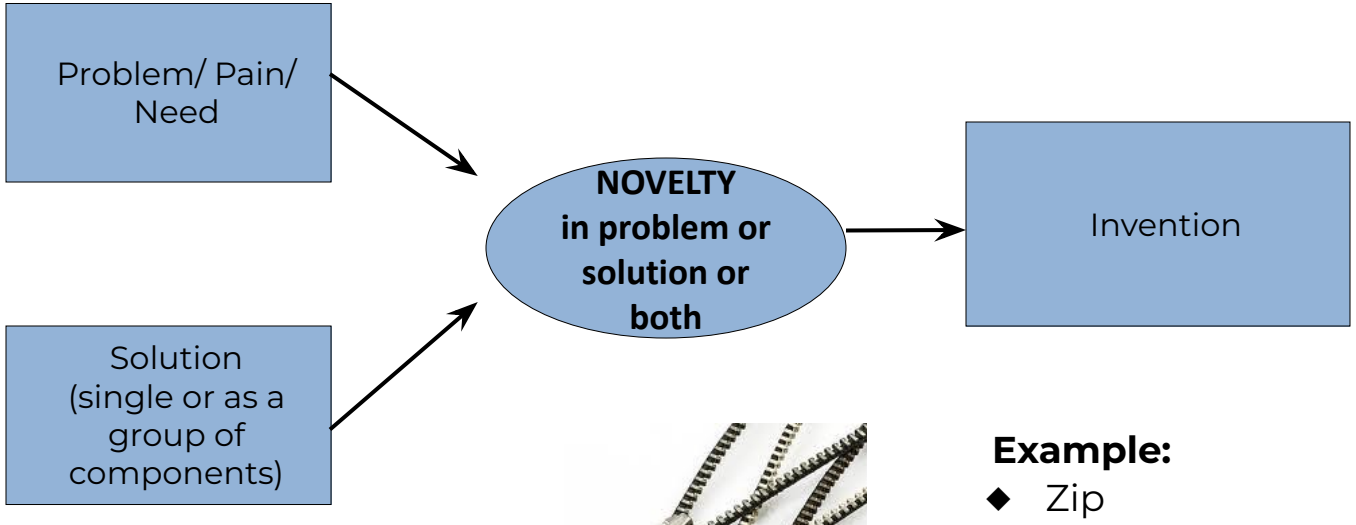
SESSION 2: Tech development, De-risking & Commercialization

25 slides

- **Premnath V.**

Technology Development & Commercialization

Invention



Example:

- Zip
- Velcro
- Bundling tie
- Punkah pulling machine

Patentable inventions

- **Invention**: An invention is the **creation** (by a human) of a **new** configuration, composition of matter, device, or process (that does not already exist in nature or is a law of nature) that serves a **useful** purpose.

- **Patentable**: An invention that is **(industrially) useful**, **novel** and **not obvious** to those who are skilled in the same field may be able to obtain the **legal** protection of a patent as allowed by the law of the land.

Modified from http://www.wikipedia.org/

Invention: Fosbury Flop

The Washington Post
Democracy Dies in Darkness

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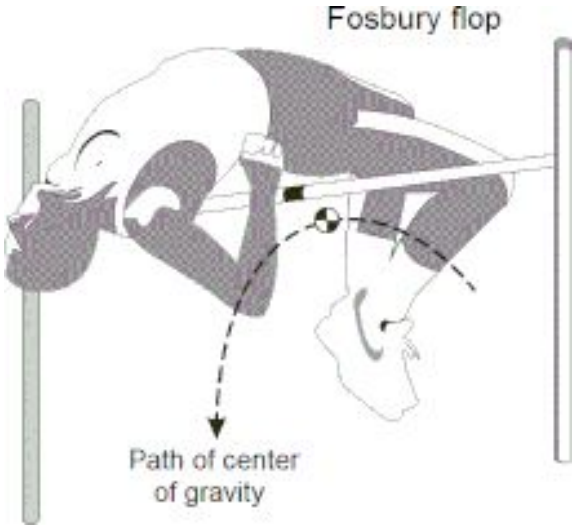
Dick Fosbury, whose 'Fosbury Flop' revolutionized high jump, dies at 76

