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# How to mitigate the risk of shortage in the global vaccines marketplace: a modern manufacturing approach

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Paolo Golfetto, Ompi | A Stevanato Group Brand  
DCVMN - Taipei, March 6-10

**Stevanato**Group

## **Who is Stevanato Group?**

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**EZ-fill: How to mitigate the risk of shortages in Vaccines supply**

**Stevanato** Group

Stevanato Group is a producer of glass **parenteral packaging**, drug delivery **devices** and manufacturing **technology** for the pharmaceutical industry, worldwide.

Our Mission:

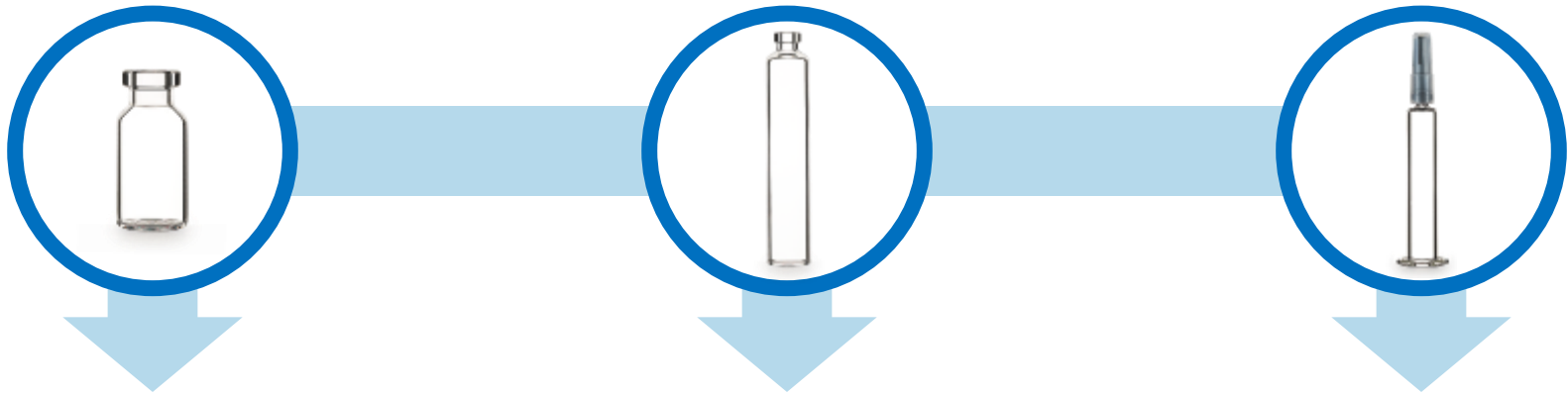
# StevanatoGroup

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To create systems,  
processes and services that  
guarantee the integrity of  
parenteral medicines



# Ompi EZ-fill | Ready-to-fill Containers



**A Complete Range of Sterile Containers**

# StevanatoGroup

Who is Stevanato Group?

**EZ-fill: How to mitigate the risk of shortages in Vaccines supply**



## **The Context:**

**Infectious diseases are  
a global problem, with  
«unpredictable»  
escalations**

# Infectious diseases are a global problem

\$60 BILLION

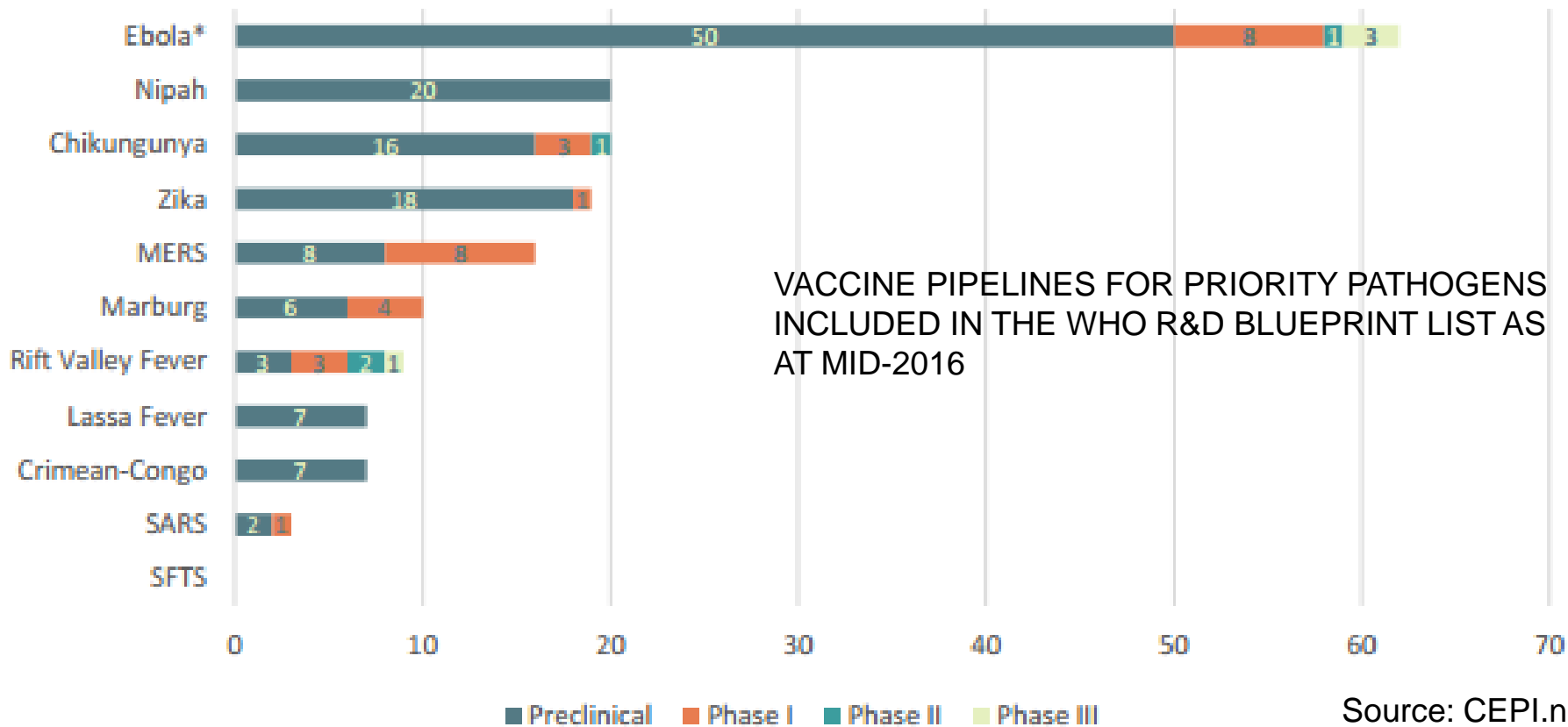
is what infectious diseases cost the world economy each year

