Trivalent Hepatitis B (HepB) Vaccine Yields Superior Seroprotection Rates in Adults

Results from the Phase 3 Double-Blind, Randomized Study Comparing Immunogenicity and Safety of a 3-Dose Regimen of Sci-B-Vac™ and Engerix B® (PROTECT)

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for the PROTECT Study Group

October 2-6 • Washington, DC • www.idweek.org
IDWeek 2019™
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Disclosure Information

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Disclosure Information :

Financial disclosure :

- The presenter of this presentation was a Principal Investigator of this study and her institution received financial support for the services performed in conducting the study at her study center(s).

Investigational/unapproved use disclosure:

- The presenter will be discussing Sci-B-Vac™ which is an investigational vaccine and has not been approved for use in the United States, with the European Medicines Agency, or in Canada. The data shown is from Phase III studies

Trial Sponsor : VBI Vaccines Inc.

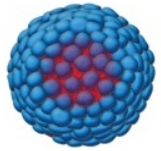
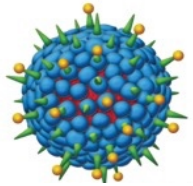
Prevention of Hepatitis B (HepB)

- Primary prevention of HepB by immunization is the most important strategy to reduce the disease burden, including acute and chronic illness, increased risk of death from cirrhosis, and liver cancer in HepBsAg carriers

- Although monovalent HepB vaccines are effective in children and healthy young adults, reduced immunologic responses (<10 mIU/mL) occur in:
  - Older adults, diabetics, obese persons, smokers, and males *[Yang S et al Sci Rep 2016;6:27251]*
  - Additionally, up to 5% of healthy persons are “non-responders” *[Saco TV et al Ann All Asthma Immunol 2018;121:320]*

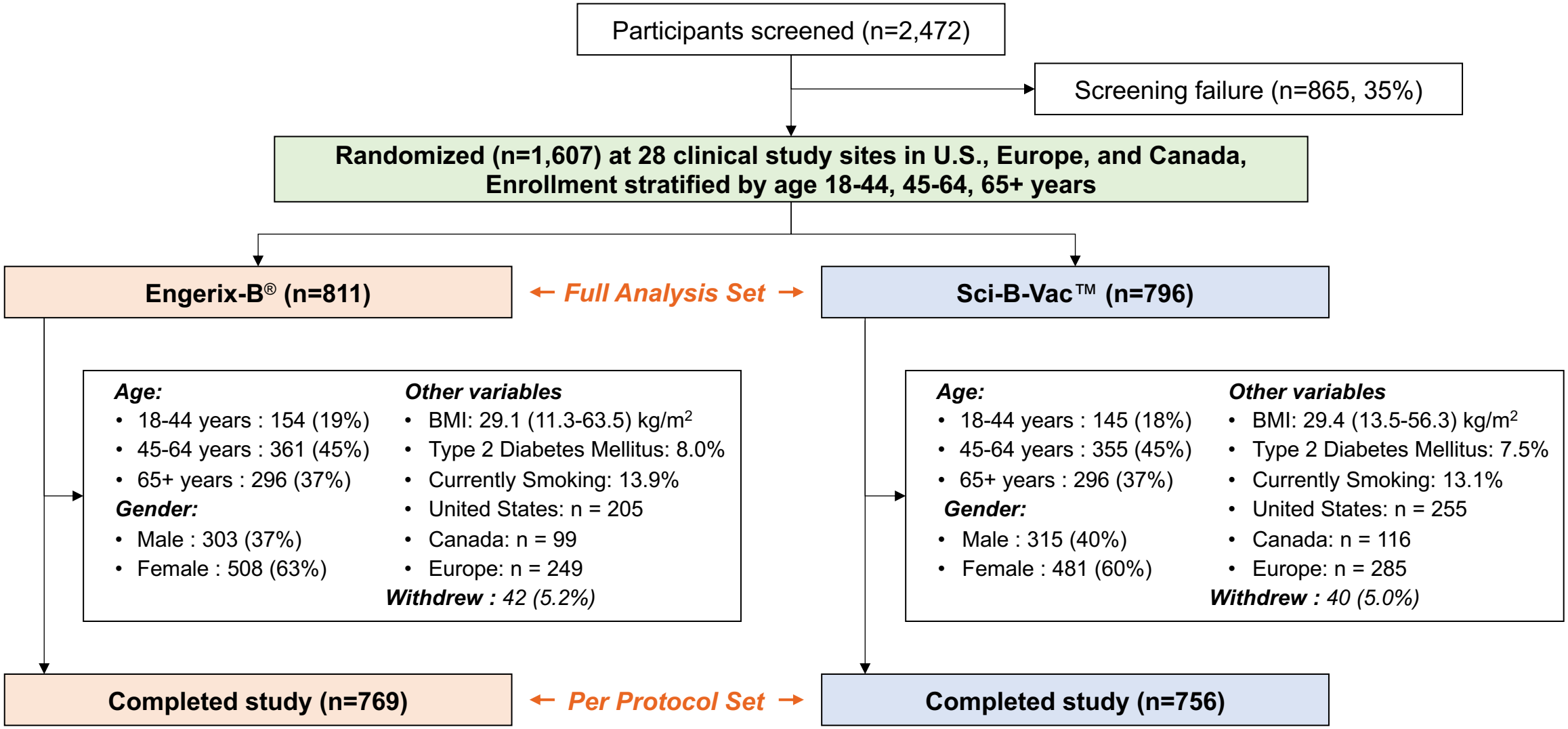
- We conducted a randomized, controlled, blinded, multicentre trial to compare safety and immunogenicity of a trivalent HepB vaccine (Sci-B-Vac™) to a monovalent HepB vaccine (Engerix-B®) given at days 0, 28 and 168, in healthy adults in stable health *[NCT03393754]*

