# PROTECTION OR TREATMENT?

**Pharmacology in the Time of Covid-19**

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***Founder and MD, Biotech Advisory Services***

# CONTENTS

# COVID-19 TREATMENT

- Do nothing
- Administer oxygen
- Administer medicines
- Hospital and ICU care

# COVID-19 PROTECTION

Vaccines are considered the most effective form of healthcare intervention.

In 2013, it was estimated that 103 million cases of childhood diseases in the United States had been prevented by the use of vaccines since 1924.

# REGULATION AND MANUFACTURING

**How do you fast track a vaccine or a medicine?**

Pharmaceutical breakthroughs usually take many years, but the Covid-19 pandemic has shown us it doesn't have to be this way.

Companies such as Pfizer, Moderna and AstraZeneca have overcome the hurdles to get their candidates through Phase III clinical trials in record time.

**Safety testing and safety assessment is the same as any other medicine so why are COVID vaccines being approved for use so quickly?**

*The ethics approval process needs work:*

The research ethics regulatory system has protected us against these risks for 50 years. It ensures newly released products will be safe and effective.

But the system has problems. It has become deeply bureaucratised and ethical discourse has often been replaced by rigid administrative rules and the slavish completion of forms.

Often the approval process can take months, and involve an extensive cycle of quibbling with little or no ethical content.

# CLOSE COLLABORATION AND CO-OPERATION BETWEEN THE FDA, EMA, MHRA AND EACH VACCINE MANUFACTURER.

MINISTRY OF HEALTH
MANATŪ HAUORA



REGULATORY BODY:

Medical & Healthcare Products Regulatory Agency (MHRA)

MHRA

# DEVELOPING VACCINES

Prof Martin Landray, co-chair of Recovery, said both vaccines and treatments are vitally important. Setting one above the other is a bit like saying “if you don’t want your house to catch fire or burn down, that because you’ve got all flame-retardant materials you don’t need the fire brigade”, he said. “We’re going to have to have treatments. And when you’re sick, whether you’ve had a vaccine or not, being told prevention is better than cure is not really terribly helpful.”

*the Guardian on line*

# TYPES OF VACCINE

**COVID-19**

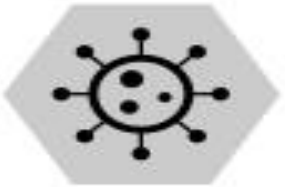
## What are the different kinds of vaccine?

### RNA

RNA vaccines work by introducing an mRNA sequence (the molecule which tells cells what to build) to the system which is coded for a specific antigen.

### DNA

Short for deoxyribonucleic acid, DNA is another of the crucial macromolecules for life. A DNA vaccine involves the direct introduction into appropriate tissues of a plasmid - a doubled-stranded molecule which exists in bacterial cells.

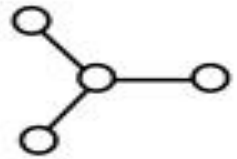


### Viral vector

Vaccines use live viruses to carry DNA into human cells.

### Virus-like particle

This type of vaccine contains molecules that mimic the virus but are not infectious and, therefore, not a danger. VLP has been an effective way of creating vaccines against diseases such as human papillomavirus (HPV), hepatitis and malaria.



### Protein sub-unit

This kind of vaccine uses a part of the virus, in this case the protein component. These vaccines can also be used on almost anyone, including people with weakened immune systems and long-term health problems.

### Inactivated virus

These vaccines use the dead version of the virus that causes a disease.

