UPDATE: Vaccine Candidate Against *C. difficile*

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If Nothing Else, You Should Remember…

Clostridium (Clostridioides) difficile: A Significant Unmet Medical Need

C. difficile **bacteria express toxins, causing severe diarrhea[1]**

Antibiotic use causes CDI[1]

>450,000 cases and >29,000 deaths/year in US[2]

1 in 5 recurrence[2]

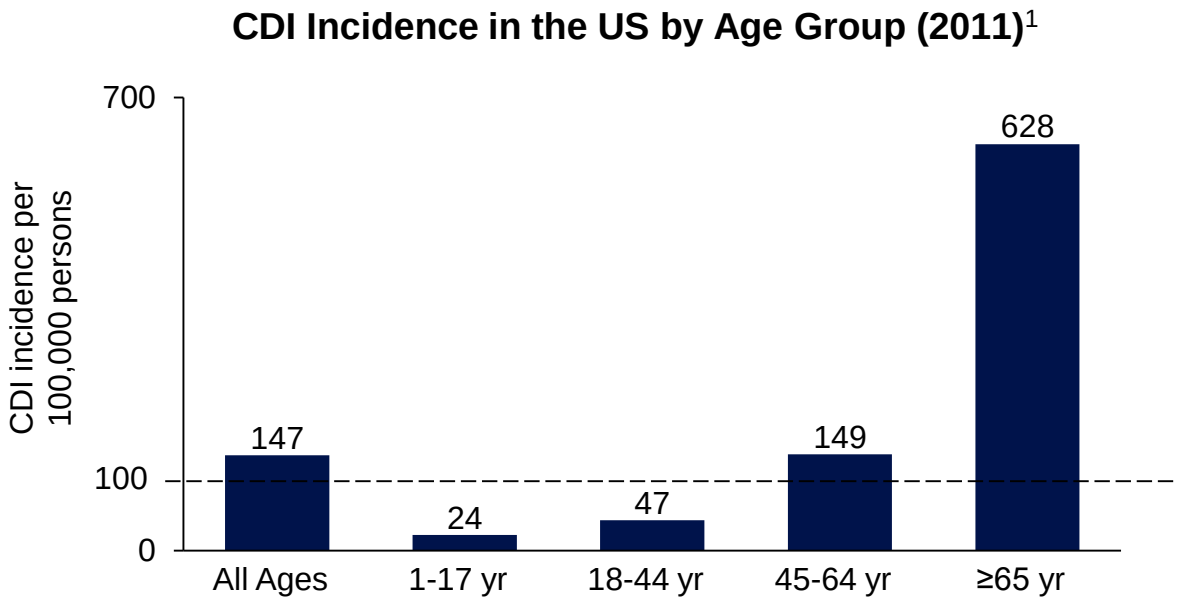
C. difficile **at "Hazard Level – Urgent" (CDC)[3]**

Currently, there is *no vaccine* to prevent initial or recurrent CDI

CDI=*Clostridium difficile* infection.

1. *Clostridium difficile* Infections in Hospital Stays, 2009. https://www.hcup-us.ahrq.gov/reports/statbriefs/sb124.pdf. Accessed May 9, 2019.
2. Lessa FC, et al. *N Engl J Med*. 2015;372(24):2369-2370.
3. Centers for Disease Control and Prevention: Biggest threats and data. https://www.cdc.gov/drugresistance/biggest_threats.html. Accessed May 9, 2019.

A Nationwide Surveillance Program by the CDC Demonstrates That the Incidence of *C. difficile* Increases With Age



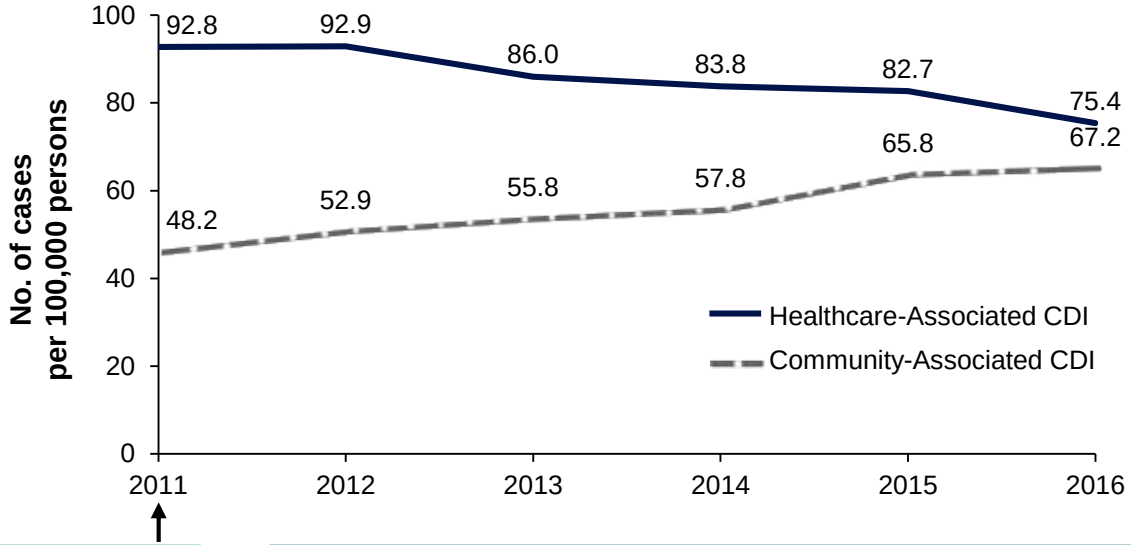
1 in 11 patients aged ≥65 years died of healthcare-related CDI within 1 month of diagnosis[2]