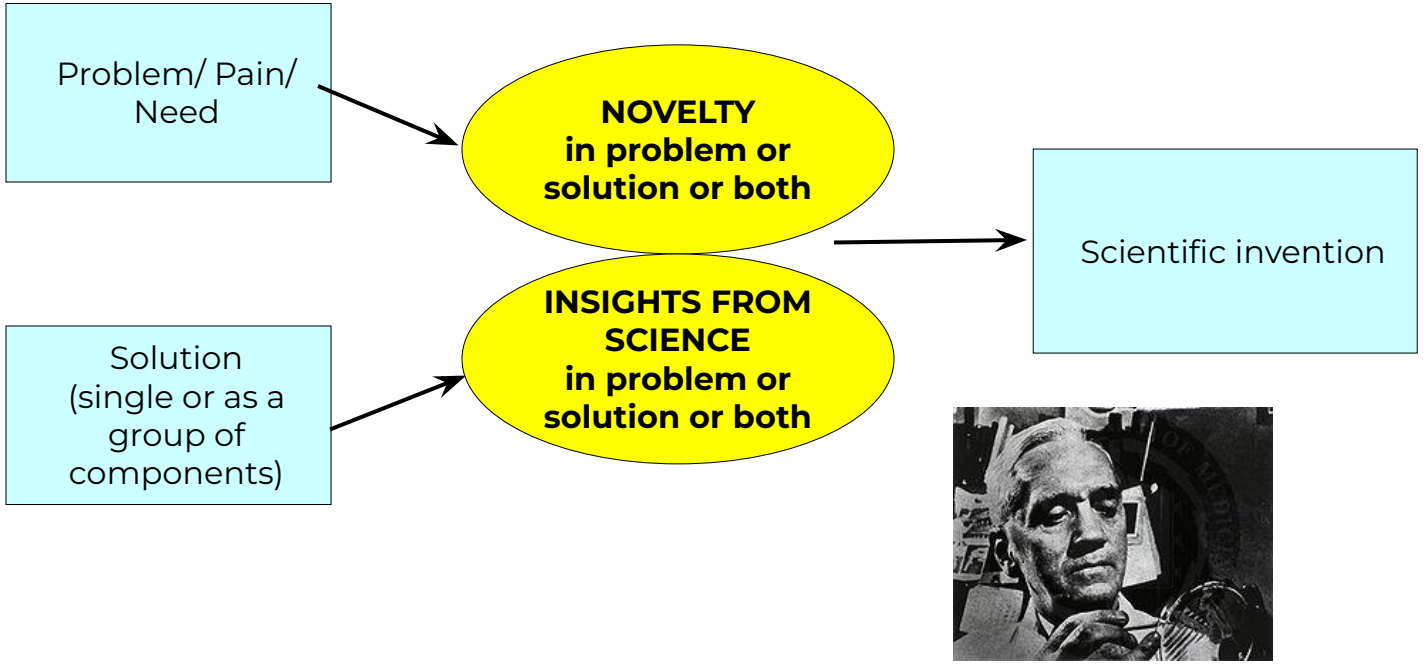
By Brian Murphy

March 14, 2023 at 3:11 p.m. EDT



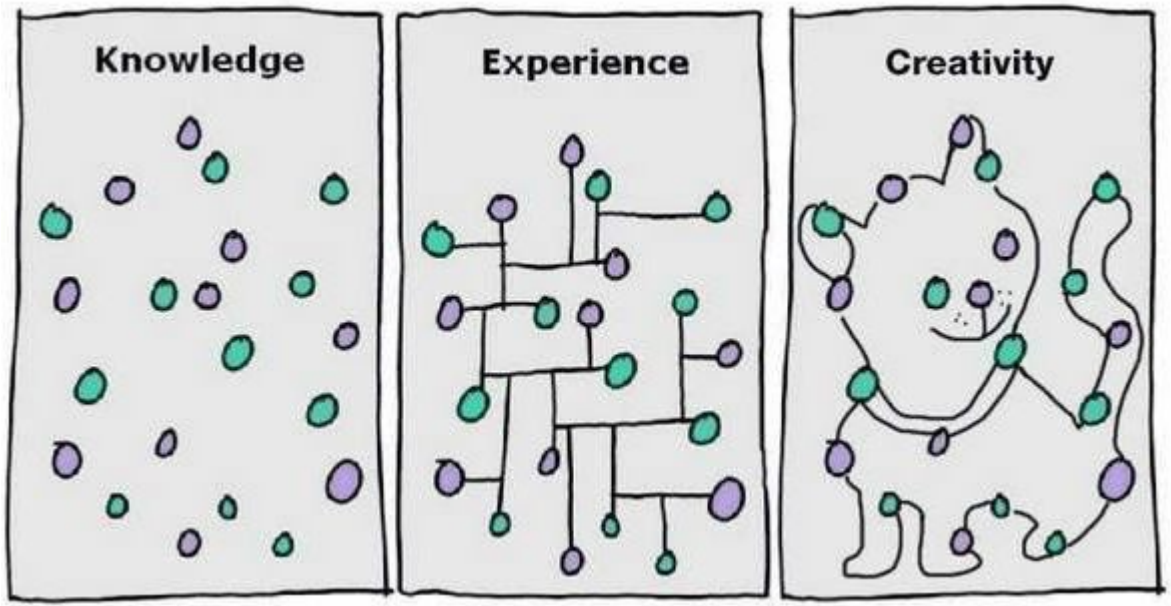
https://en.wikipedia.org/wiki/Fosbury_flop