28,616

people caught Ebola in the most recent outbreak in West Africa

11,310

people died from Ebola in the West Africa outbreak





# Pandemic and Epidemic Diseases: WHO's list

## • Epidemic and pandemic diseases

- **Airborne diseases:** **influenza** (seasonal, pandemic, avian), severe acute respiratory syndrome (SARS), Middle East respiratory syndrome coronavirus (MERS-CoV)
- **Vector-borne diseases:** **yellow fever**, chikungunya, Zika fever, West Nile fever
- **Water-borne diseases:** **cholera**, shigellosis, typhoid fever
- **Epidemic meningitis**
- **Rodent-borne diseases:** **plague**, leptospirosis, hantavirus, Lassa fever, rickettsia (murine typhus)
- **Haemorrhagic fevers:** **Ebola virus disease**, Marburg virus disease, Crimean-Congo haemorrhagic fever, Rift Valley fever
- **Smallpox, monkeypox**
- **Other zoonotic diseases:** Nipah virus infection, Hendra virus infection
- **Any other emerging disease**

### Diseases

Avian influenza

Cholera

Coronaviruses (MERS-CoV, SARS)

Emerging diseases (e.g. nodding disease)

Ebola virus disease

Hendra virus infection

Influenza (seasonal, pandemic)

Leptospirosis

Meningitis

Nipah virus infection

Plague

Rift Valley fever

Smallpox and human monkeypox

Tularaemia

Viral haemorrhagic fevers (Ebola, Marburg, Lassa, Crimean-Congo haemorrhagic fever, etc.)

Yellow fever

Zika virus

# The Time to Market is Essential... H1N1 Flu

UPMC CENTER FOR HEALTH SECURITY

## CLINICIANS' BIOSECURITY NEWS

ANALYSIS OF ADVANCES AND CHALLENGES IN CLINICAL BIOSECURITY

ABOUT | AUTHORS | SUBSCRIBE | HEALTH SECURITY HEADLINES | PREPAREDNESS PULSEPOINTS

Archive by Year

- 2015
- 2014
- 2013
- 2012
- 2011
- 2010
- 2009
- 2008
- 2007
- 2006
- 2005

Archive by Topic

UPMC Center for Health Security

### A Closer Look at WHO Pandemic Declaration

2009 H1N1 Influenza Issue Brief

By Jennifer Nuzzo, SM

On June 11, 2009, the World Health Organization (WHO) officially declared that the 2009 H1N1 virus had reached pandemic status, or Pandemic Alert Phase 6.<sup>1</sup> U.S. Centers for Disease Control and Prevention (CDC) Director Thomas Frieden noted at a June 11, 2009, press conference that the declaration of a pandemic does not indicate a change in severity of the 2009 H1N1 virus, but rather describes what health officials have observed for several weeks—that transmission of the virus is occurring across the globe.<sup>2</sup>

The WHO pandemic alert phases were initially outlined in WHO's 2005 global influenza preparedness plan. The 2005 plan made recommendations for international and national measures to be taken during each of the 6 phases of pandemic alert. However, in April 2009, WHO revised its pandemic plan and alert scale to reflect "advances in many areas of preparedness and response planning" that have occurred since 2005, including "increased understanding of past pandemics, strengthened outbreak communications, greater insight on disease spread and approaches to control, and increasingly sophisticated statistical modeling of various aspects of influenza."<sup>3</sup>

A brief overview of WHO's 2009 pandemic alert levels is provided below:

**Phase 1:** Influenza viruses may be circulating among animals, but there are no reports of such viruses causing infections in humans.

**Phase 2:** An animal influenza virus has caused infection in humans.

**Phase 3:** An "animal or human-animal influenza reassortant virus has caused sporadic cases or small clusters of disease in people, but has not resulted in human-to-human transmission sufficient to sustain

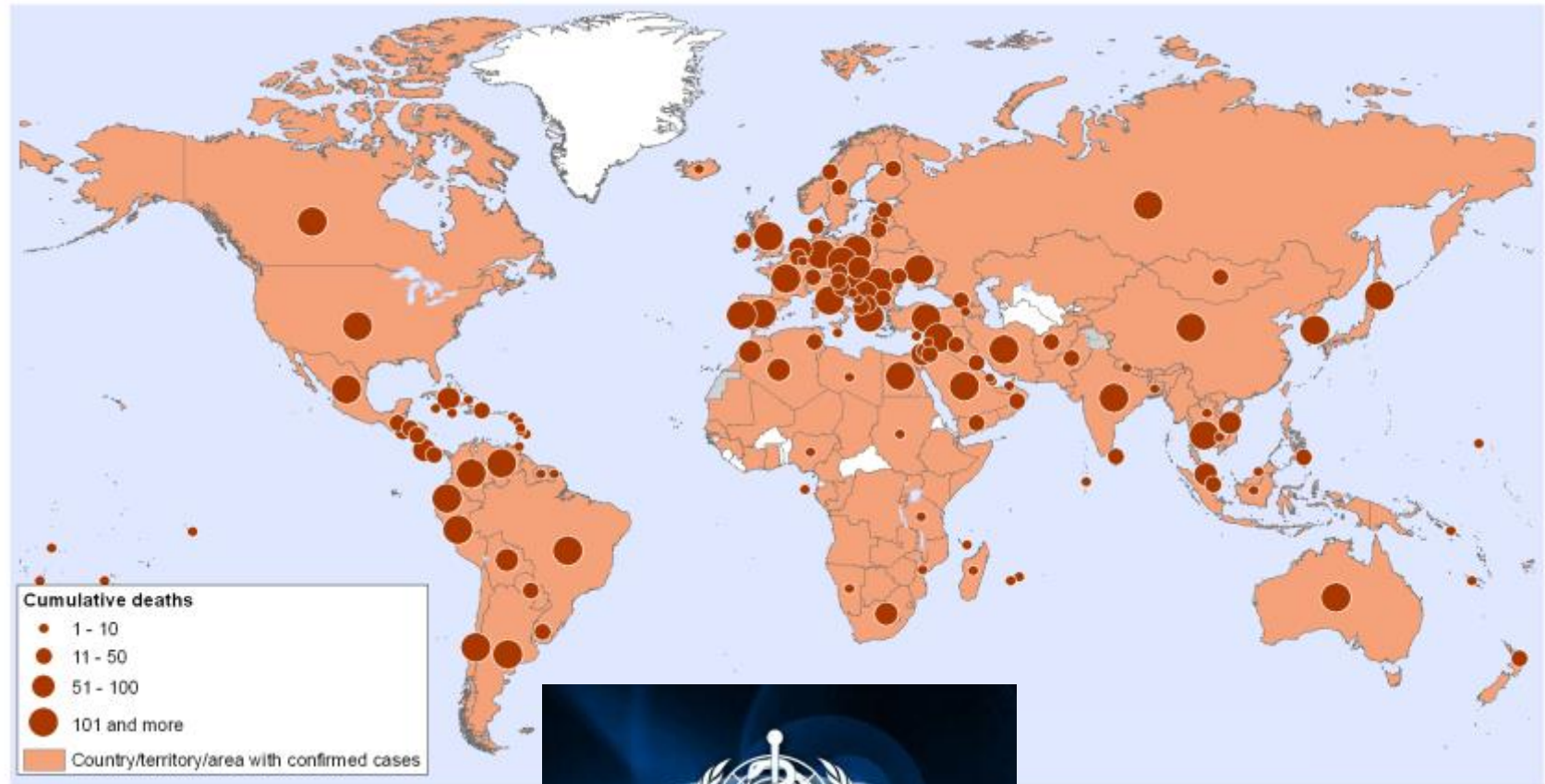
Useful Links

- CDC
- BioPast

On June 11, 2009, the World Health Organization (WHO) officially declared that the 2009 H1N1 virus had reached pandemic status, or Pandemic Alert Phase 6