Typical recommendation threshold (100 per 100k)

1. Lessa FC, et al. *N Engl J Med*. 2015;372(24):2369-2370.
2. Centers for Disease Control and Prevention: What is *C. diff*?. https://www.cdc.gov/cdiff/what-is.html. Accessed May 9, 2019.

CDC Emerging Infections Program *C. difficile* US Surveillance Data: 2011-2016

Reported Crude Incidence of Community-Associated and Healthcare-Associated CDI Among the 10 Emerging Infections Program Sites, 2011-2016[1,2]



19% decrease in healthcare-associated CDI from 2011-2016[2]

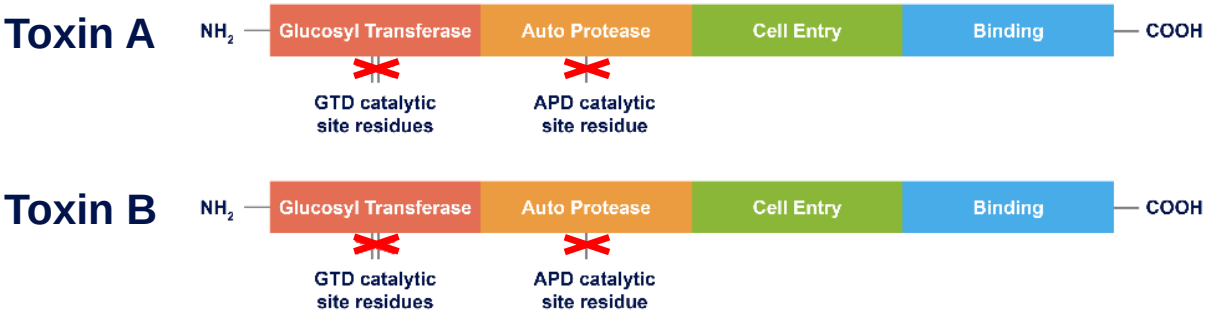
39% increase in community-associated CDI from 2011-2016[2]

In 2011: 453,000 cases, 29,000 deaths[1]

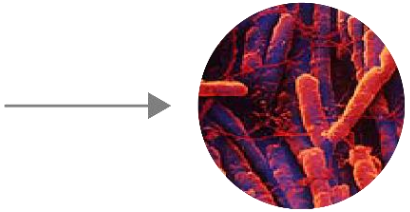
Overall 3% decrease in CDI from 2011 to 2016[2]

1. Lessa FC, et al. *N Engl J Med.* 2015;372(24):2369-2370.
2. Center of Disease Control and Prevention. Data Summary of HAIs in the US: Assessing Progress 2006-2016. Unpublished data (2016) courtesy of Dr. Alice Guh.

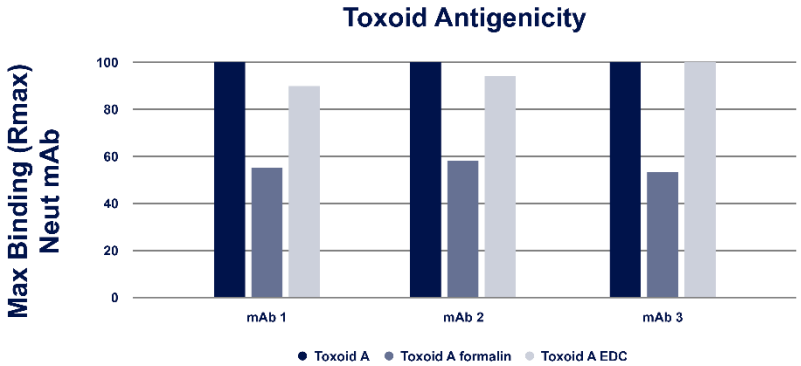
Pfizer's Bivalent Toxoid Vaccine Preserves Important Antigenic Epitopes