SOURCE: VACCINES.GOV, NEWS MEDICAL LIFE SCIENCES, SCIENCE MEDIA CENTER | NOVEMBER 24, 2020

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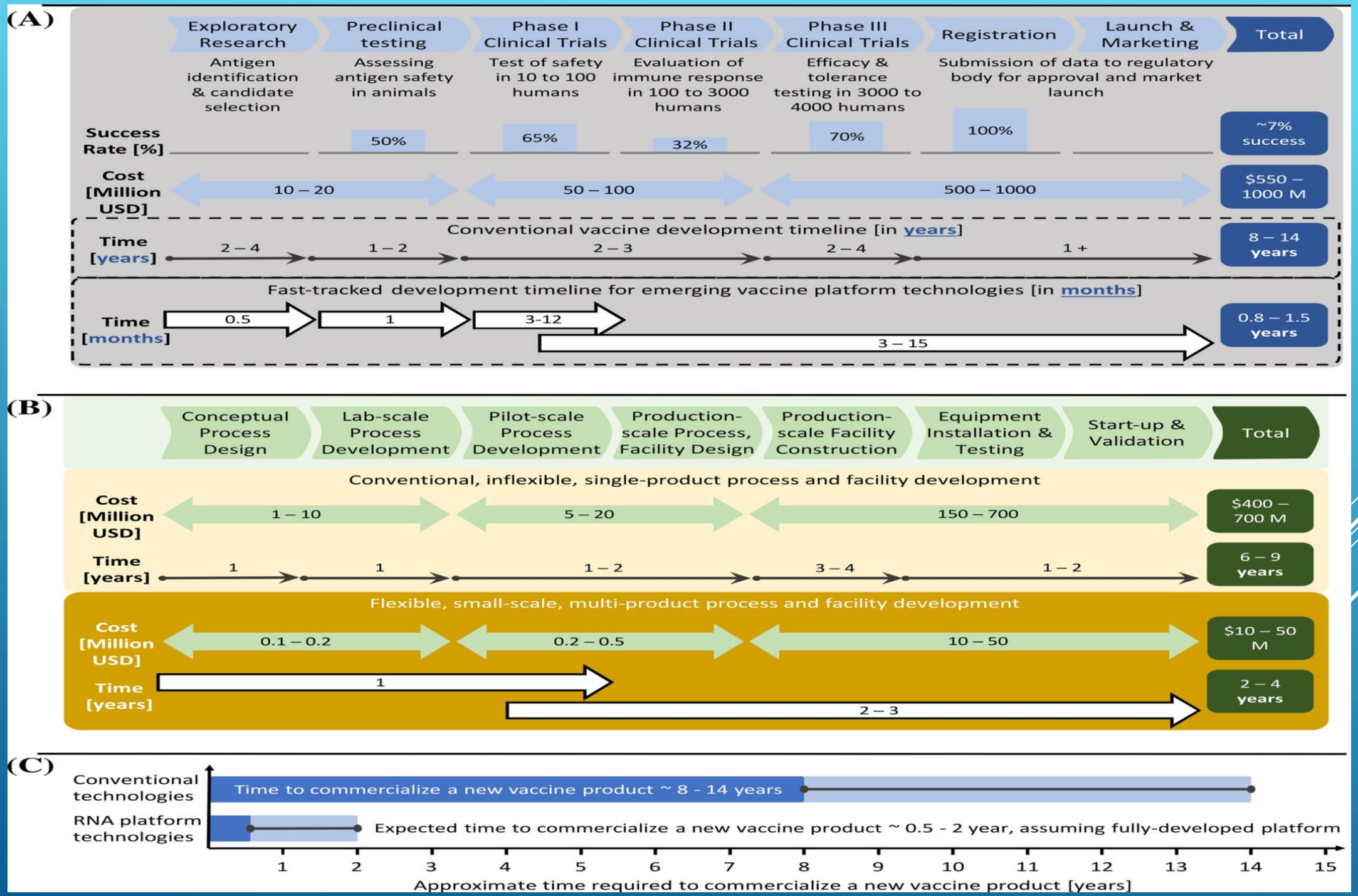
# SO WHAT ARE THOSE TREATMENTS? WHAT WORKS?

- **Steroids -** In July, Horby and others published a paper showing that 12,000 lives in the UK and 650,000 worldwide could be saved by January by the widespread use of **dexamethasone**. The drug is now standard treatment for those who are on ventilators.
- **Anti-virals - Colchicine** is the latest drug to turn in exciting results, according to Horby. A Canadian study showed  it may end up with 20% reduced risk of hospitalisation or death.
- **Mono-clonal antibodies** - There are quite a few positive results from monoclonal antibody studies to prevent people becoming seriously ill, such as **tocilizumab**, which is a monoclonal antibody given to rheumatoid arthritis patients.
- **Drugs to prevent blood** clots are looking promising. Clotting is a big issue in severe Covid as a result of inflammation – such as **aspirin, heparin**.