Sci-B-Vac™ vs. Engerix-B®: Design and Function

	Engerix-B®	Sci-B-Vac™
		
Viral antigens mimicked:		
S Antigen	✓	✓
Pre-S1		✓
Pre-S2		✓
Dose of S Antigen:	20µg	10µg
Adjuvant:	Alum	Alum
Derivation:	rDNA yeast	Mammalian cell

- Pre-S1 antigen induces key neutralizing antibodies that block virus receptor binding
- Published data demonstrates that T cell response to pre-S1 and pre-S2 antigens can further boost responses to the S antigens, resulting in a more immunogenic response

PROTECT Study Participant Disposition

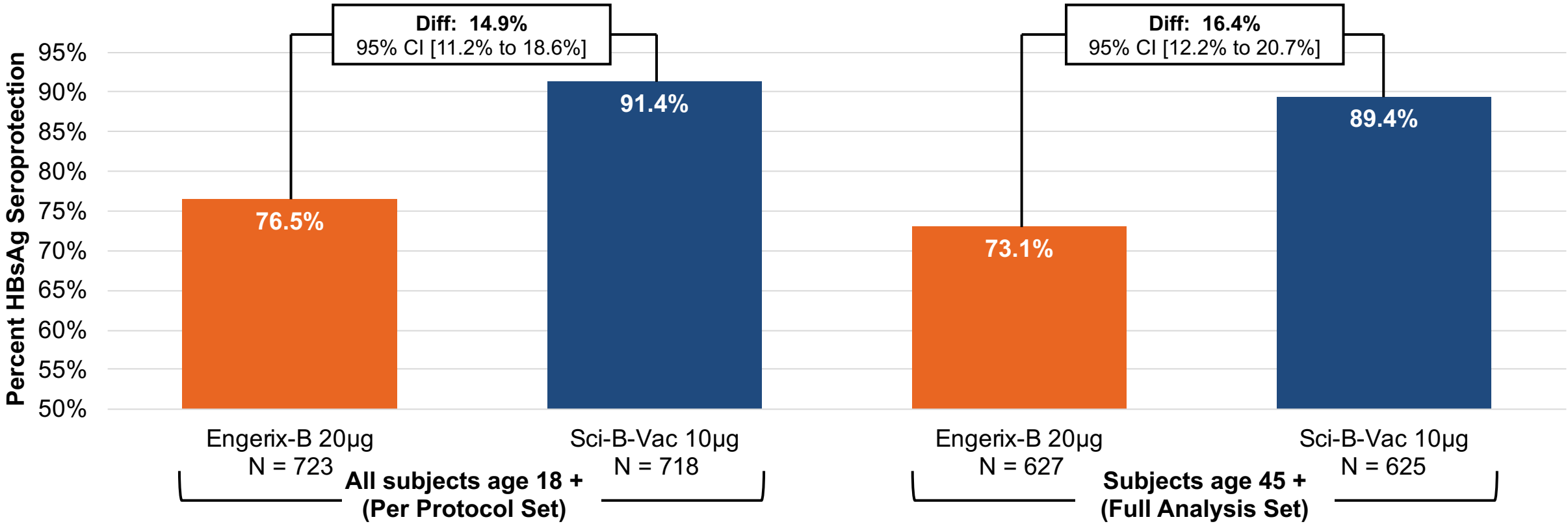


Both PROTECT Co-Primary Endpoints Met

Co-Primary Endpoints at Day 196, 4 weeks post-3rd vaccination:

1. Non-Inferiority of seroprotection rate (SPR) achieved in all subjects age 18+

2. Superiority of seroprotection rate (SPR) achieved in subjects age 45+

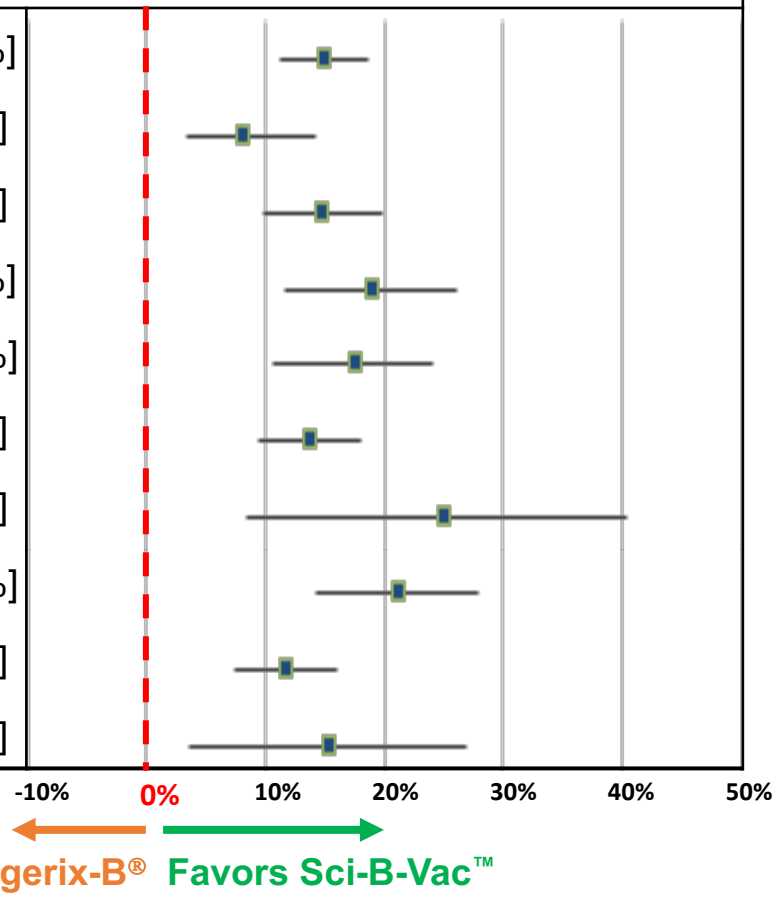


- *Non-inferiority :* If the lower bound of the 95% confidence interval (CI) of the difference between the SPR in the Sci-B-Vac™ arm minus the SPR in the Engerix-B® arm is > -5%, Sci-B-Vac™ will be declared non-inferior to Engerix-B®
- *Statistical superiority :* If the lower bound of the same 95% CI is greater than 0%, Sci-B-Vac™ will be declared statistically superior to Engerix-B®
- *Clinical superiority :* If the lower bound of the same 95% CI is > 5%, Sci-B-Vac™ will be declared clinically superior to Engerix-B®

Seroprotection Rates in Subgroup Populations

Sci-B-Vac™ achieved statistically significantly higher SPR vs. Engerix-B® in all subgroup analyses below at Day 196, at 4 weeks post-3rd vaccination

Population	Engerix-B® N	Engerix-B® SPR (%)	Sci-B-Vac™ N	Sci-B-Vac™ SPR (%)	Difference in SPR (%) [95% Confidence Interval]
All subjects	723	76.5%	718	91.4%	14.9% [11.2%, 18.6%]
18-44 years	135	91.1%	125	99.2%	8.1% [3.4%, 14.2%]
45-64 years	322	80.1%	325	94.8%	14.7% [9.8%, 19.8%]
65+ years	266	64.7%	268	83.6%	18.9% [11.6%, 26.1%]
Men	269	69.5%	282	86.9%	17.4% [10.6%, 24.2%]
Women	454	80.6%	436	94.3%	13.7% [9.5%, 18.0%]
Diabetics	60	58.3%	54	83.3%	25.0% [8.4%, 40.4%]
Obese (BMI > 30)	254	68.1%	269	89.2%	21.1% [14.3%, 28.0%]
Non-Obese (BMI ≤ 30)	469	81.0%	449	92.7%	11.6% [7.4%, 16.0%]
Current Smokers	95	70.5%	92	85.9%	15.3% [3.5%, 27.0%]