Expression in *C. difficile*



Recipient VPI 11186
SPO-A and Toxin minus



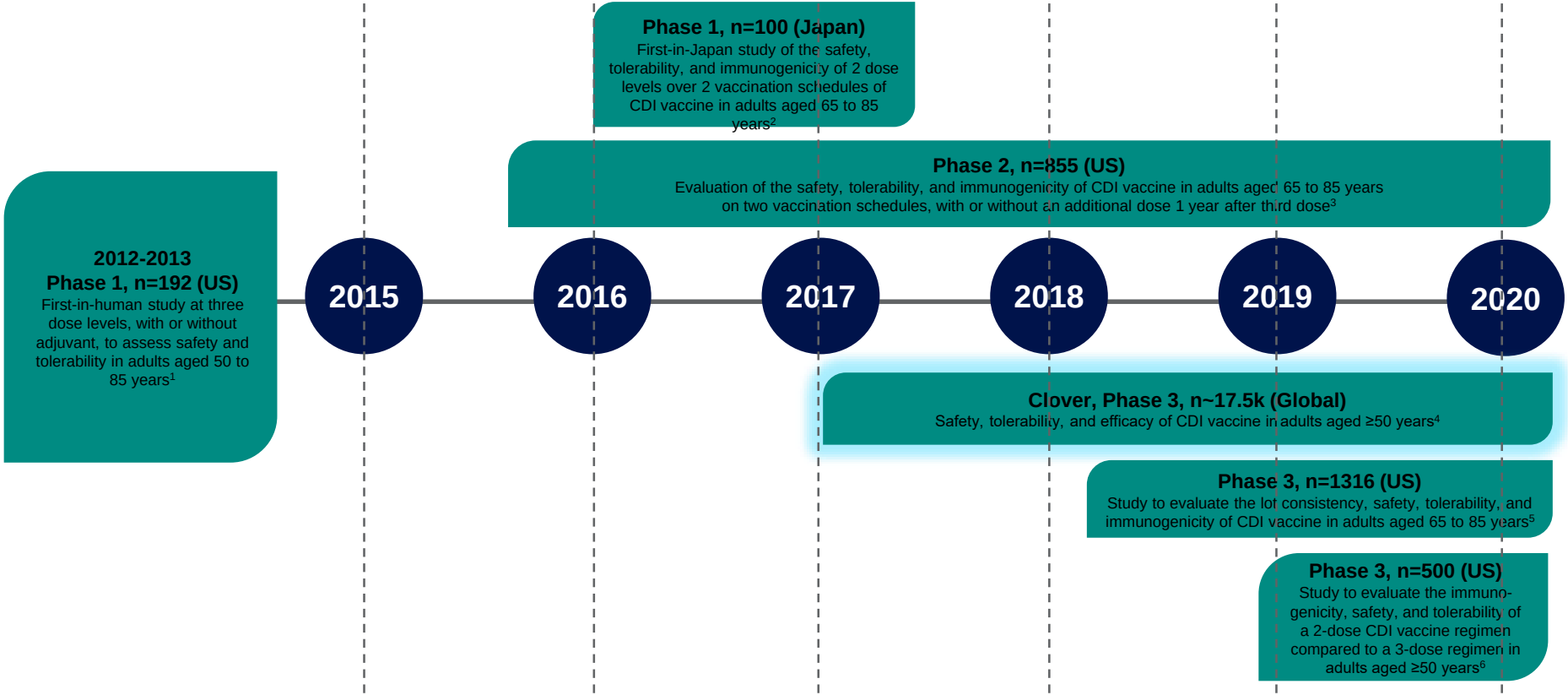
Key Advantages:

- **Safety:** Genetically detoxified toxin
- **Efficacy:** Preservation of neutralizing epitopes
- **Implementation:** Ease of manufacturing

APD=autoprotease domain; GTD=glucosyltransferase domain.

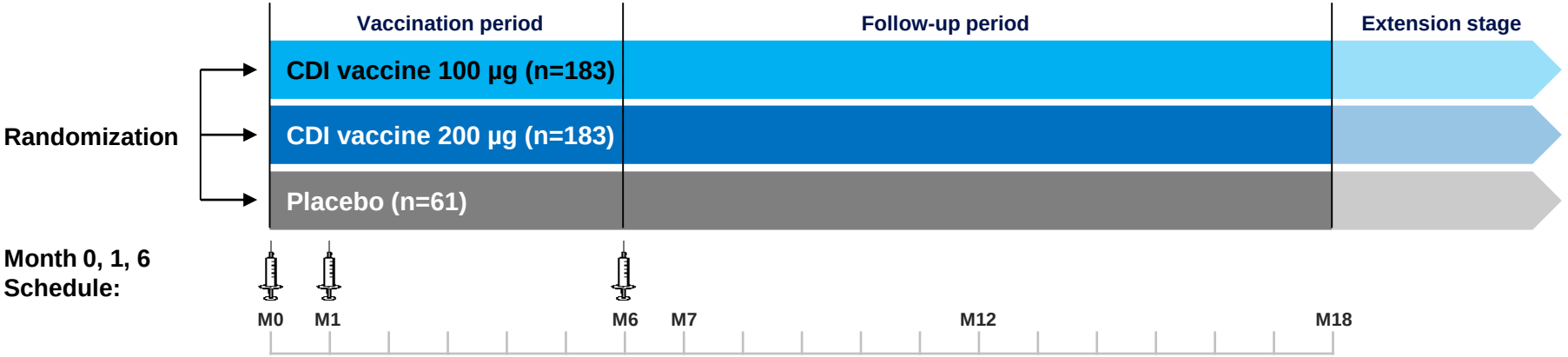
1. Donald RG, et al. *Microbiology*. 2013;159(Pt 7):1254-1266.
2. Gribenko A, et al. *Biochem Biophys Rep*. 2017;9:193-202.

