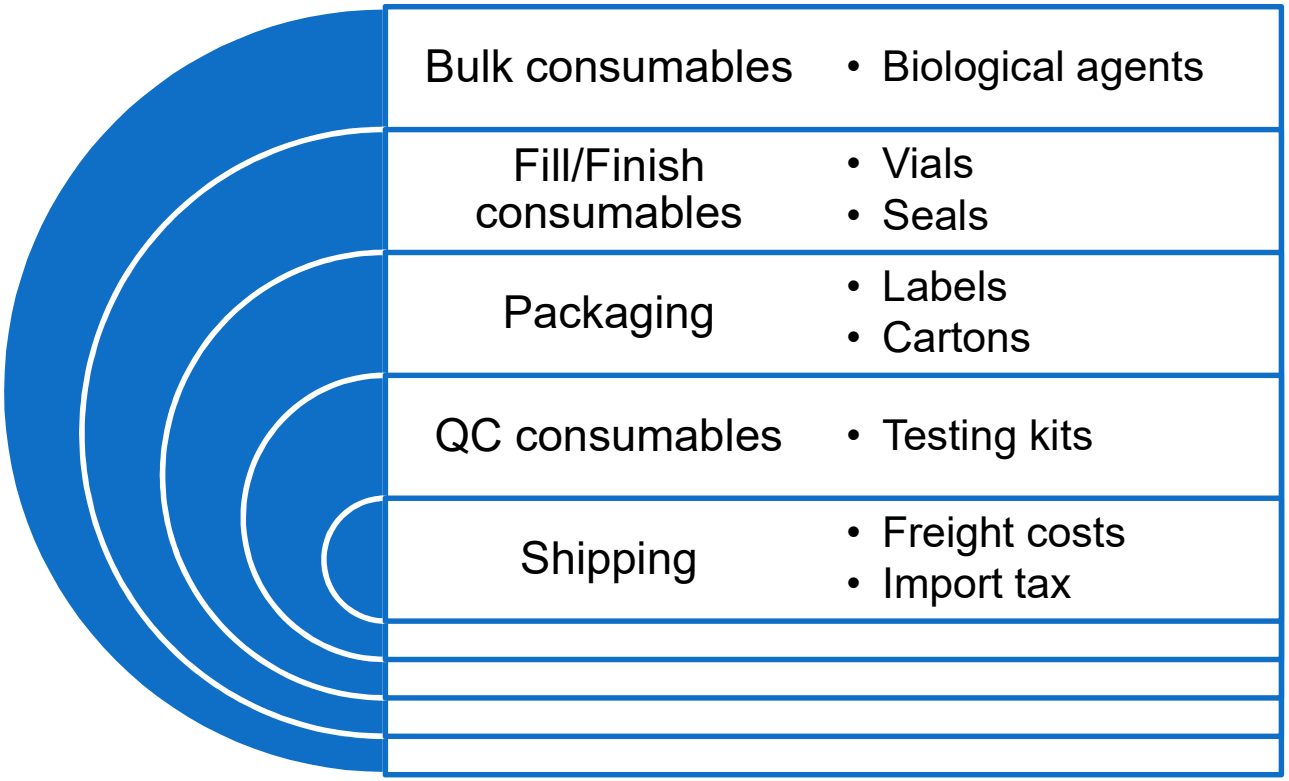
Function of technology, and capital and labor inputs – substitutability within these parameters normalizes MRT to one.



https://policonomics.com/lp-welfare-economics1-production-possibility-frontier/

Further Production Economics Costs

Consumables – Materials used as inputs in production, including materials



Further Production Economics Costs

Consumables are the key variable cost in vaccine manufacturing – they increase (decrease) directly with output.

Further Production Economics Costs

Direct labor- fully loaded costs that include all employee costs directly attributable to a specific vaccine e.g. wages, benefits.

→Costs vary by product and manufacturer based on market labor rates, manufacturing labor intensity, worker skill-level required, and complexity of manufacturing processes.

Labor costs differences between developed and developing countries is shrinking?