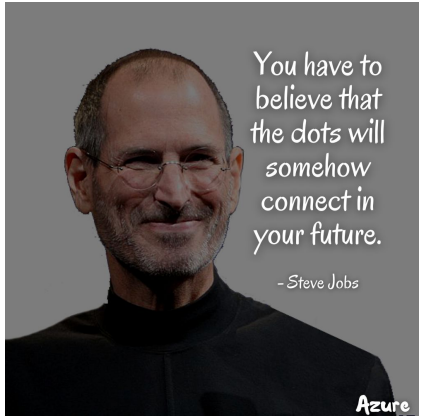
Scientific Inventions



Alexander Fleming: Penicillin

Secret sauce: How you connect the dots





https://www.linkedin.com/pulse/knowledge-experience-creativity-dr-anadi-sahoo/

Innovation

"market introduction"

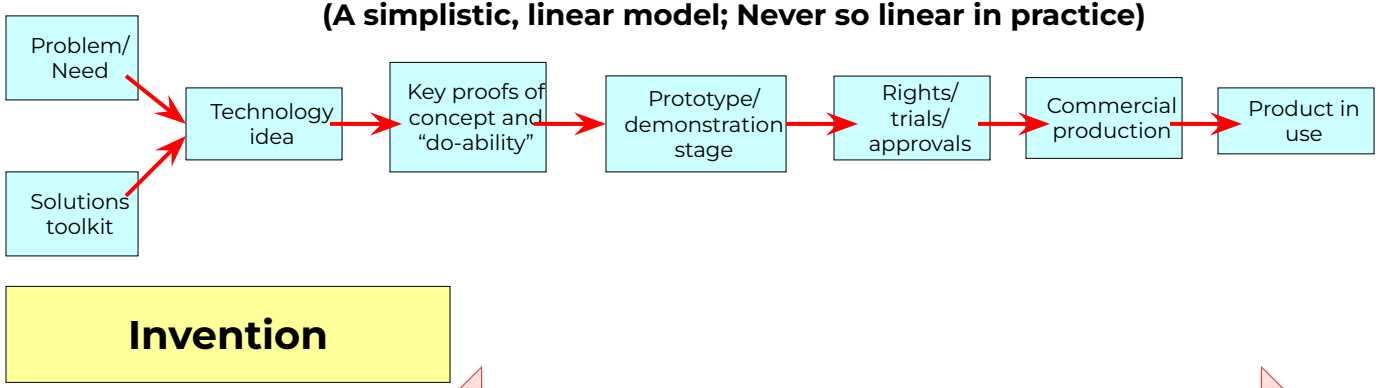
"novelty"

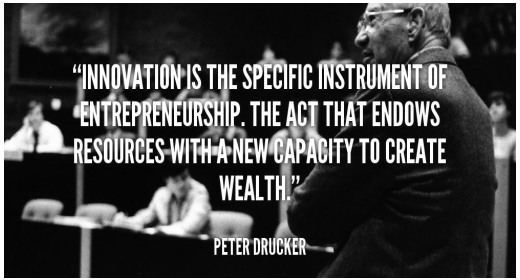
Organizational novelty

Technical novelty

Innovation: Taking to the market

(A simplistic, linear model; Never so linear in practice)



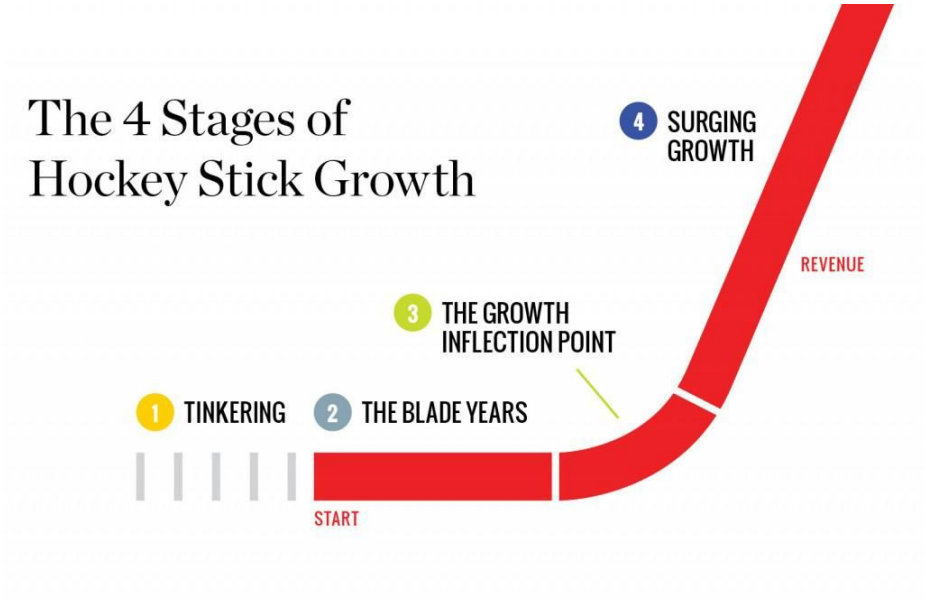


~ 80% of work, time, investment

Entrepreneurship – The vehicle for delivering innovations in a sustainable and scalable manner!