Summary of Safety Results

- No safety signals observed – Sci-B-Vac™ safety profile consistent with previous studies and post-marketing use (Israel)

- Higher rates of mild-to-moderate injection site pain, tenderness, and myalgia reported by subjects receiving Sci-B-Vac™ compared to Engerix-B®
  - Symptoms generally resolved without intervention within 1-7 days
  - No increase in reactogenicity symptoms over the 3-dose vaccination schedule

- Vaccine acceptability:
  - High rate of completion of vaccinations − 96.8% Engerix-B® and 95.2% for Sci-B-Vac™
  - Low rate of vaccine discontinuation due to non-serious adverse events (AEs) of 0.4% vs. 0.4% and due to SAEs of 0.2% vs. 0.3% for Engerix-B® and Sci-B-Vac™, respectively

Serious Adverse Events (SAEs) and Unsolicited AEs

SAEs

	Engerix-B®	Sci-B-Vac™
Total SAEs (62) throughout the study	**21 (2.6%)**	**32 (4.0%)**
SAEs occurring in ≥ 2 subjects:		
Atrial Fibrillation	2 (0.2%)	1 (0.1%)
Cardiac failure congestive	-	2 (0.3%)
Colon cancer	2 (0.2%)	-
Cholelithiasis	1 (0.1%)	1 (0.1%)
Ankle fracture	1 (0.1%)	1 (0.1%)
Osteoarthritis	1 (0.1%)	1 (0.1%)
Cerebrovascular accident	1 (0.1%)	1 (0.1%)

- Only one SAE, viral gastroenteritis, reported by site investigator as probably related to study vaccine Sci-B-Vac™
- No clusters or unusual patterns of SAEs – generally consistent with characteristics of study population (age 18-90 years)

Unsolicited AEs

	Engerix-B®	Sci-B-Vac™
1+ AEs reported (% of sub.) throughout the study	**54.5%**	**52.5%**
AEs reported by ≥ 1% of subjects:		
Headache	8.3%	8.5%
URI	6.7%	6.3%
Fatigue	4.9%	4.1%
Nasopharyngitis	3.5%	3.9%
Injection site pain	1.6%	2.9%
Back pain	2.8%	4.4%
Arthralgia	2.5%	2.1%
Diarrhea	2.6%	1.3%
UTI	2.1%	2.1%
Oropharyngeal pain	2.2%	1.9%
Dizziness	1.2%	1.5%
Sinusitis	2.1%	1.4%
Hypertension	1.6%	1.3%
Respiratory rate increase	0.9%	1.3%
Gastroenteritis	0.5%	1.3%
Nausea	1.2%	0.4%
Cough	1.0%	1.1%
Neck pain	1.1%	0.8%
Bronchitis	0.7%	1.0%
Muscle strain	0.7%	1.0%

PROTECT Data Summary

When compared to Engerix-B® at 20µg, PROTECT study demonstrated Sci-B-Vac™ at 10µg to have:

- Higher rates of protection in all adults aged ≥ 18 years (91.4% vs. 76.5%) with superiority in adults age 45 years and older (89.4% vs. 73.1%)
- Statistically significantly higher seroprotection rates in key immunocompromised populations including obese individuals (89.2% vs. 68.1%), diabetics (83.3% vs. 58.3%), and subjects age 65+ (83.6% vs. 64.7%)
- Safety in-line with the known profile of Sci-B-Vac™, with no safety signals observed

Next Steps:

- Data from CONSTANT, the Phase III lot-to-lot consistency study, is expected to expand the safety data base as well as provide additional seroprotection data in the adult population age 18-45 years *[NCT03408730]*

Acknowledgements

- All study participants

- Principal Investigators:

Finland

- Timo Vesikari and Aino Forsten (Coordinating P.I.)
- Miia Virta
- Ilkka Seppä
- Anitta Ahonen
- Solli Henriksson
- Benita Ukkonen
- Satu Kokko
- Outi Laajalahti
- Pauliina Paavola

Canada

- Joanne Langley (Coordinating P.I.)
- Brian Ward
- Curtis Cooper
- Marc Dionne
- Soren Gantt
- P. Guillaume Poliquin
- Janet Elizabeth McElhaney

U.S.

- Nathan Segall
- Bruce Rankin
- Mary Beth Manning
- Carl Griffin
- Amina Z. Haggag
- Mark E. Kutner
- Mark Turner
- Barbara E. Rizzardi
- Michael Levin
- Hayes Williams

Belgium

- Isabel Leroux-Roels
- Pierre Van Damme

|| Questions? ||