**The problem is all drugs have side-effects, some are dangerous and require discontinuation of the drug, possibly leading to less chance of surviving the infection.**

# TIMELINES


(A)
Exploratory Research
Antigen identification & candidate selection
Preclinical testing
Assessing antigen safety in animals
Phase I Clinical Trials
Test of safety in 10 to 100 humans
Phase II Clinical Trials
Evaluation of immune response in 100 to 3000 humans
Phase III Clinical Trials
Efficacy & tolerance testing in 3000 to 4000 humans
Registration
Launch & Marketing
Submission of data to regulatory body for approval and market launch
Total
Success Rate [%]
50%
65%
32%
70%
100%
~7% success
Cost [Million USD]
10 – 20
50 – 100
500 – 1000
$550 – 1000 M
Conventional vaccine development timeline [in years]
Time [years]
2 – 4
1 – 2
2 – 3
2 – 4
1 +
8 – 14 years
Fast-tracked development timeline for emerging vaccine platform technologies [in months]
Time [months]
0.5
1
3-12
3 – 15
0.8 – 1.5 years
(B)
Conceptual Process Design
Lab-scale Process Development
Pilot-scale Process Development
Production-scale Process, Facility Design
Production-scale Facility Construction
Equipment Installation & Testing
Start-up & Validation
Total
Conventional, inflexible, single-product process and facility development
Cost [Million USD]
1 – 10
5 – 20
150 – 700
$400 – 700 M
Time [years]
1
1
1 – 2
3 – 4
1 – 2
6 – 9 years
Flexible, small-scale, multi-product process and facility development
Cost [Million USD]
0.1 – 0.2
0.2 – 0.5
10 – 50
$10 – 50 M
Time [years]
1
2 – 3
2 – 4 years
(C)
Conventional technologies
Time to commercialize a new vaccine product ~ 8 - 14 years
RNA platform technologies
Expected time to commercialize a new vaccine product ~ 0.5 - 2 year, assuming fully-developed platform
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
Approximate time required to commercialize a new vaccine product [years]

COVID-19

# Vaccines under development

According to the World Health Organization (WHO), there are more than 150 vaccines under development for the coronavirus that has swept across the world.

Some of the vaccines are closer to release as they pass through the third phase of human trials. Vaccines made in Russia and China were released prior to the third phase of human trials.


** One dosing regimen showed vaccine efficacy of 90 percent when it was given as a half dose, followed by a full dose at least one month apart. Efficacy was 62 percent when it was given as two full doses at least one month apart. The combined analysis from both dosing regimens resulted in an average efficacy of 70 percent.*

SOURCE: REUTERS, WHO | NOVEMBER 24, 2020

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# MANUFACTURING VACCINES

# COMPLIANCE

Good Manufacturing Practice (GMP) is a manufacturing control philosophy, that is applied by all approved manufacturers and health authorities to ensure that medicines and technologies used in health:

**are safe,**

**that they work and**

**that they are reliable…and available**

# VACCINES: A COMPLEX MANUFACTURING PROCESS

### 1 BACTERIA, VIRUS OR CELL CULTURE

The antigens are developed using raw material

### 2 HARVESTING

The antigens produced from microorganisms are extracted

### 3 PURIFICATION

Impurities are removed and concentrated through physical and chemical processes

### 4 INACTIVATION

Pathogenicity is suppressed while retaining immunological properties

### 5 VALENCE ASSEMBLY

The active antigenic substances are combined in a single component

### 6 FORMULATION

All the ingredients are melt together

### 7 FILLING

The vaccine is filled into a vial or a syringe

### 8 FREEZE-DRYING

This step makes it possible to remove the water in a product by transforming it into powder, which ensures a better stability and therefore a better conservation

### 9 PACKAGING

The vaccine is labeled in accordance with regulatory requirements and packed, ready for shipping

### 10 BATCH RELEASE

Quality assurance confirms the product has been manufactured and tested in accordance with the correct procedures. The national regulatory authority gives the final authorization to release the product for distribution

### 11 TRANSPORT

Our vaccines are distributed all around the world, respecting the cold chain and a temperature between 2 and 8 degrees C

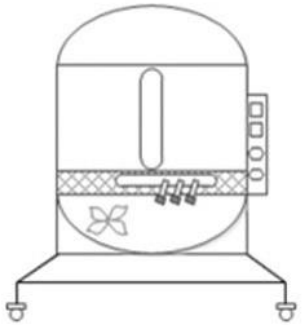
PRODUCTION TAKES BETWEEN
**6 AND 36 MONTHS**