Note: All the inventions that are remembered have successfully navigated this process!

Startups: An important category of business for a country aiming to pole vault ahead



- An early bet on uncertain, emerging/ **future opportunities** by a committed **entrepreneur**
- A new way to solve a problem; **Innovation**
- Systematic **de-risking** while you wait for the tide to turn
- Rapid **scaling**
- Raise/ attract **risk capital** to fuel rapid growth in a timely manner

https://www.forbes.com/sites/sageworks/2016/10/23/navigating-the-make-or-break-years-as-you-create-hockey-stick-growth/

Examples

UBER

Unmet need:
Easy, predictable transport from A to B

Vision of the future:
Nobody will want to own a car

Solution:
App-based taxi hailing

Innovation:
Business process innovation

Revenue model:
Commissions

Type:
Disruptive, high risk

Resourcing:
- Venture Capital investments
- Partner (driver) investments

Unmet need:
Way to reduce COVID19 risks

Vision of the future:
Human body manufacturing biopharma molecules

Solution:
Vaccine for COVID19

Innovation:
Technical innovation

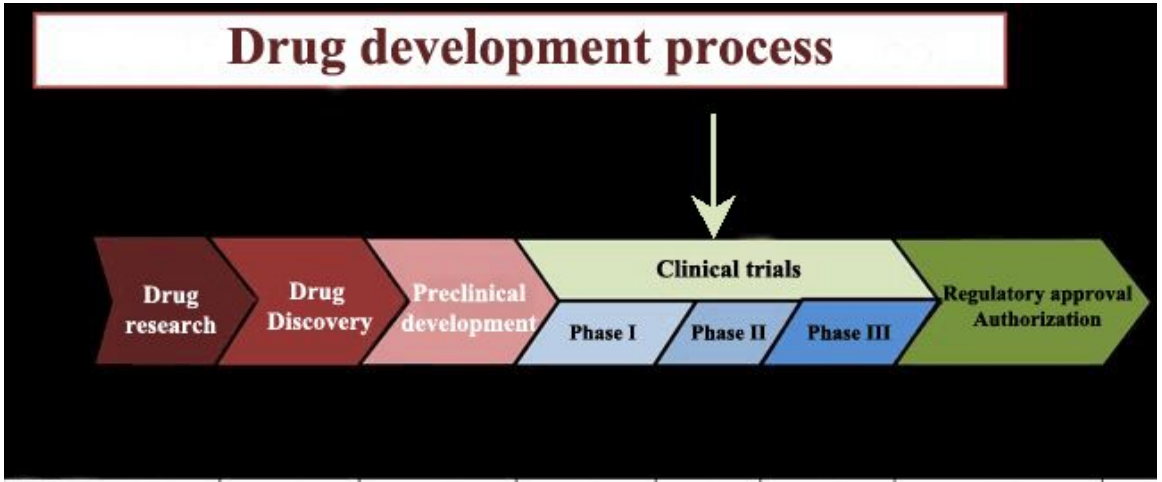
Revenue model:
Sale of vial of vaccine

Type:
Disruptive, high risk

How costs are covered:
-- Grants
-- Venture Capital investments
-- Strategic partnerships
-- Forward POs, sovereign indemnity
-- Now revenues