C. difficile Vaccine Clinical Development Program

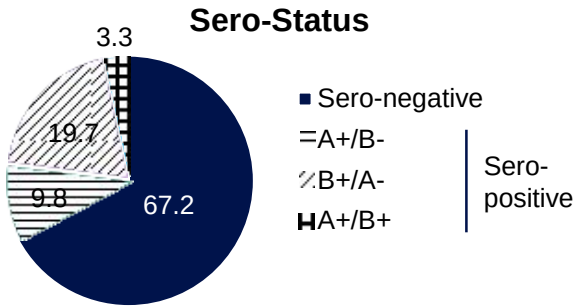


1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT01706367. Accessed May 9, 2019. 2. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02725437. Accessed May 9, 2019.
3. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02561195. Accessed May 9, 2019. 4. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03090191. Accessed May 9, 2019.
5. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03579459. Accessed May 14, 2019. 6. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03918629. Accessed May 14, 2019.

Proof of Concept Phase 2 Study to Evaluate the Safety, Tolerability, and Immunogenicity of CDI Vaccine in Adults Aged 65 to 85 Years (NCT02561195)

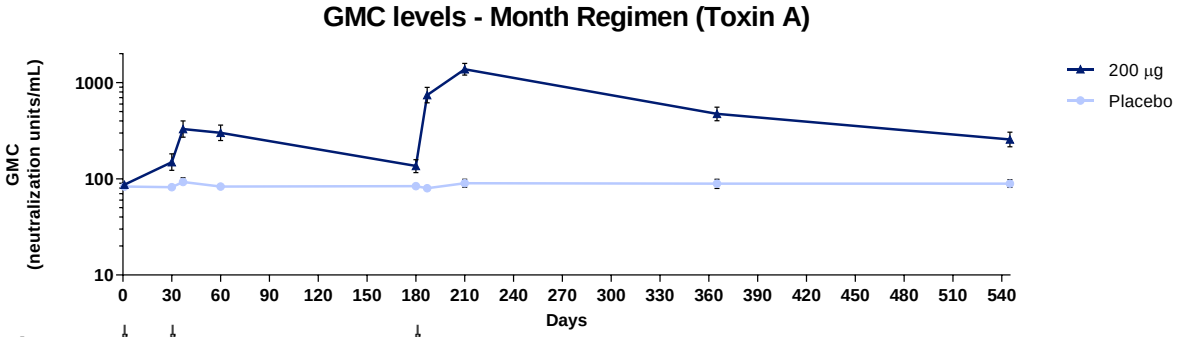


Patient Demographics | (200 µg – Month 0, 1, 6)

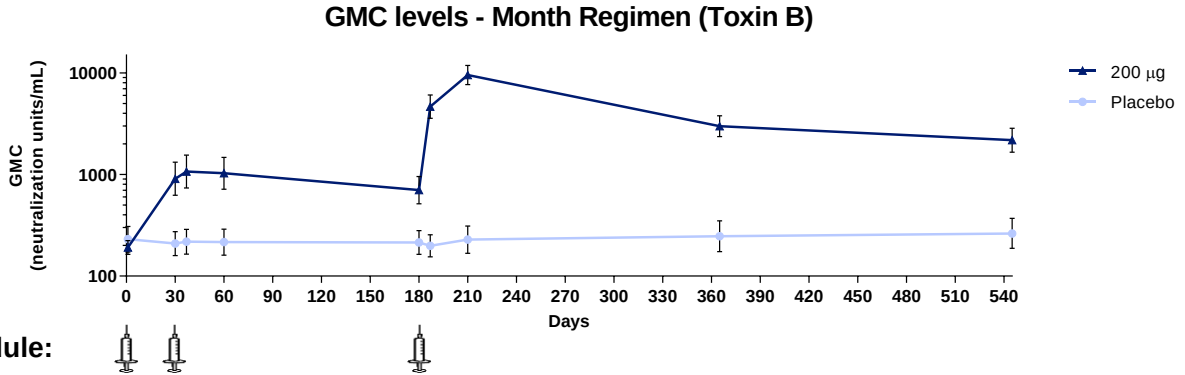


Remich S, et al. A phase-2, placebo-controlled, randomized, observer-blinded study to evaluate the safety, tolerability and immunogenicity of two 3-dose regimens of a *Clostridium difficile* vaccine in healthy adults 65 to 85 years of age. Poster presented at: ECCMID; April 21-24, 2018; Madrid, Spain.