- Requirements of cGMP practices are increasing
- More developing countries hire consultants and import skilled labor

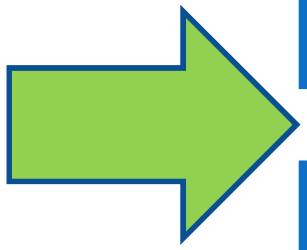
Increase automation and single-use production technologies	• Must be balanced with potential increase in equipment or consumable costs • E.g. Single-use, or disposable bioreactors reduce cleaning and sterilization requirements
Standardize and streamline processes across as many steps and vaccines as possible	• E.g. PCV assays are streamlined across multiple serotypes

Further Production Economics Costs

Overhead – Indirect costs that are necessary for the manufacturer to function, but are not directly attributable to a specific product e.g. management, quality systems, IT systems.

High if company has few products

Low if overhead can be allocated across multiple products



Invest in quality systems that can streamline quality practices and reduce costs over long term

Ensure management team has broad expertise to be leveraged across a portfolio of vaccines

Further Production Economics Costs

Licensing, regulatory and commercialization

- Expenses paid for the right to use product-related IP
- Expenses to comply with regulatory requirements to produce either for domestic markets or exports
- Costs of WHO PQ Process
- Sales and marketing costs

Further Production Economics Costs

Costs minimization strategies:

Request royalty reductions or waivers for vaccine sold in low income countries (LICs)

- Royalty for HPV antigens waived for volumes sold in Gavi markets

Produce reagents in-house or seek viable alternatives rather than license

Differentiate originator production processes sufficiently to be considered a novel process

Accelerate approval by seeking NRA or WHO priority review for vaccines for neglected diseases or emergency use

Allocation of Costs

To isolate the costs of resources used in the manufacturing of a specific vaccine, where resources may be used to manufacture and commercialize multiple products.

To isolate the costs of production and introduction for the vaccine specific to a particular geography when the product is sold in multiple markets

To isolate production costs of a specific vaccine between production steps

Manufacturers generally allocate costs to different products and market based on **relative revenues or volumes**

Use of accurate, simple and equitable cost allocations are critical in strategic decision-making and assessments

Example – technology for cost-effective vaccine manufacturing

Applying process intensification and continuous bioprocessing principles:

- Chaining equipment to semi- or fully continuous format to automate the process
- Reduces equipment, cleanrooms and overall facility cost
- Rapid deployment
- Reduces time and cost to market (demand flexibility)