Source:  
<http://www.pharmtech.com/can-new-vaccine-manufacture-method-cut-time-market-half>

# Pandemic (H1N1) 2009 | Countries, territories and areas with confirmed cases and number of deaths



# The Time to Market is Essential...

## Getting Ebola treatments to market may take time



Health workers in protective suits treat a woman and her two children at Ebola treatment center in Monrovia, Liberia.

LOS ANGELES (MarketWatch)—Just how long will it take to get Ebola treatments ready for use by an increasingly nervous public?

The truth is, it may take some time—a year or more to get an effective therapy on the market and perhaps longer for a vaccine, health officials say.

The good news? There seems to be little danger of an Ebola outbreak in the U.S. despite the first diagnosed case confirmed in Dallas this week.

Dr. Anthony Fauci, director of the National Institutes of Health's allergy and infectious disease branch, says drug companies and regulators are taking a two-pronged approach in finding a way to treat the virus. There are therapies for those who already have Ebola, and vaccines to prevent the deadly disease from ever infecting humans.



"It's usually a slow process," Fauci said. "It tends to get accelerated in an emergency situation."

How accelerated is anyone's guess.

Source: <http://www.marketwatch.com/story/getting-ebola-treatments-to-market-may-take-time-2014-10-01>

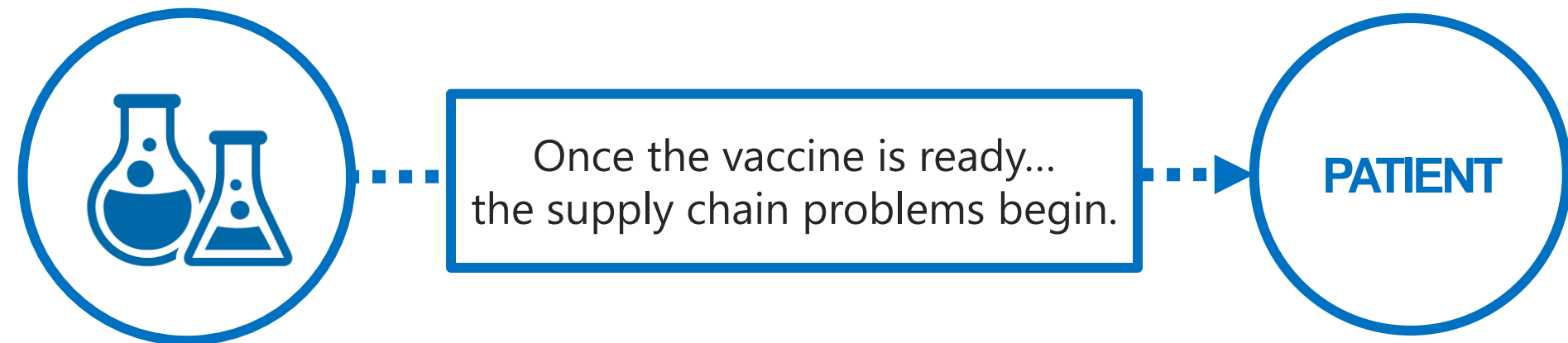
# Flexibility and Vaccine paradigm: Yellow fever

The screenshot shows the WHO Media Centre page. The main headline is "Lower doses of yellow fever vaccine could be used in emergencies". Below it, a WHO statement dated 17 June 2016 is displayed. A red box highlights a key paragraph: "Experts agreed with this proposal at a meeting convened by WHO to consider potential shortages in yellow fever vaccine due to the outbreak in Angola and Democratic Republic of the Congo." To the left of this text is a red warning triangle icon. The page also includes a sidebar with navigation links like "News", "Statements", "Events", and "Fact sheets". On the right, there are links to "Share", "Print", and "More on yellow fever".

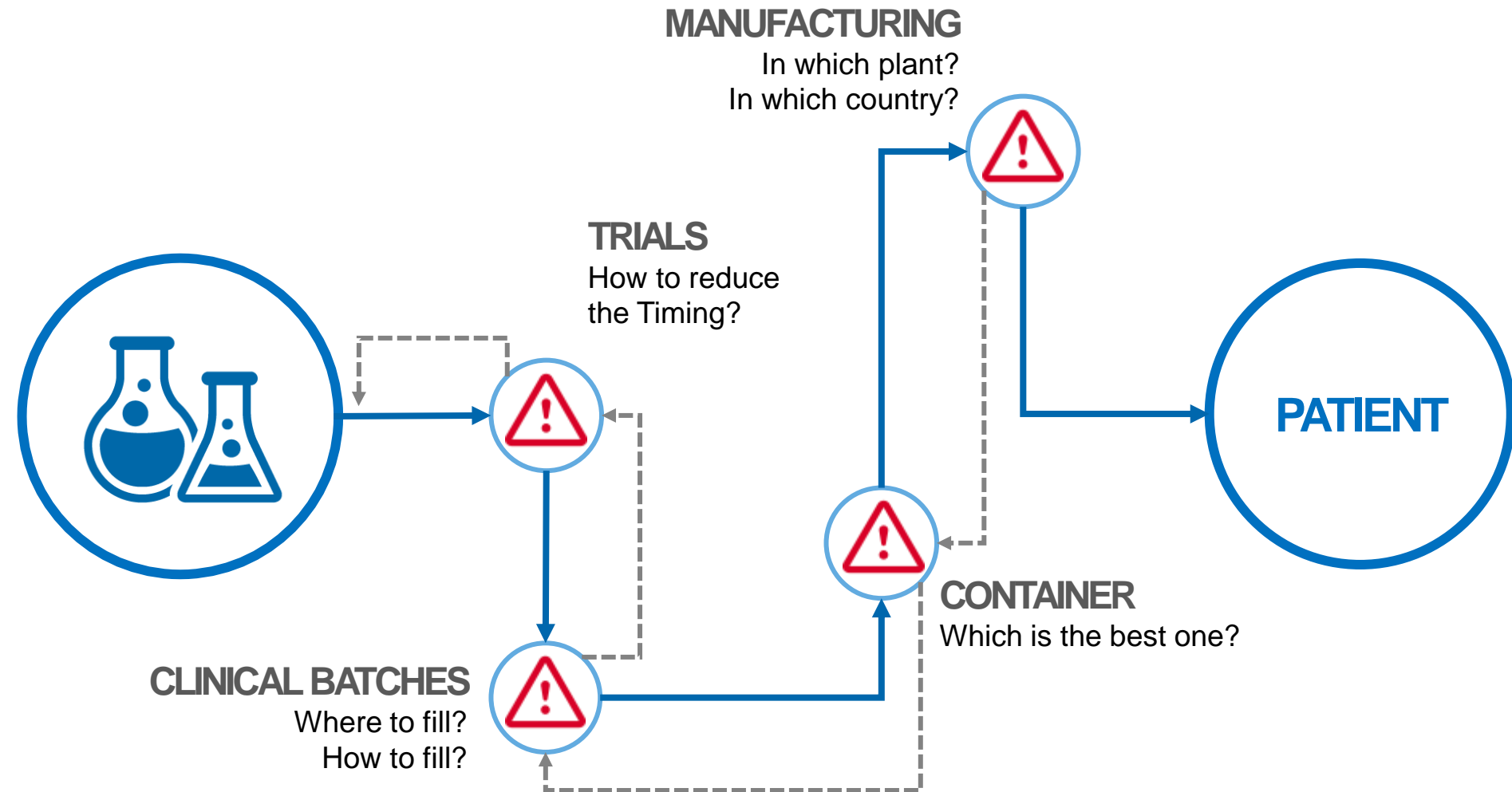
**Shortage** in Yellow fever vaccine due to due to the outbreak in Angola and Democratic Republic of the Congo