Month Regimen Geometric Mean Concentration (GMC) Levels
(200 µg vs Placebo)



Month 0, 1, 6 Schedule:



Month 0, 1, 6 Schedule:

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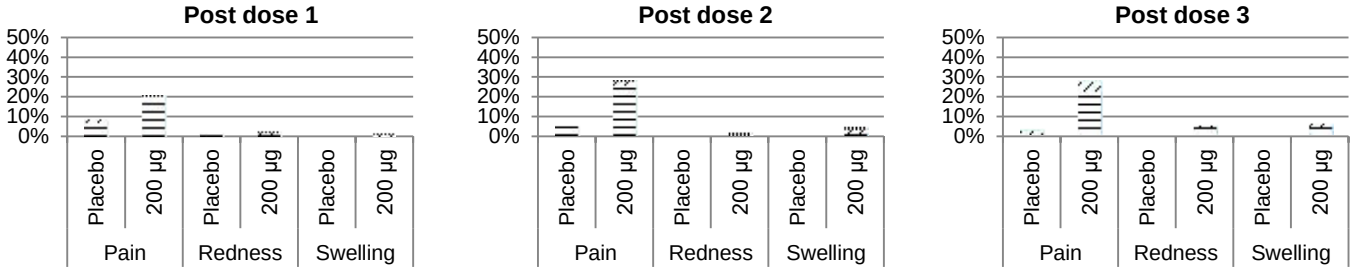
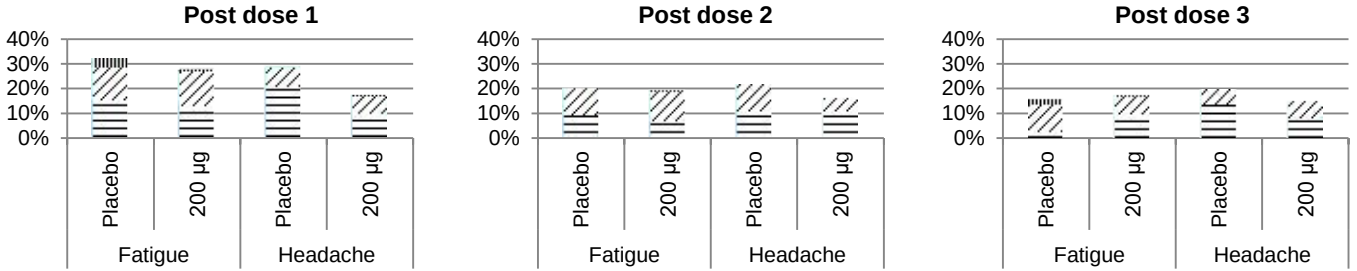
E-diary Reported Events: Month 0, 1, 6 Regimen
(Follow-up 14 Days After Each Dose)

Local Reactions



Fatigue and Headache



Grade 1 (mild) Grade 2 (moderate) Grade 3 (severe) Grade 4

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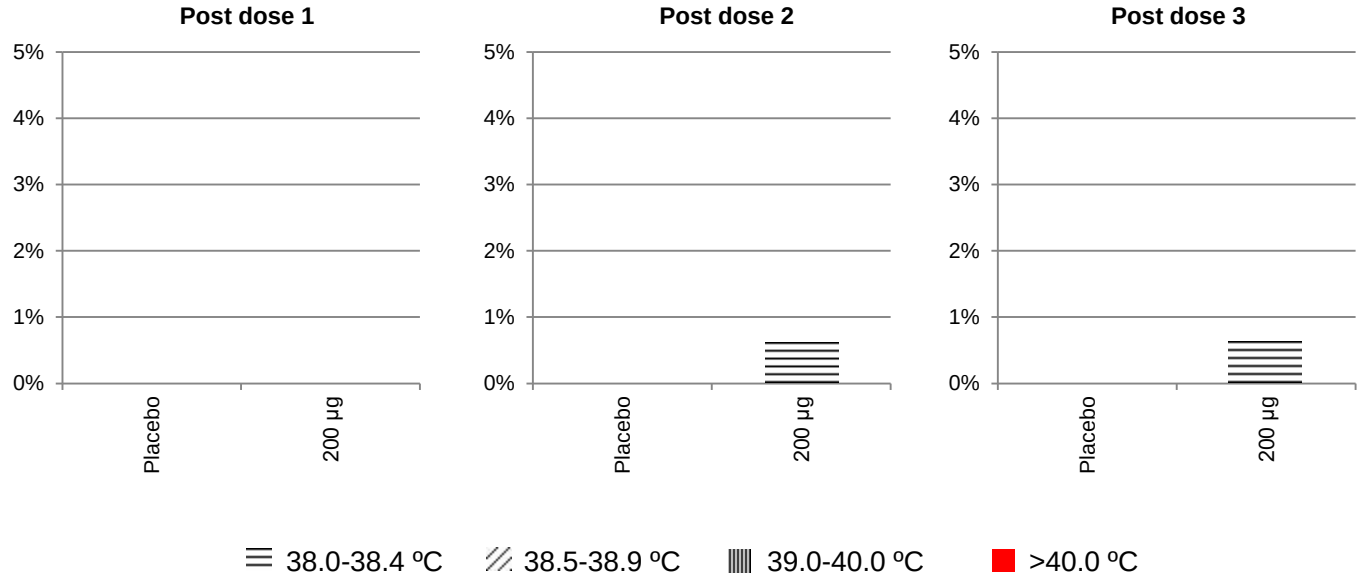
E-diary Reported Fever: Month 0, 1, 6 Regimen
(Follow-up 14 Days After Each Dose)



