

**Consortium PMTA Efforts and Costs**

	Cost	Per Company Cost with Total Number of Consortium Partners		
		20 Partners	30 Partners	35 Partners
<b>Phase I - Research and Development Stage</b>				
Literature reviews <sup>A</sup>	\$750,000	\$37,500	\$25,000	\$21,429
Literature database maintenance (monthly ongoing)	\$20,000	\$1,000	\$667	\$571
Prepare state-of-the-science review and recommendations/considerations for product testing, non-clinical, and clinical study design for the PMTA briefing package	\$240,000	\$12,000	\$8,000	\$6,857
Keller Heckman Legal Strategy, Regulatory Compliance and Coalition Building Support	\$125,000	\$6,250	\$4,167	\$3,571
Phase I - Total	\$1,135,000	\$56,750	\$37,833	\$32,429
<b>Phase II - FDA Briefing Package and Meeting</b>				
Gather and assess product information	TBD	TBD	TBD	TBD
Descriptive information <sup>B</sup> per flavor	\$15,000	\$15,000	\$15,000	\$15,000
Screening level evaluation of flavor chemicals - flavor risk ranking (assumes 100 unique sharable chemicals)	\$300,000	\$15,000	\$10,000	\$8,571
Keller Heckman Legal Strategy, Regulatory Compliance and Coalition Building Support	TBD	TBD	TBD	TBD
Company-Specific Briefing Package	TBD	TBD	TBD	TBD
<b>Phase III - Execution Stage: Product Analysis and Non-clinical Studies</b>				
Quality Manufacturing Systems summary/development	\$12,000/TBD	\$12,000/TBD	\$12,000/TBD	\$12,000/TBD
Initial environmental compliance	\$11,000 plus travel costs	\$11,000 plus travel costs	\$11,000 plus travel costs	\$11,000 plus travel costs
Toxicological profiles <sup>C</sup>	\$465,000	\$23,250	\$15,500	\$13,286
Liquid & aerosol testing (Base PG/VG formulation for 2 device types) <sup>D</sup>	\$935,000	\$46,750	\$31,167	\$26,714
Liquid & aerosol testing (1 flavor, 1 device temp) <sup>E</sup>	\$72,000	\$72,000	\$72,000	\$72,000
Additional aerosol testing as determined by topography	TBD	TBD	TBD	TBD
Cost for devices	TBD	TBD	TBD	TBD
Extractable/leachable/storage	TBD	TBD	TBD	TBD
Literature review <sup>F</sup> Comparator products <sup>G</sup> Risk assessment of 29 HPHCs <sup>G</sup>	\$170,000	\$8,500	\$5,667	\$4,857
Computational modeling/ Tox review of additional chemicals <sup>H</sup>	\$750/ \$4,000 - 10,000 per chemical	\$750/ \$4,000 - 10,000 per chemical	\$750/ \$4,000 - 10,000 per chemical	\$750/ \$4,000 - 10,000 per chemical
Risk assessment of leachable/ extractable chemicals	\$4,000 - 10,000 per chemical	\$4,000 - 10,000 per chemical	\$4,000 - 10,000 per chemical	\$4,000 - 10,000 per chemical

## Per Company Cost with Total Number of Consortium Partners

	Cost	20 Partners	30 Partners	35 Partners
In vitro studies (Base PG/VG formulation) (Assumes 3 common PG/VG ratios; Ref Cigarette)	\$1,150,000	\$57,500	\$38,333	\$32,857
In vitro studies <sup>1</sup> (1 flavor, 1 device temp)	\$450,000	\$450,000	\$450,000	\$450,000
Environmental compliance	\$11,800	\$11,800	\$11,800	\$11,800
<b>Execution Stage: Clinical Studies</b>				
Clinical health, pharmacokinetic (1 base PG/VG and flavor) <sup>1</sup>	\$1,100,000 - 2,400,000	\$55,000 - 120,000	\$36,667 - 80,000	\$31,429 - \$68,571
Additional base PG/VG and flavor for PK study, if necessary, based on FDA response	\$1,840,000 - 2,400,000	\$92,000 - 120,000	\$61,333 - 80,000	\$52,571 - \$68,571
Clinical Topography Study (up to 4 flavor groups)	\$1,265,000 - 1,725,000	\$63,250 - 86,250	\$42,167 - 57,500	\$36,143 - 49,286
Clinical product surveys	\$60,000 - 240,000	\$60,000 - 240,000	\$60,000 - 240,000	\$60,000 - 240,000
Consumer product surveys	\$80,000	\$4,000	\$2,667	\$2,286
Environmental assessment (plus individual chemical assessment)	\$27,000	\$27,000	\$27,000	\$27,000
Keller Heckman Legal Strategy, Regulatory Compliance and Coalition Building Support	TBD	TBD	TBD	TBD
FDA meeting package	\$95,500	\$95,000	\$95,000	\$95,000
<b>Phase IV - Report Preparation Stage</b>				
Summary of research findings	\$60,000 per flavor \$150,000 per 10 flavors	\$60,000 per flavor \$150,000 per 10 flavors	\$60,000 per flavor \$150,000 per 10 flavors	\$60,000 per flavor \$150,000 per 10 flavors
Keller Heckman Legal Strategy, Regulatory Compliance and Coalition Building Support	TBD	TBD	TBD	TBD
Compilation of FDA submission package	TBD	TBD	TBD	TBD
Totals - flat costs <sup>k</sup>	\$8,657,300 - 11,157,300	\$639,300 - 935,300	\$489,938 - 755,967	\$458,443 - \$704,729
Totals - Per flavor	\$597,000	\$597,000	\$597,000	\$597,000
Totals - Tox Evaluations	\$4,000 - 10,000 per chemical	\$200 - 500 per chemical	\$133 - 333 per chemical	\$114 - 286 per chemical
Totals - Leachable/extractable	\$4,000 - 10,000 per chemical	\$4,000 - 10,000 per chemical	\$4,000 - 10,000 per chemical	\$4,000 - 10,000 per chemical

<sup>A</sup>Includes 9 topics (in vivo/in vitro toxicology, clinical health, abuse liability and pharmacokinetic, initiation, cessation, topography, human factors, consumer perception, PATH) of studies published since the NAS report; <sup>B</sup>Sales and marketing, adverse reporting, product descriptive information, labeling and packaging; <sup>C</sup>Based on evaluation of 33 HPHC chemicals; <sup>D</sup>Assumes 3 PG/VG formulations, 2 devices, 3 temperatures, 1 superbatch per PG/VG formulation, 7 replicates. Does not include particle size costs; <sup>E</sup>Assumes 3 nicotine concentrations per flavor, 3 batches and 7 replicates per batch, 1 high temperature device setting; <sup>F</sup>Literature review of liquid and aerosol constituents; <sup>G</sup>Comparator product and risk assessments evaluated only for highest concentrations; <sup>H</sup>Common flavor ingredients can be shared across relevant partners. Tox screen costs range \$750-4,000 per chemical; <sup>I</sup>Assumes 1 device, 1 max temperature, 1 max nicotine concentration, 1 PG/VG and a reference cigarette;

<sup>J</sup>Excludes additional clinical study costs that may be required for each flavor; <sup>K</sup>Does not include costs per chemical or TBD items