Source: <http://www.marketwatch.com/story/getting-ebola-treatments-to-market-may-take-time-2014-10-01>

# The Time to Market is Essential...



# The Time to Market is Essential...







# How the Pharma Industry

is  
adapting?



# How to be faster



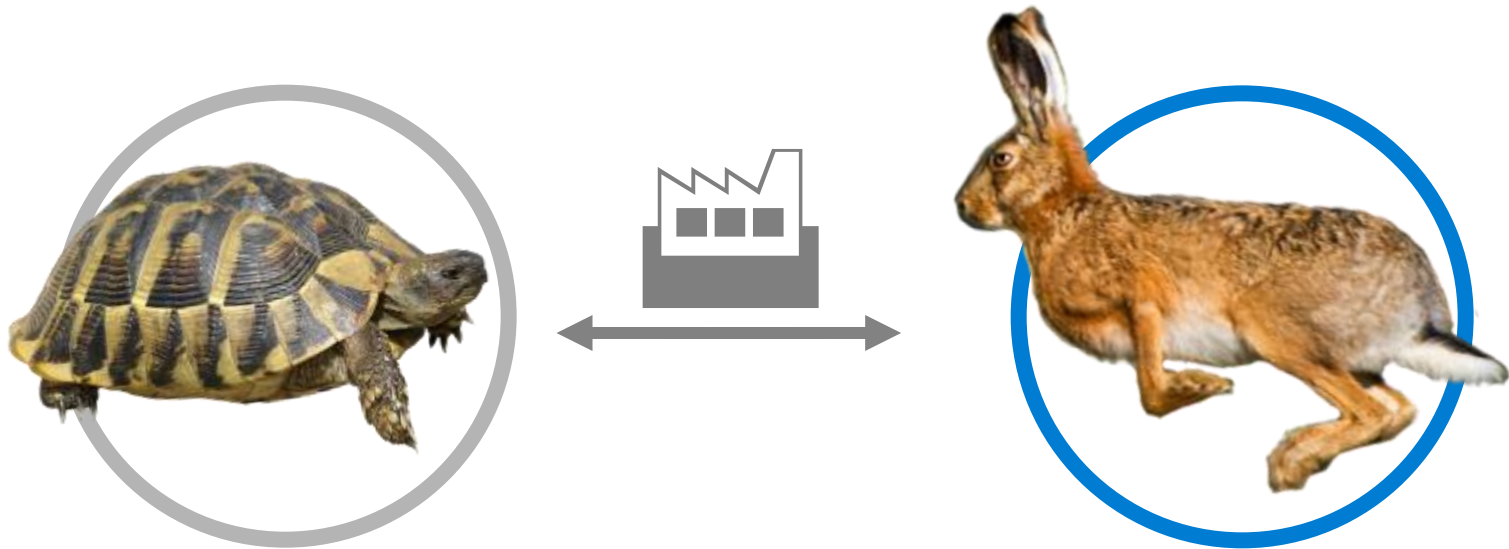
It is no longer about stable production alone.

”Production facilities must be ready for **adaption to changes** in corporate strategy, in market dynamics and in short-term targets.”

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SOURCE: NNE PHARMAPLAN

# Something has changed so far



“The success of a manufacturing site is moving  
**from site stability to site agility:**

in addition to maintaining stable production, pharmaceutical sites are now required to accommodate more changes and deliver on unexpected targets”

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SOURCE: NNE PHARMAPLAN

# How to be faster

## SITE STABILITY



*Mono Product*  
*Core and Non core Activities*  
*High Capex*  
*High Running Costs*