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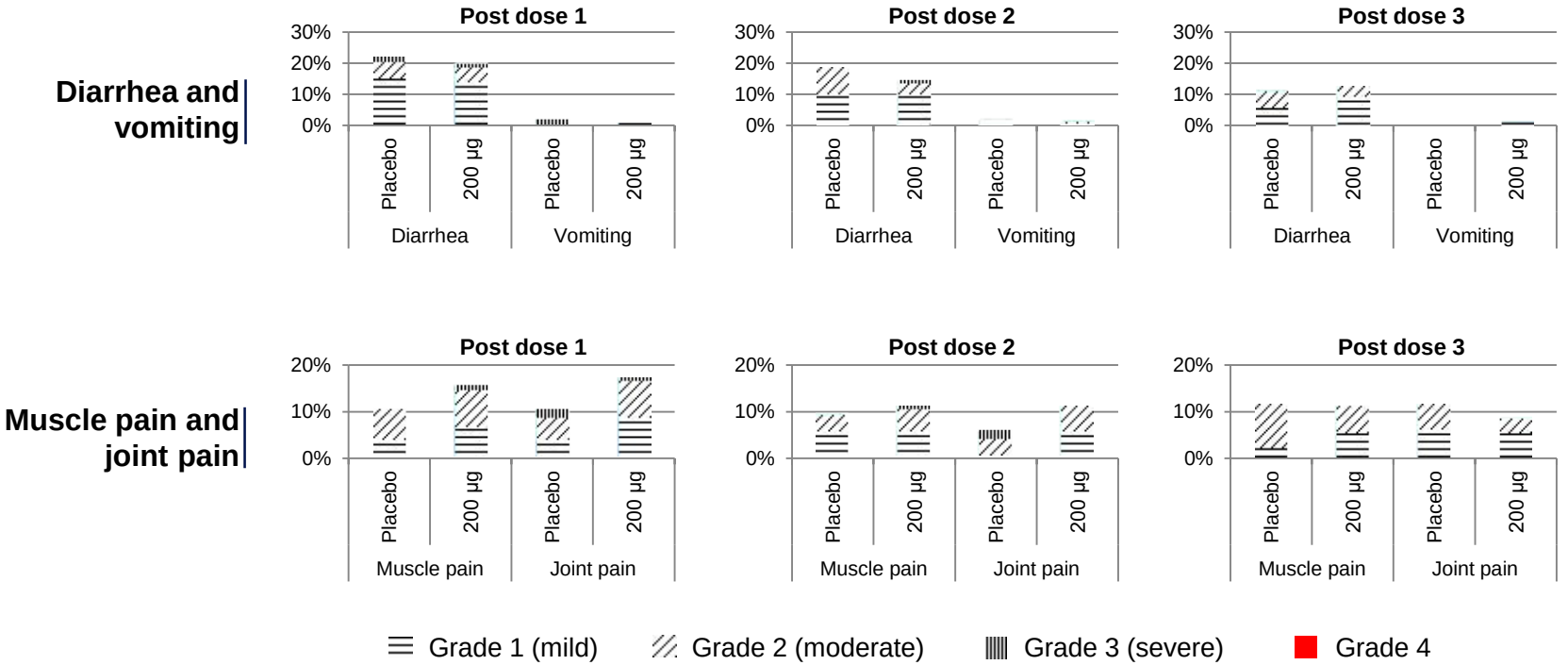
E-diary Reported Events: Month 0, 1, 6 Regimen
(Follow-up 14 Days After Each Dose)