NevoLine polio vaccine production platform

- 50 million doses at <$0.30
- Approx. 7-fold reduction in CAPEX

Addressing the need for cost-effective vaccine manufacturing

1-Oct-2019

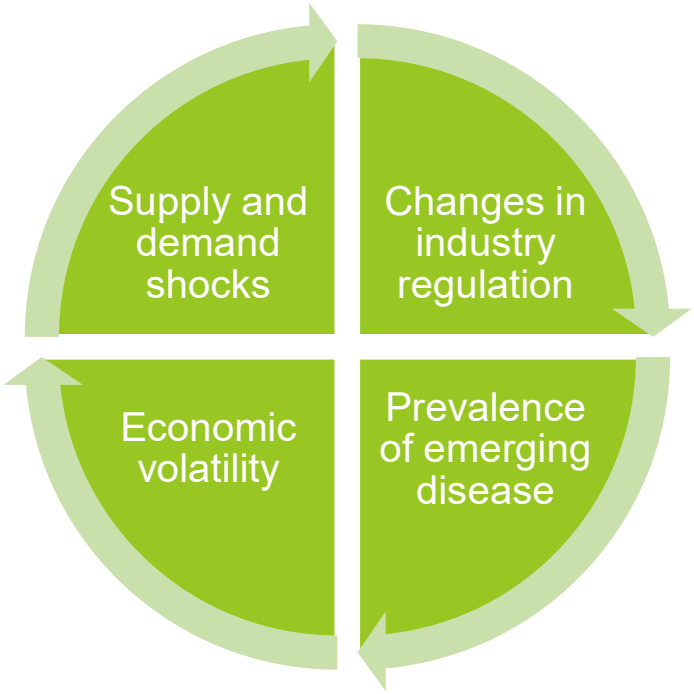
FINANCE | EQUIPMENT

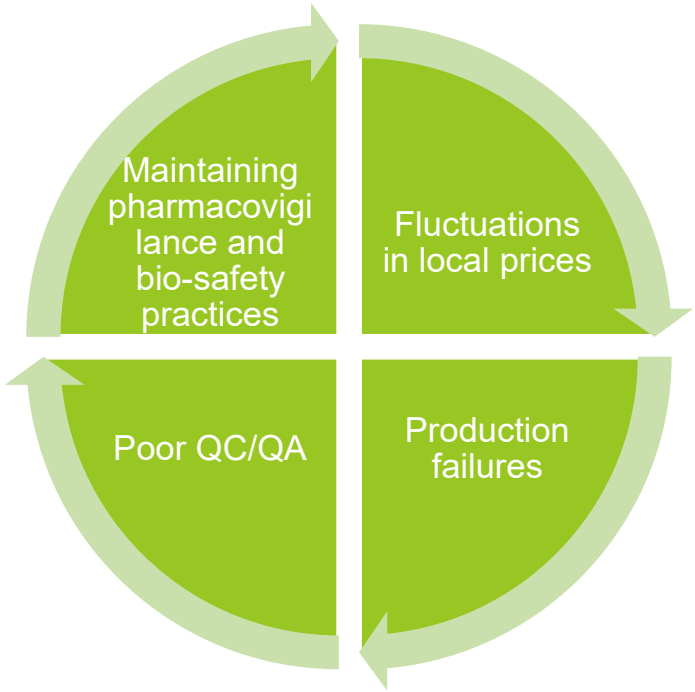
Process intensification and integrated continuous bioprocessing are two approaches that can be used to achieve cost-effective, local production of high-quality biologic products. Tania Pereira-Chilima, Product Manager at Univercells, explains

https://www.manufacturingchemist.com/news/article_page/Addressing_the_need_for_cost-effective_vaccine_manufacturing/158112

Economic shocks

Systematic vs **non-systematic risk**





Economic fluctuations

Inflation Rates

-Can increase costs of inputs, increasing production costs.

Foreign Exchange rates

- From the time raw materials are purchased to the time the final product (vaccine) is sold exchange rates can fluctuate greatly.
- Exchange rate variability influences costs and revenues of importing and exporting. Simple model: appreciated domestic currency makes importing raw materials more affordable while exports may be less price competitive
- Hedging against currency fluctuations has proven successfully and is an method adopted by many manufacturers.

In any case – forecasts of future inflation and exchange rates should be incorporated in business and product level decisions

→ Using multi-year averages effectively smooth the effect of business cycles.

Decisions based on production economics

Economics, in its simplest form is the science of decision-making:

- Maximizing utility subject to constraints
- Optimizing short and long term effects
- Aligning decision with values
- Accounting for macroeconomic variables

Two key methods in making economic evaluations are **Cost-Benefit Analysis (CBA)** and **Cost-Effectiveness Analysis (CEA and also iCEA).**

Cost-Benefit Analysis

Decision rule: choosing projects based on positive net present value (NPV) – in monetary terms is the present values of benefits is greater the present value of cost the project should go ahead.

$$\textbf{NPV}\text{of a project} = CF_0 + \frac{CF_1}{(1+r)^1} + \frac{CF_2}{(1+r)^2} + \frac{CF_3}{(1+r)^3} + \ldots + \frac{CF_n}{(1+r)^n}$$

Accounts for time value of money and risk.

If NPV is positive should you undertake the project?

Steps in Cost-Effectiveness Evaluation

Before conducting CEA, there are four preliminary considerations to be identified:

Baseline
- To determine the baseline to which the alternative program is compared. May include others alternatives i.e. different production platforms

Outcome
- Clearly define outcomes based on objective (maximizing profit, reaching target markets, achieving mandate)
- Must be discussed with stakeholders, funders, etc.