Technology De-risking Projects

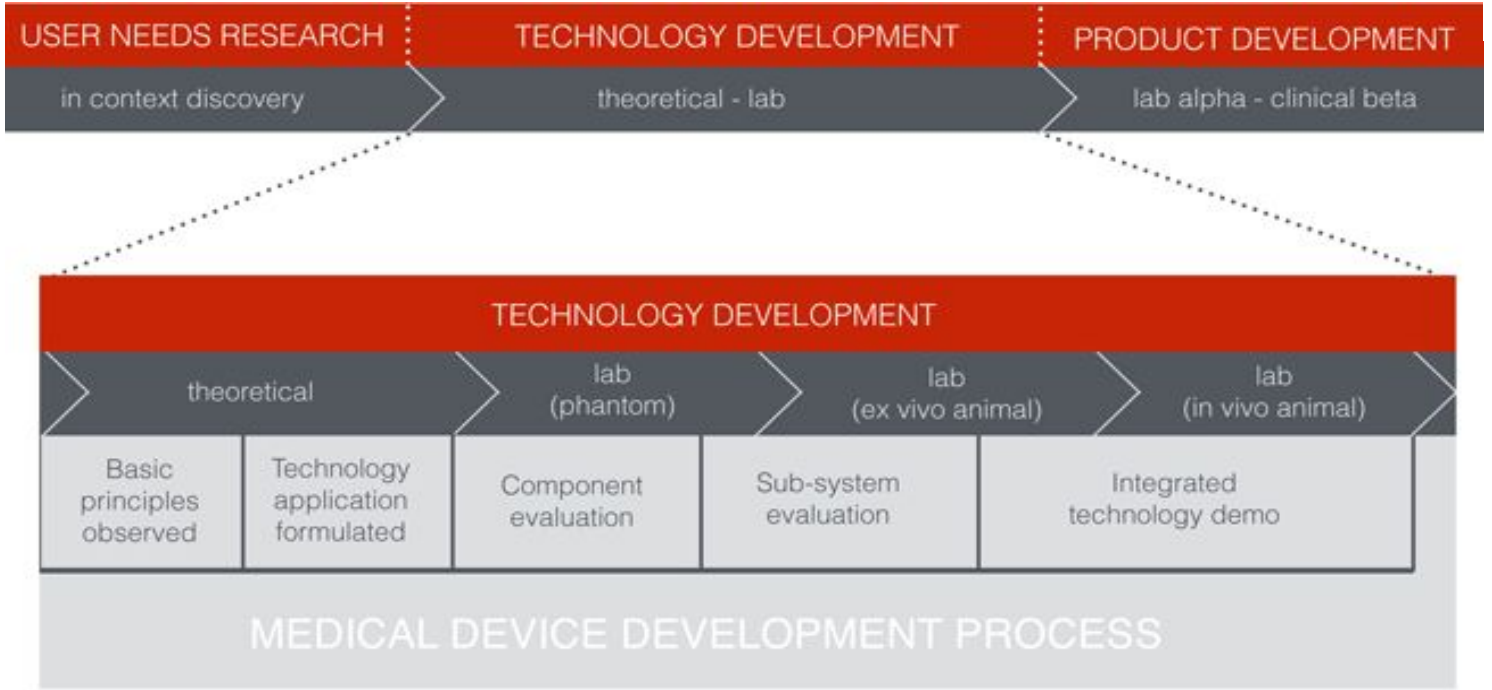
De-risking in drug development



Time (years)	2,5	3	1	1,5	2	2,5	1,5
Cost (% total)	4%	15%	10%	15%	22%	31%	3%
Success probability		0,0001%	1-5%	10%	30%	80%	95%

Source: http://www.davidfunesbiomed.eu/2016/03/141-clinical-research-overview.html

De-risking in medical device development

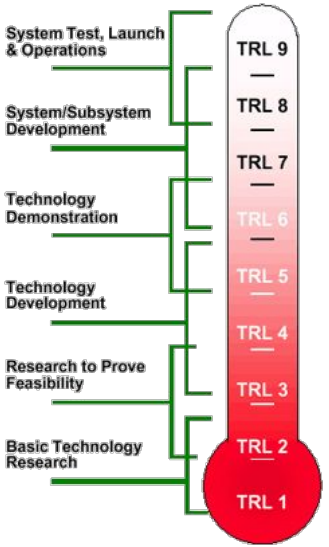


https://www.mddionline.com/how-cut-risk-and-score-more-medtech-home-runs?cid=nl.mpmn01.20150604

TRLs

Table Technology Readiness Levels based on those of the European Commission with modifications based on the US Army Technology Readiness Levels for a pharmaceutical product[2] [in blue]

Technology Readiness Level	Description
TRL 1.	Basic principles observed [scientific technical watch maintained]
TRL 2.	Technology concept formulated [research ideas and protocols are developed]
TRL 3.	Experimental proof of concept (PoC) [Hypothesis testing and initial proof of concept (PoC) is demonstrated in a limited number of *in vitro & in vivo* models]
TRL 4.	Technology validated in lab [PoC and safety of candidate formulation/device or system is demonstrated in a defined laboratory or animal model]
TRL 5.	Technology validated in relevant environment (industrially relevant environment in the case of key enabling technologies) [Pre-clinical studies, including GLP animal safety & toxicity, sufficient to support further trials]
TRL 6.	Technology demonstrated in relevant environment (industrially relevant environment in the case of key enabling technologies) [Phase 1 clinical trials support proceeding to phase 2 clinical trials or Class III device safety is demonstrated and in line with predictions]
TRL 7.	System prototype demonstration in operational environment [Phase 2 clinical trial is completed. Phase 3 clinical trial plan is approved. For devices the final product design is validated and final prototypes are produced and tested]
TRL 8.	System complete and qualified [Phase 3 clinical trial is complete and licencing/ authorisation given. For devices market approval given]
TRL 9.	Actual system proven in operational environment (competitive manufacturing in the case of key enabling technologies) [Post marketing studies and surveillance]



NASA's TRL

- http://www.npl.co.uk/upload/pdf/background-to-life-sciences-survey-and-TRL-scale.pdf
- **BIRAC's TRLs- https://www.birac.nic.in/desc_new.php?id=443**

BIRAC TRL Scale

- Website: https://www.birac.nic.in/desc_new.php?id=443
- Scales:
  - -- Drugs (including Drug Delivery)
  - -- Vaccines
  - -- Biosimilars
  - -- Regenerative Medicine
  - -- Medical Devices and Diagnosis
  - -- Artificial Intelligence, Big Data Analysis, IoT's, Software Development & Bioinformatics
  - -- Industrial Biotechnology (including secondary agriculture)
  - -- Agriculture
  - -- Aqua Culture and Fisheries
  - -- Veterinary