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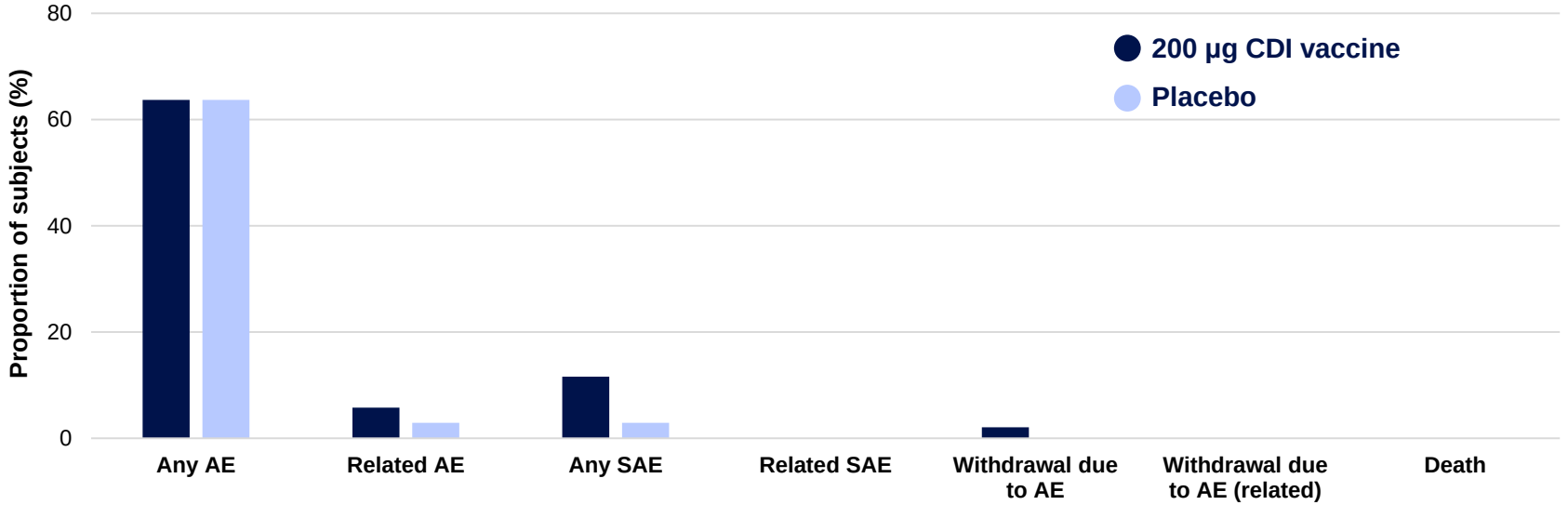
Safety Profile: Adverse Events and Serious Adverse Events



Safety profile of 200 µg dose at 0, 1, and 6 months in this phase 2 study is consistent with previous studies

AE=adverse event; SAE=serious adverse event.