**Big Size**  
**Full Process**

**FILL**  
**FINISH**

## SITE AGILITY

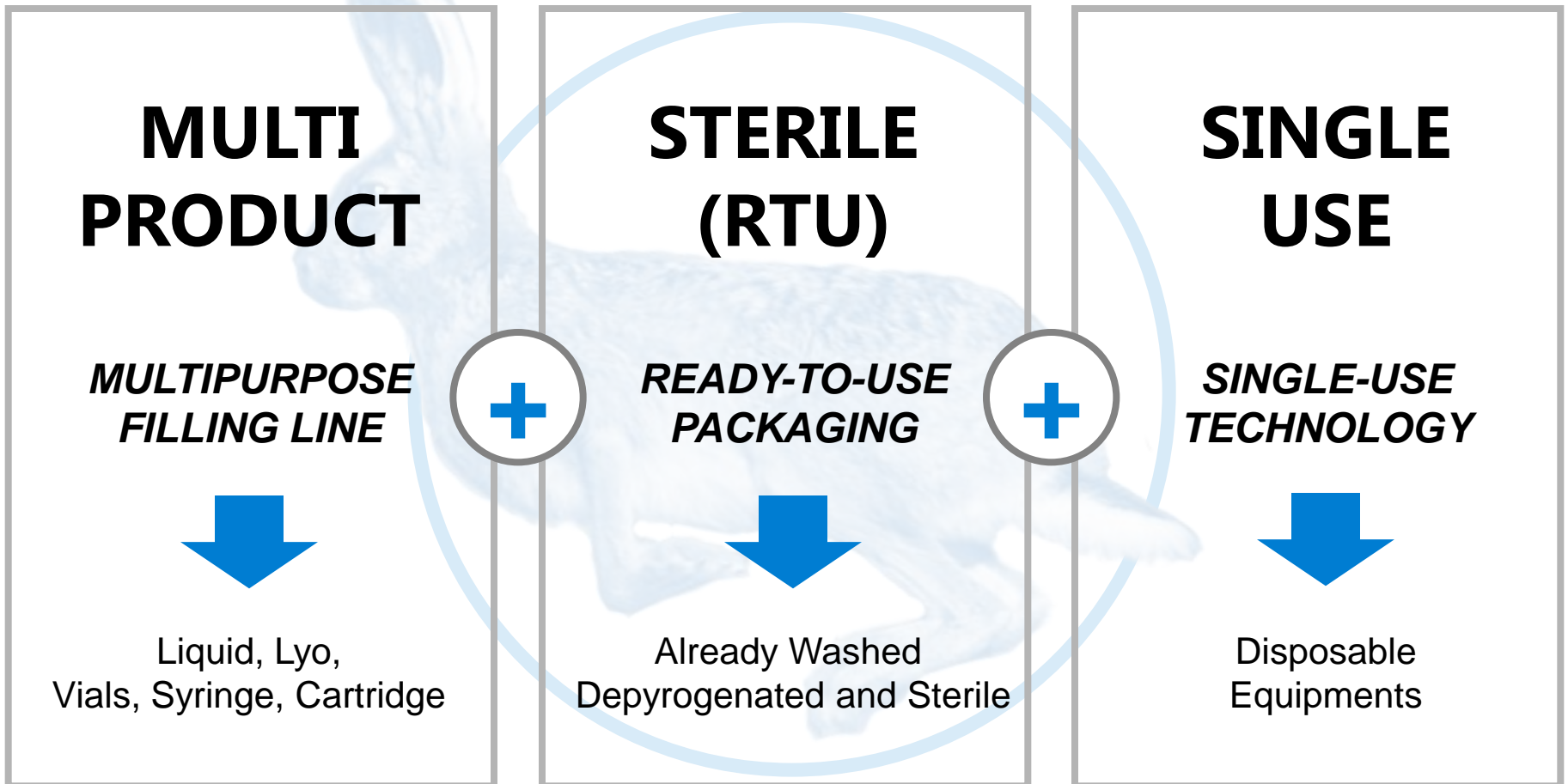


*Multi Product*  
*Only Core Activities*  
*Very Limited Capex*  
*Reduced Running Costs*

**Flexibility**  
**Fast Reaction**

# A Fast Track Facility

## SITE AGILITY



# Multi Product Filling Line: one machine for many products

**MULTI  
PRODUCT**

**STERILE  
(RTU)**

**SINGLE  
USE**



Pictures::Courtesy of  
Sartorius Stedim

**Single Use Equipments allow lower investment costs  
and no cleaning procedures**

# Reasons for increasing use of RTU components

Factor	Biotherapeutic Developers (exclusive of CMOs)	Vaccines Producers Only
1. Reduce time to get facility up and running	43.3%	60.0%
2. Eliminate cleaning requirements	43.1%	41.7%
3. Eliminate use of hazardous cleaning fluids	14.4%	40.0%
4. Decrease documentation requirements	20.0%	36.4%
5. Ability to sterile-sample	14.7%	36.4%
6. Reduce capital investment in facility & equipment	36.4%	30.0%
7. Faster campaign turnaround time	35.7%	30.0%
8. Increase total annual capacity at my facility	17.5%	30.0%
9. Decrease risk of endogenous contamination (e.g. bacterial)	24.0%	27.3%
10. Disposable filters more convenient	17.5%	27.3%
11. Avoid hazardous waste disposal	14.3%	25.0%
12. Decrease risk of product cross-contamination	41.2%	20.0%
13. Greater assurance of sterility	25.0%	20.0%

**Source:** 9<sup>th</sup> Annual Report and Survey of Biopharmaceutical Manufacturing  
BioPlan Associates, Inc., April 2012



# Reasons for increasing use of RTU components

14. Lower annual maintenance costs	24.8%	20.0%
15. Improve scheduling ability	23.2%	20.0%
16. Reduce space requirements	22.2%	20.0%
17. Flexibility of a 'modular' approach	31.3%	10.0%
18. Strength and reliability of disposable components were shown to be comparable to fixed systems	19.1%	9.1%
19. Avoid costs associated with system re-design and modifications	18.0%	9.1%
20. Simplify operations, and reduce learning curve for new operators	8.3%	9.1%
21. Easier QA/QC	15.6%	0.0%
22. Reduce water requirements	15.5%	0.0%
23. Faster process optimization (flexibility to try different processes)	12.6%	0.0%
24. Reduce operations staff	9.0%	0.0%
25. Ease of control of bioreactor (use of probes, etc.)	8.4%	0.0%

**Source:** 9<sup>th</sup> Annual Report and Survey of Biopharmaceutical Manufacturing  
BioPlan Associates, Inc., April 2012

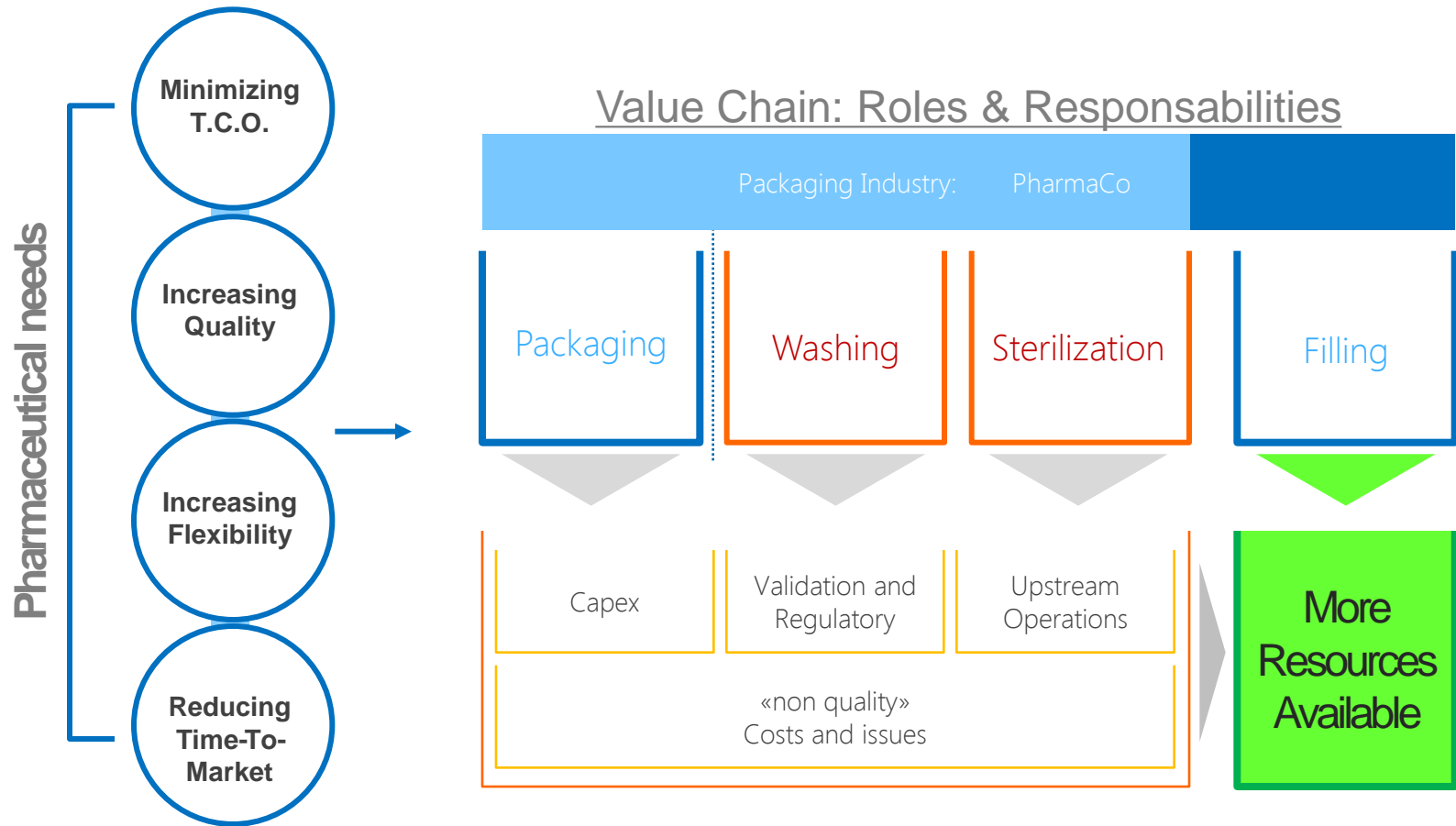
The Next Generation, now.