BIRAC TRL Scale: Example

5. Medical Devices and Diagnosis

Stage	Technology Readiness Level	Definition (Medical Devices including diagnostic devices)	Definition (In vitro Diagnostic Kits & reagents)	Definition (Biomedical implants)
Ideation	TRL-1	Need identified, Basic principles observed and reported (Scientific research begins which can be translated into applied research and development)	Need identified, Basic principles observed and reported (Scientific research begins which can be translated into applied research and development)	Need identified, Basic principles observed and reported (Scientific research begins which can be translated into applied research and development)
Proof of Principle	TRL-2	Market surveillance data and competitor analysis available to support the idea. Basic device design ready and product specifications defined based on the competitor analysis and patent landscaping. FTO ensured. Development of individual components initiated.	Hypothesis formulated and protocols developed. Market surveillance data and competitor analysis available to support idea. Individual core components of kit/reagents(Antibodies/ Antigens/Aptamers/Nano particles) finalized, developed/procured for testing	Market surveillance data and competitor analysis available to support the idea. Basic implant design ready, candidate materials shortlisted and product specifications defined based on the competitor analysis and patent landscaping. FTO ensured
Proof of Concept demonstrated	TRL-3	Individual modules/Components/PCBs/Software s/Systems developed and tested separately for its functionality on a breadboard/laboratory level. Material safety, electrical safety & biocompatibility of the systems demonstrated	Individual core components optimized at lab scale. Demonstrated the limit of detection/Sensitivity with metabolite serial dilution or ELISA or spiked biological sample studies.	Material research completed and material properties of the finalized material/composites compared against benchmarks. Relevant ASTM standard tests (strength, ductility, corrosion, surface properties, antimicrobial activity, usability, shelf life etc.) on the material performed successfully. Material sterilization method finalized. Biocompatibility (ISO 10993) proven in *in vitro* cytotoxicity assays.

Technology De-risking vs. Exploratory Research

Technology de-risking projects

Starting point:
- Idea of a solution for a problem

Purpose:
- Evidence that solution works
- De-risking/ validation

Exploratory research projects

Starting point:
- Curiosity

Purpose:
- Discovering new knowledge
- Develop new tools, methods of study

Designing experiments

Purposes of experiments

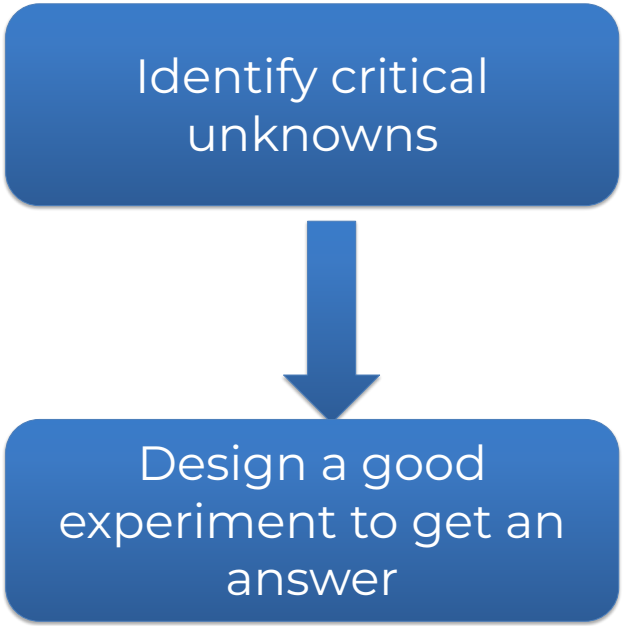
- Proof that the proposed solution works
- Standardizing SOPs and de-risking
- Proof that the solution delivers value being claimed
- Data that funders/ investors want to see to convince themselves
  - -- Technical feasibility
  - -- Commercial viability
  - -- Proof of Value, Quality, Superiority
- Data that customers want to see
- Data that KOLs want to see (can include publications, white papers)
- Data that regulators or certifying bodies want to see
  - -- Safety
  - -- Efficacy
  - -- Evidence supporting regulated claims