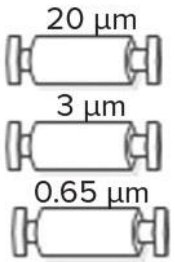
**70%** OF THE TIME OF PRODUCTION OF A VACCINE IS DEDICATED TO **QUALITY CONTROL**, WHICH REPRESENTS SEVERAL HUNDREDS OF TESTS

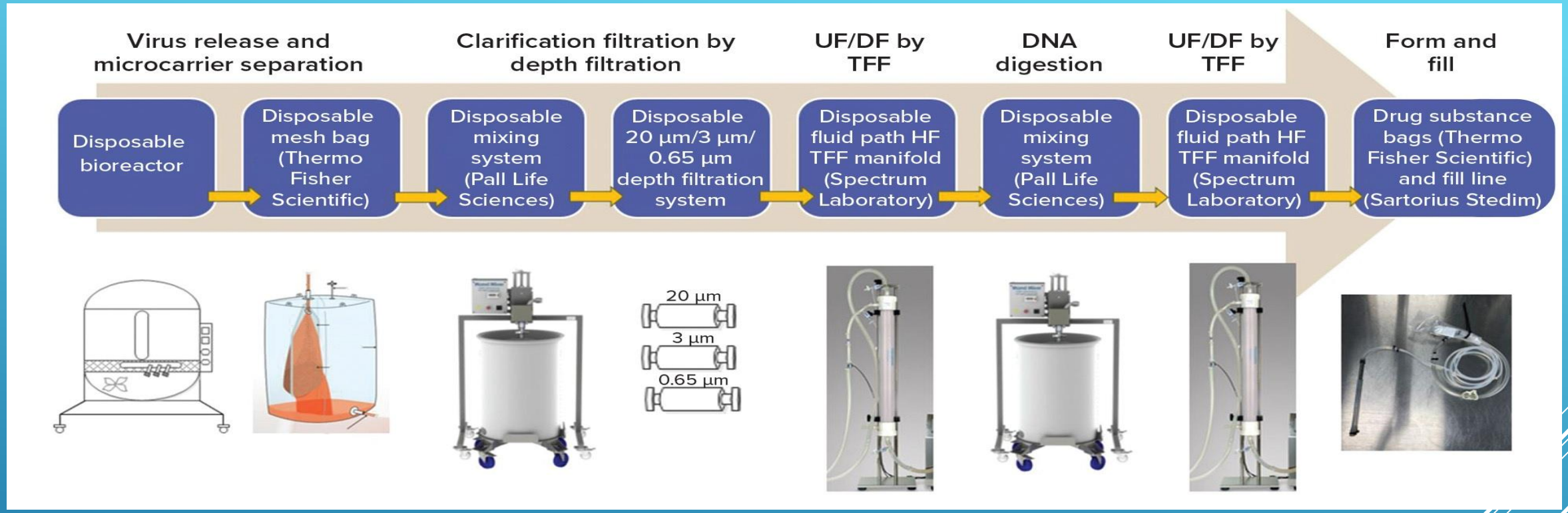
SANOFI

# The Manufacturing Process

| Virus release and microcarrier separation | | Clarification filtration by depth filtration | | UF/DF by TFF | DNA digestion | UF/DF by TFF | Form and fill |
|---|---|---|---|---|---|---|---|
| Disposable bioreactor | Disposable mesh bag (Thermo Fisher Scientific) | Disposable mixing system (Pall Life Sciences) | Disposable 20 µm/3 µm/ 0.65 µm depth filtration system | Disposable fluid path HF TFF manifold (Spectrum Laboratory) | Disposable mixing system (Pall Life Sciences) | Disposable fluid path HF TFF manifold (Spectrum Laboratory) | Drug substance bags (Thermo Fisher Scientific) and fill line (Sartorius Stedim) |






# CELL CULTURE AND PURIFICATION

BioProcess International

# FILLING VIALS – DOSAGE FORM

GSK
photo library

# HEALTH OUTCOMES

What about the ‘end’ game?

Medicines treat the disease once you have it and there are often lifelong side effects.

Vaccines prevent disease

– like building a house to stay warm and dry.

# THANK YOU