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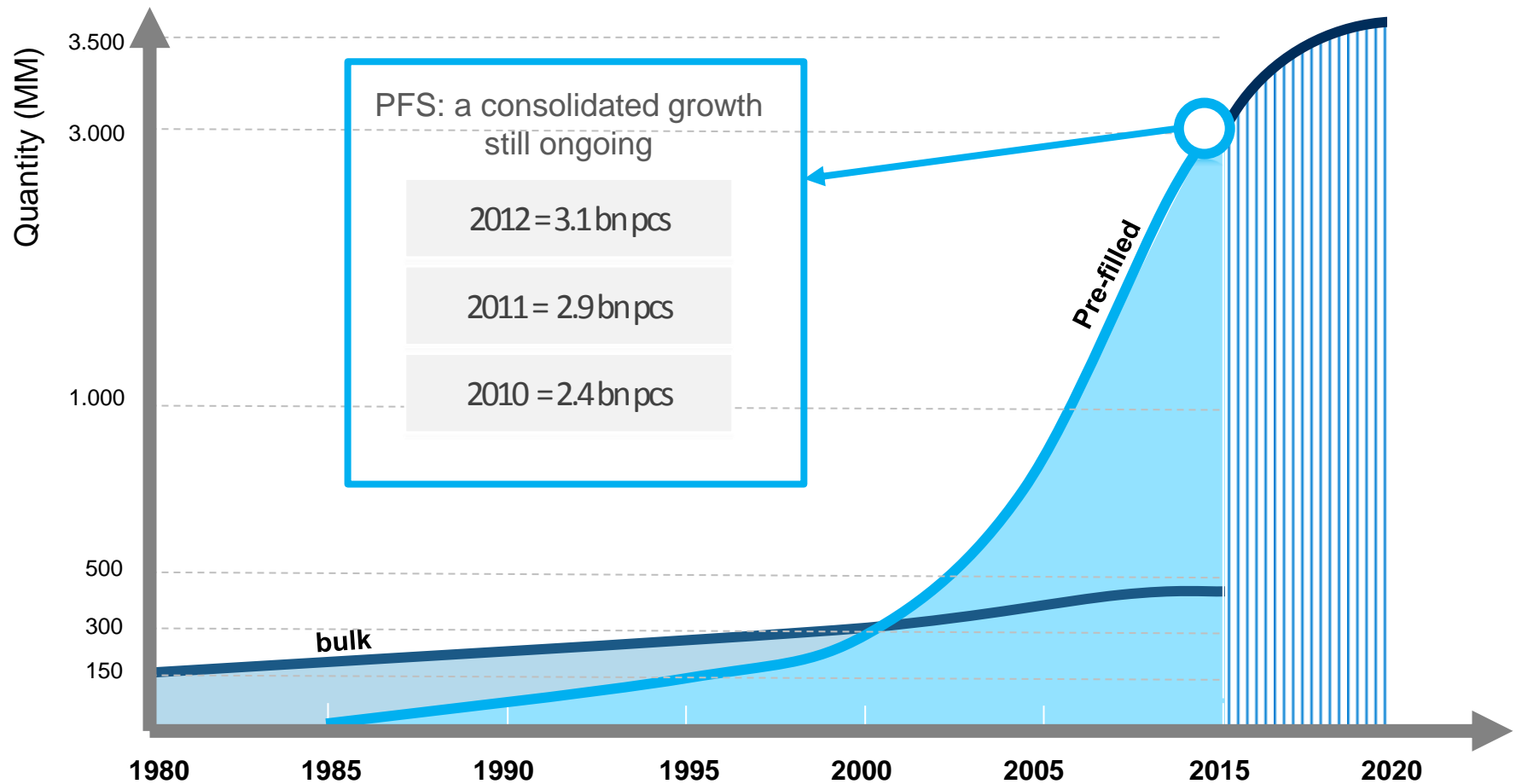
# What Glass Suppliers can do for improving flexibility?



# Sterile Containers have changed Pharmaceutical Operations



# A Real Example: Pre-filled Syringes Growth



Source: Greystone Associates:  
"PREFILLED SYRINGES Drugs, Devices and Disease Therapeutics" 2009