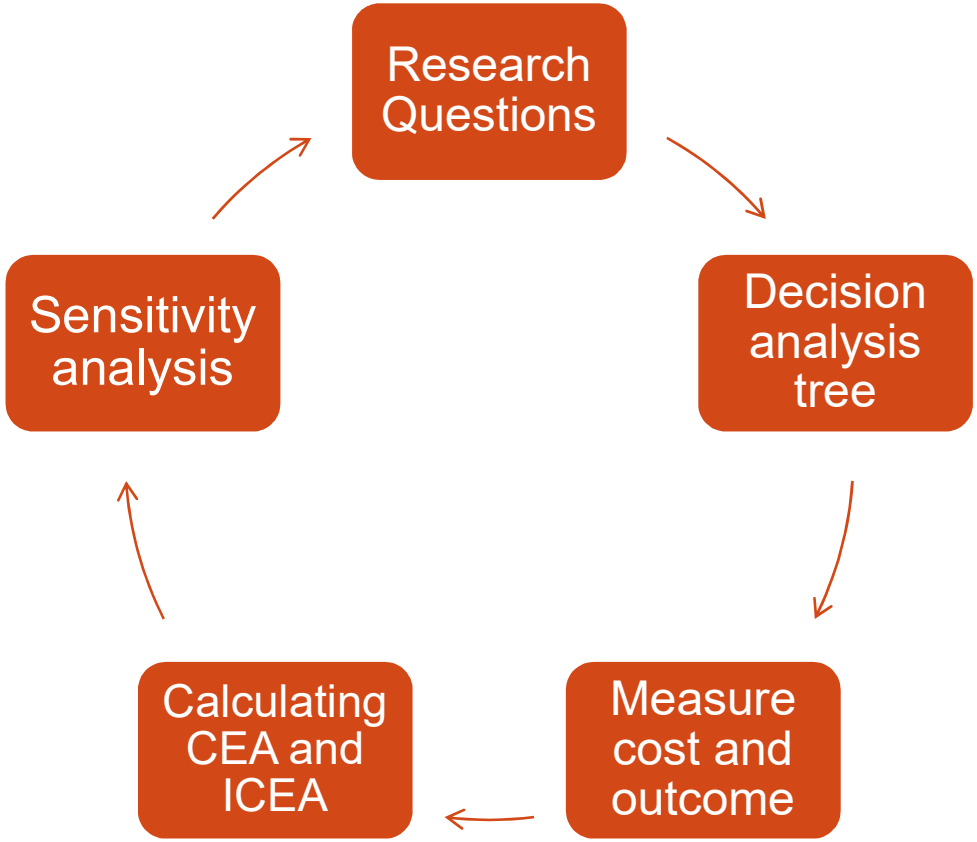
Perspectives
- Viewpoint of the analysis, which costs will be included and attributed to the outcomes
- Societal, funder, company perspectives

Time frame
- Analytic horizon in which outcomes and costs are collected must be ascertained

Haslinda et al, 2007

Cost-Effectiveness Analysis

Decision rule: choose the project with the lowest costs per outcome variable (in health care this is QALYs).



Cost-Effectiveness Analysis

CEA will tell us how efficiently the costs can produce an additional unit of effect.

$$CEA = \frac{cost}{units\ of\ effectiveness}$$

What is the shortcoming?

Economic analysis is concerned with costs and outcomes of all alternatives (opportunity costs).

$$ICEA = \frac{costs(B) - costs\ (A)}{effect(B) - effect\ (A)}$$

We want to know the cost-effective relative to other alternatives, or a threshold (current state)

Multi-Criteria Decision-Making

→ Prioritizing, or ranking, or choosing from amongst competing alternatives or individuals, based on considering multiple criteria (or objectives)

1) Alternatives to be prioritized

- E.g. Technology platforms

2) Criteria by which alternatives are to be prioritized/ranked

- Quantitative (future cash flow) or qualitative (platform substitutability)

3) Relative importance of the criteria

- By using weights or points system

→ Make decision subject to budget constraint

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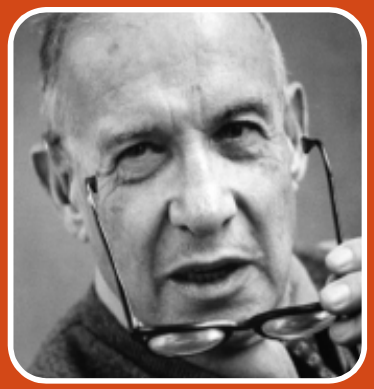
"Man is man because he is free to operate within the framework of his destiny. He is free to deliberate, to make decision, and to choose between alternatives"

- Martin Luther King



"Making good decisions is a crucial skill at every level"

- Peter F Drucker