… for technology de-risking

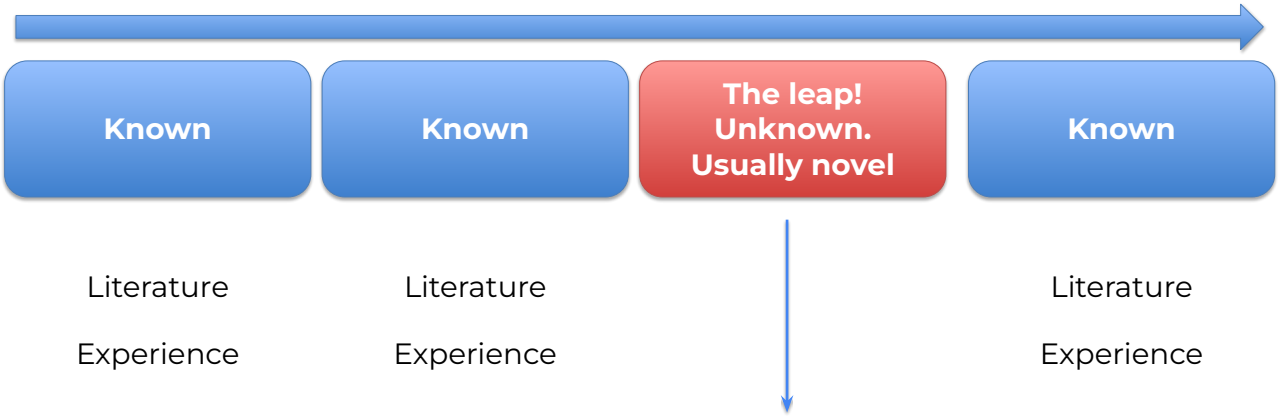
Risk associated with tech development

- ❑ Raw materials risk
- ❑ Equipment risk
- ❑ Method/process risk
- ❑ Expertise/knowhow risk
- ❑ Measurement risk
- ❑ IP risk
- ❑ Regulatory risks
- ❑ Safety and EHS risk
- ❑ Effectiveness (functionality) risk
- ❑ Cost effectiveness risk
- ❑ Environmental impact risk
- ❑ Scale up risk
- ❑ Trials and testing risk
- ❑ External environment risk

Technology de-risking through experimentation



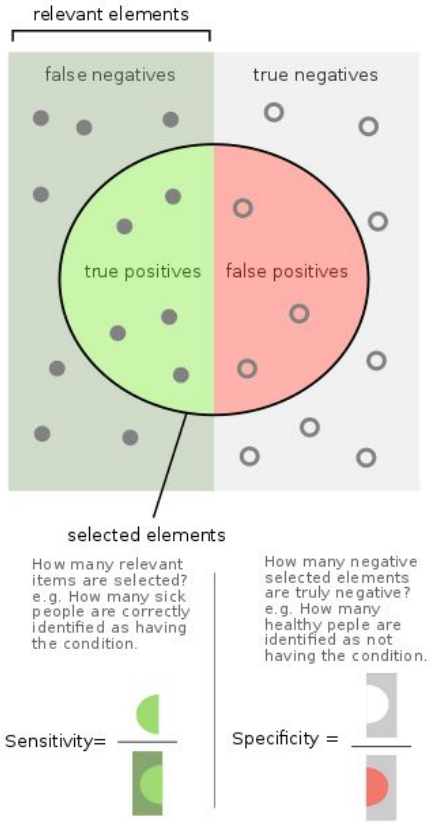
The balance between novelty and knowns



The leap: Why is it feasible?

-- Prelim data
-- Comparable
-- Reasonable chance

EXAMPLE --> Risk: Validating diagnostics



Typical progression:

- ❑ Marker identification, relationship, relevant concentrations, how sensitive?, R&R, etc
- ❑ Specificity studies
- ❑ Range (of variations) over which it works. Explore many situations where it works and where it doesn't, including interferences.

Depending upon the intended use (screening vs diagnosis) appropriate choice of sensitivity and specificity values is necessary

Source: https://en.wikipedia.org/wiki/Sensitivity_and_specificity

… for IP strategy

Risk: IP risk

- **Do you have freedom to operate/practice? Any uncertainty there that needs checking? Do you need back up plans?**
  - File early
  - Do a FTO analysis.
  - Research alternatives for sourcing, methods etc.

- **What is the risk to your own patents/ IP getting granted? Contested? Invalidated?**
  - Quality of drafting
  - Expedited grant

- **What is the risk of somebody bypassing your IP?**
  - Draft carefully. Structure claims smartly.
  - Create a portfolio instead of standalone IP

- **Risk of theft of IP**
  - Sign contracts with employees, partners etc
  - Sign NDAs with collaborators
  - Keep paper trail of sharing confidential information
  - File patents/ IP

Example: Rapid diagnostics

Knowns

❖ Need in undisputed and known

-- There is a need for a 30 min rapid RTPCR for airports to rule out C19 carriers with 100% accuracy.

❖ Problem is well understood

-- Air travelers are carriers. Air travel is higher risk. Current tests take too long or false negatives are high.

❖ Underlying science has been established

-- C19 virus signature known. RT-PCR method known and established.

Unknowns

- POC: Can the RT-PCR be done in 30 min?
- De-risking: R&R, S&S ?
- Certification: Do you have third party test data? Ex IEC.
- ***POV: Does it give quicker AND low false negatives compared to rapid antigen and conventional RT-PCR?***
- FTO: Does SOP/ method/ tools not infringe another patent? If it does, what is a work around?
- Own patent: Does data illustrate novelty and non-obviousness?
- IP coverage: Does it block competitors? Is there data for adequate variations?
- For KOLs: Is the data suitable and high quality for a peer reviewed publication?
- For clinical PI: Is the data convincing and credible? Was it done with credible methods and partners?
- For CDSCO submission: Is it safe? Does it do what it claims (efficacy)? Is data

Example POV study

Question: Was the detection accurate accurately? How reliable is “rule out”?