# Sterile (RTU) containers are the «core element» of this change

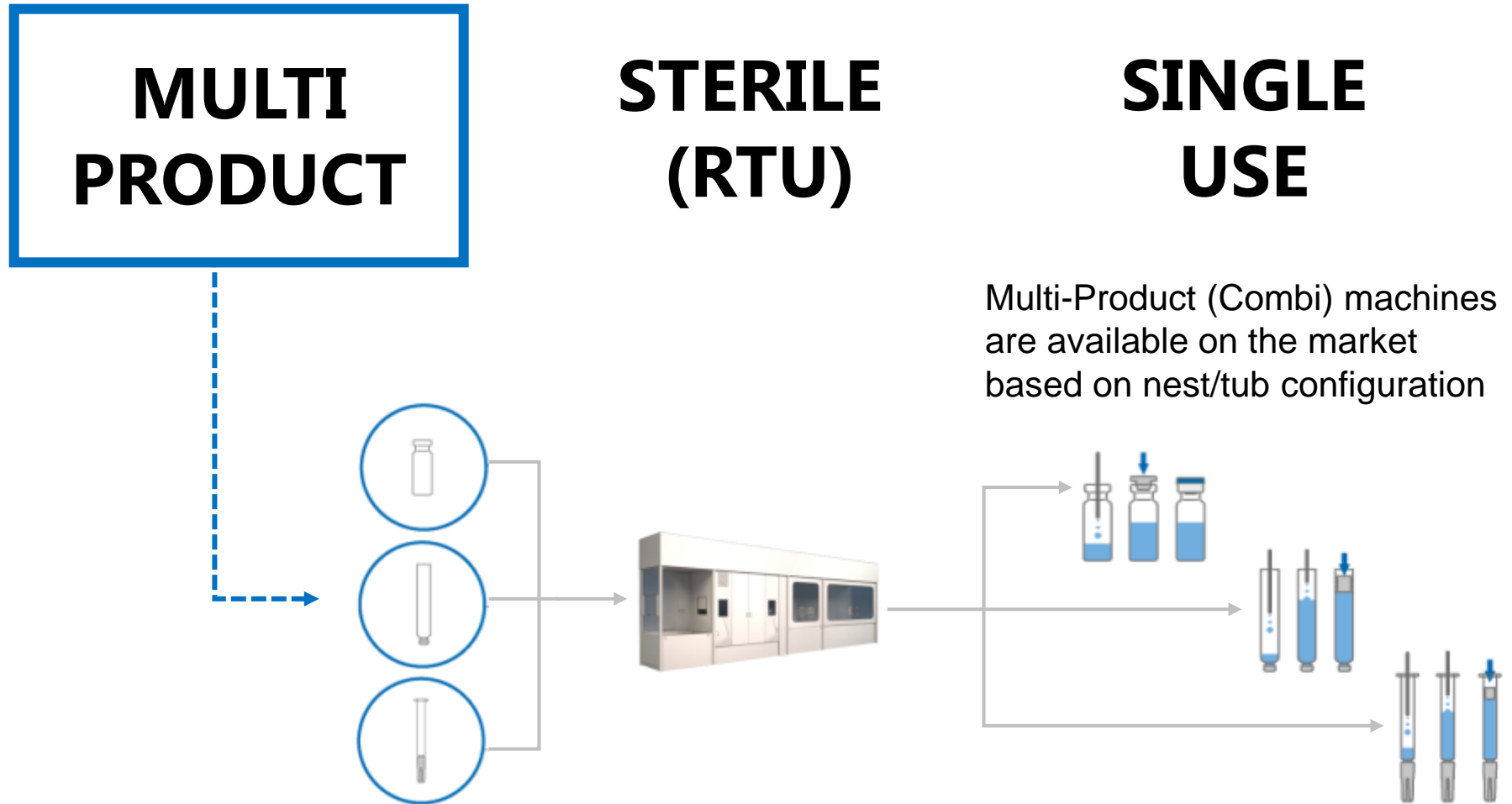


**Multiproduct machine are  
based on sterile containers,  
nest&tub configuration**



**OMPI has allowed this  
change presenting its EZ-  
fill® vials and cartridge in  
2010**

# Multi Product Filling Line: one machine for many products



# Multi Product Filling Line: one machine for many products

**MULTI  
PRODUCT**

**STERILE  
(RTU)**

**SINGLE  
USE**



**VIALS**

**CARTRIDGES**

**SYRINGES**

**CLOSURES**



*Picture: Courtesy of West Pharma*

**Primary Packaging and components are  
available Ready-to-Use (already sterile) on the Market**

# Comparison between «stability model» vs «agility model»

	<u>SITE</u> <u>STABILITY</u>	<u>SITE</u> <u>AGILITY</u>
Flexibility	-	✓
Time-to-market	Slow	Fast
Regulatory Compliance	High	Higher
Business Risk	High	Low
Capex/Opex	Higher	Lower
Validation Costs	High	Low
Cleaning Costs	High	Low
<b>Costs of NON-QUALITY</b>	Significant	Low

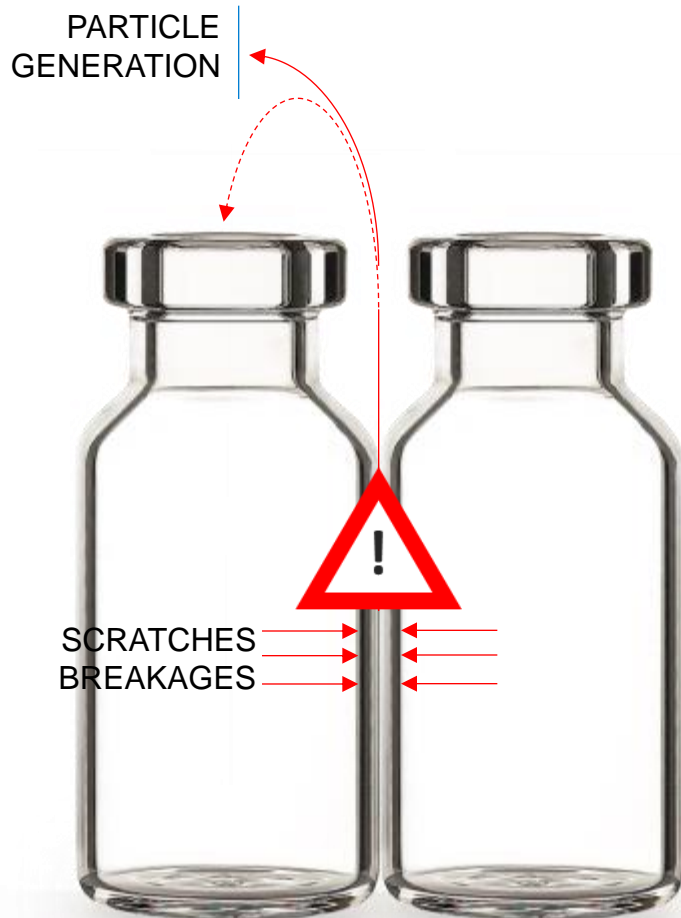
The Next Generation, now.

**EZ-fill**

**Nested Glass Vials and  
Cartridges for vaccines:**

**a model for  
reducing the  
T.C.O.**

# Glass-to-Glass Contact in the traditional lines



## Glass-to-Glass contact is responsible for:

- Cosmetic issues,
- Breakages (stops)
- Particle generation
- **High rejection rate during inspection phase**
- Cost increase
- Risk of recalls

## High risk:

- Transportation phase
- Buffering/in-feeding operations (rotating round table)



# 60% of losses (often hidden) are caused during transportation

Mechanical damage to goods accounts for approximately 43% of insurance claims made by shippers. Environmental damage (including damage from water and humidity) account for another 15% of claims.<sup>1</sup> Some of these **Hidden damage is often left unidentified upon receipt of a shipment,** the hidden damage can be used or installed without the problem being identified. As its name implies, hidden damage cannot be seen during normal receiving inspections; however, the damage is real and discovering the source can be frustrating. You know the product was fine when it left your dock but when your customer receives the product, all they know is that it doesn't work. Hidden damage is often left unidentified upon receipt of a shipment, so the responsibility of product failure falls back to the manufacturer even if the damage occurred in transit. The result is harm to your reputation as a manufacturer, not to mention added expenses in repairing the damage or completely replacing the product. In recent years, the cost of goods damaged in transit has been more than US