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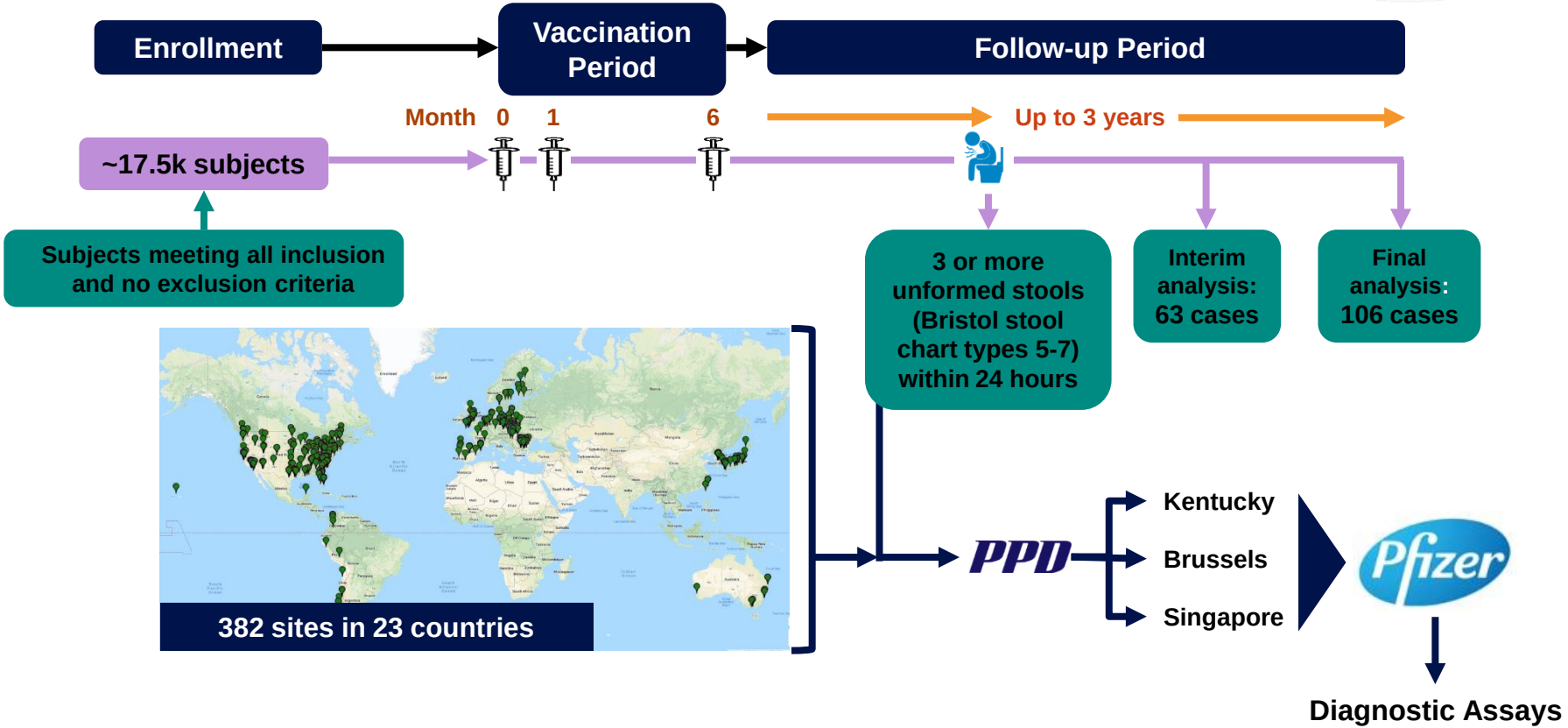
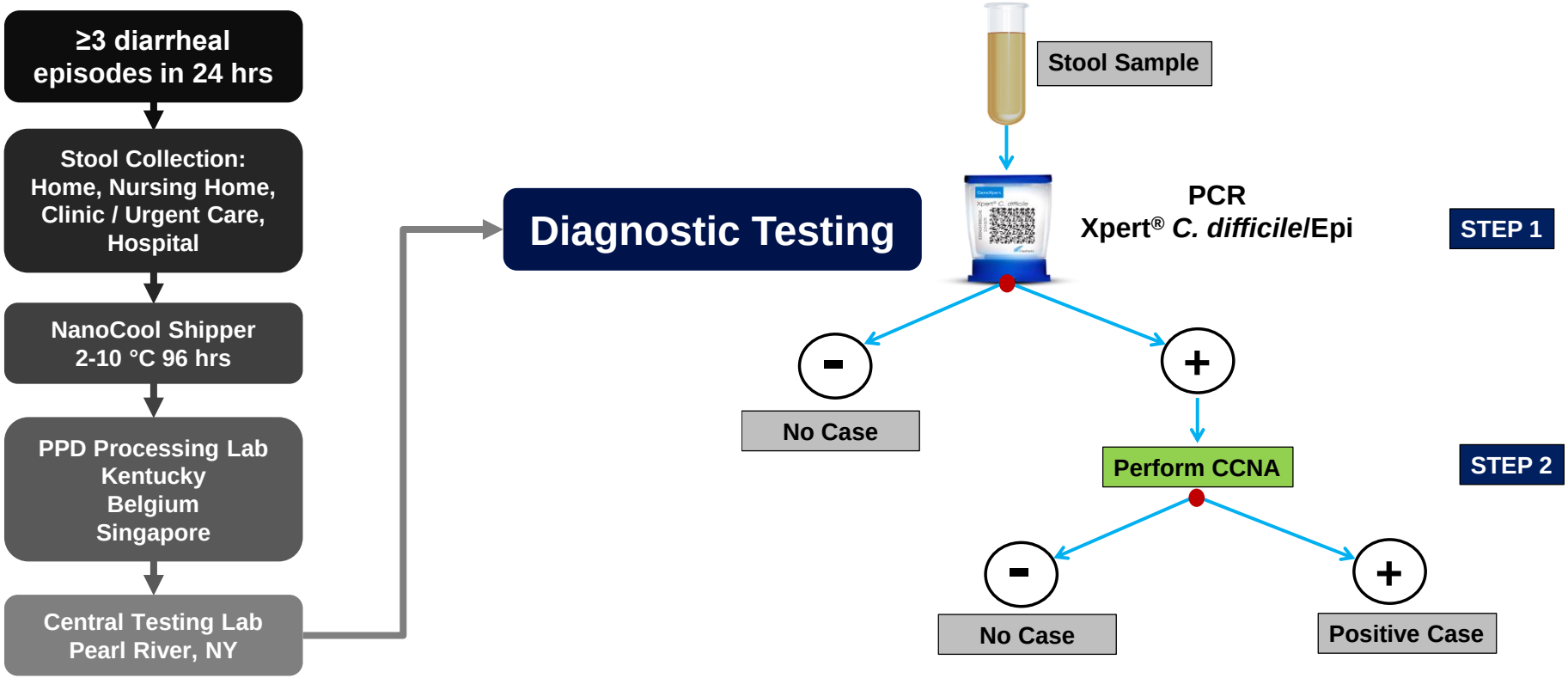
Clostridium Difficile Vaccine Efficacy Trial (Clover)



Two-Step Testing Algorithm

Endorsed by KOLs, ESCMID, ISDA, SHEA, CHMP, and the FDA



Conclusions

- CDI causes **significant disease in adults >50 years of age** in community and hospital settings
- Pfizer's vaccine was produced using a **novel detoxification process that preserves critical epitopes maximizing production of neutralizing antibodies**
- The vaccine induces polyclonal antibodies that **neutralize diverse toxins** and shows protection in preclinical models
- Vaccine program has progressed through proof of concept to phase 3 demonstrating **robust immune responses with a strong safety profile**
- Status: phase 3 Clover trial is fully enrolled and awaiting case accrual

Acknowledgments

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Pfizer Contributors

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