Raw data

Sample code	Gold standard Conventional RT-PCR	Bench mark/ comparator Rapid antigen	New method 30 min Rapid RT-PCR
1	Positive	Positive	Positive
2	Positive	Negative	Positive
3	Negative	Negative	Negative
199	Positive	Positive	Positive
200	Negative	Negative	Negative

sensitivity, recall, hit rate, or true positive rate (TPR)

$$\mathrm{TPR} = \frac{\mathrm{TP}}{\mathrm{P}} = \frac{\mathrm{TP}}{\mathrm{TP} + \mathrm{FN}} = 1 - \mathrm{FNR}$$

specificity, selectivity or true negative rate (TNR)

$$\mathrm{TNR} = \frac{\mathrm{TN}}{\mathrm{N}} = \frac{\mathrm{TN}}{\mathrm{TN} + \mathrm{FP}} = 1 - \mathrm{FPR}$$

precision or positive predictive value (PPV)

$$\mathrm{PPV} = \frac{\mathrm{TP}}{\mathrm{TP} + \mathrm{FP}} = 1 - \mathrm{FDR}$$

negative predictive value (NPV)

$$\mathrm{NPV} = \frac{\mathrm{TN}}{\mathrm{TN} + \mathrm{FN}} = 1 - \mathrm{FOR}$$

Sources: [23][24][25][26][27][28][29][30] view · talk · edit

		Predicted condition			
	Total population = P + N	**Positive (PP)**	**Negative (PN)**	Informedness, bookmaker informedness (BM) = TPR + TNR − 1	Prevalence threshold (PT) = $\frac{\sqrt{\mathrm{TPR}\times\mathrm{FPR}} - \mathrm{FPR}}{\mathrm{TPR} - \mathrm{FPR}}$
Actual condition	**Positive (P)**	**True positive (TP),** hit	**False negative (FN),** type II error, miss, underestimation	True positive rate (TPR), recall, sensitivity (SEN), probability of detection, hit rate, power = $\frac{\mathrm{TP}}{\mathrm{P}}$ = 1 − FNR	False negative rate (FNR), miss rate = $\frac{\mathrm{FN}}{\mathrm{P}}$ = 1 − TPR
	Negative (N)	**False positive (FP),** type I error, false alarm, overestimation	**True negative (TN),** correct rejection	False positive rate (FPR), probability of false alarm, fall-out = $\frac{\mathrm{FP}}{\mathrm{N}}$ = 1 − TNR	True negative rate (TNR), specificity (SPC), selectivity = $\frac{\mathrm{TN}}{\mathrm{N}}$ = 1 − FPR
	Prevalence = $\frac{\mathrm{P}}{\mathrm{P}+\mathrm{N}}$	Positive predictive value (PPV), precision = $\frac{\mathrm{TP}}{\mathrm{PP}}$ = 1 − FDR	False omission rate (FOR) = $\frac{\mathrm{FN}}{\mathrm{PN}}$ = 1 − NPV	Positive likelihood ratio (LR+) = $\frac{\mathrm{TPR}}{\mathrm{FPR}}$	Negative likelihood ratio (LR−) = $\frac{\mathrm{FNR}}{\mathrm{TNR}}$
	Accuracy (ACC) = $\frac{\mathrm{TP}+\mathrm{TN}}{\mathrm{P}+\mathrm{N}}$	False discovery rate (FDR) = $\frac{\mathrm{FP}}{\mathrm{PP}}$ = 1 − PPV	Negative predictive value (NPV) = $\frac{\mathrm{TN}}{\mathrm{PN}}$ = 1 − FOR	Markedness (MK), deltaP (Δp) = PPV + NPV − 1	Diagnostic odds ratio (DOR) = $\frac{\mathrm{LR+}}{\mathrm{LR-}}$
	Balanced accuracy (BA) = $\frac{\mathrm{TPR}+\mathrm{TNR}}{2}$	F_1 score = $\frac{2\mathrm{PPV}\times\mathrm{TPR}}{\mathrm{PPV}+\mathrm{TPR}} = \frac{2\mathrm{TP}}{2\mathrm{TP}+\mathrm{FP}+\mathrm{FN}}$	Fowlkes–Mallows index (FM) = $\sqrt{\mathrm{PPV}\times\mathrm{TPR}}$	Matthews correlation coefficient (MCC) = $\sqrt{\mathrm{TPR}\times\mathrm{TNR}\times\mathrm{PPV}\times\mathrm{NPV}} - \sqrt{\mathrm{FNR}\times\mathrm{FPR}\times\mathrm{FOR}\times\mathrm{FDR}}$	Threat score (TS), critical success index (CSI), Jaccard index = $\frac{\mathrm{TP}}{\mathrm{TP}+\mathrm{FN}+\mathrm{FP}}$

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