**During transportation, incorrect handling, securement, and/or packaging of goods cause 60% of losses.<sup>2</sup>**

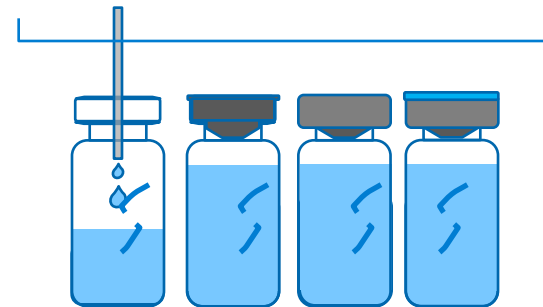
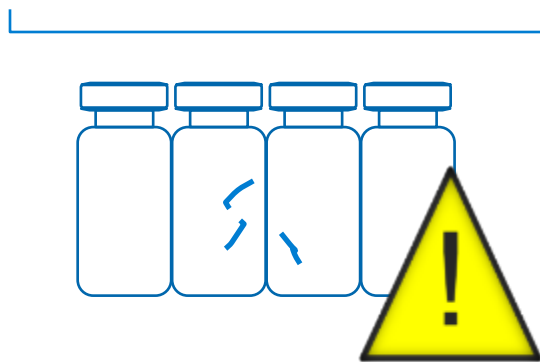
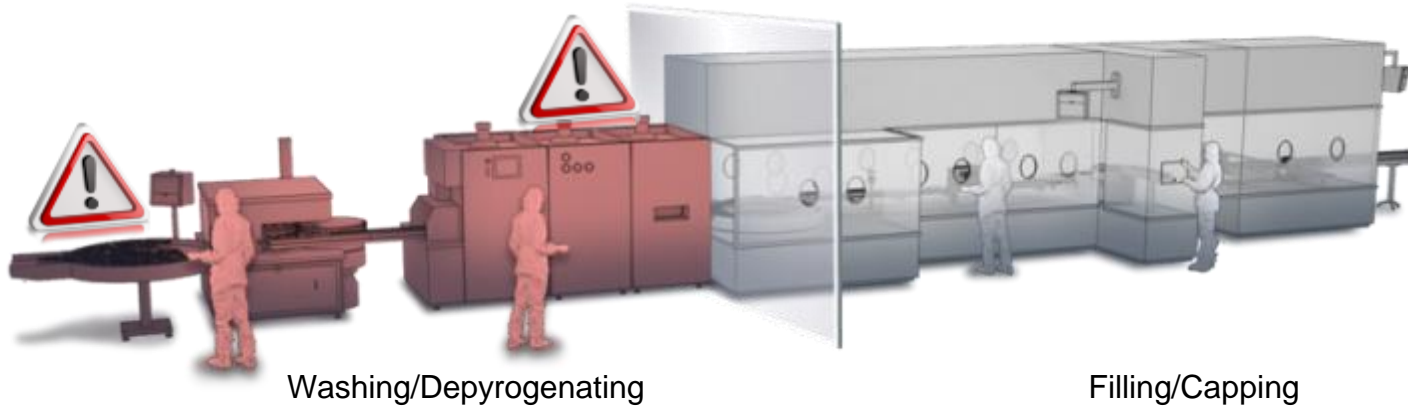
What if you knew that something unexpected happened on the trip? During transportation, incorrect handling, securement, and/or packaging of goods cause 60% of losses.<sup>2</sup> Knowing that mishandling occurred during transit allows the recipient to inspect for damage immediately and helps assign accountability for issues. Discovering that the packaging was insufficient to protect your product allows you to make enhancements. Discovering that you are over packaging a product allows you to make cost saving adjustments. The point is that you have information and that information can be used to help minimize risk in the future.

1

Understand the Source of Product Damage with Data Recorders

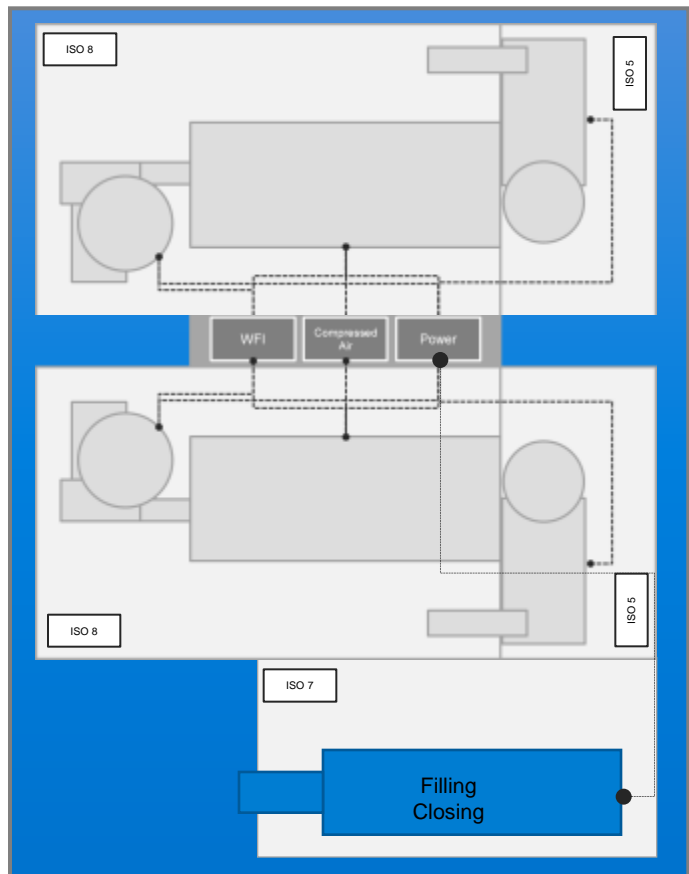
SHOCKWATCH®

# More steps mean more risks of breakages, issues and flakes throughout the process

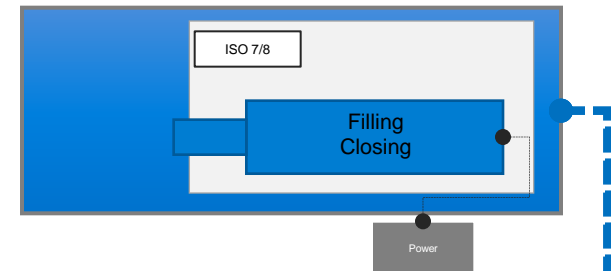


# Traditional filling operations vs RTU filling operations for 3 containers

## TRADITIONAL (BULK)



## READY-TO-USE (NESTED/STERILE)



(Courtesy of Bosch)



(Courtesy of Optima Inova)



(Courtesy of Groninger)

## EXAMPLES OF COMBI LINES



A **Stevanato** Group Brand

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Than You for your attention!

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[www.ompipharma.com](http://www.ompipharma.com)