



**December 10, 2020 - Revision**

**Contract Services Agreement For**

**Registration, Validation &  
Commercial Manufacturing and Packaging**

**Product or Project Name:**

**Pocket Naloxone – 2 applicator cartons**

**Prepared for**

**Pocket Naloxone Corporation**

Ashanthi Mathai | CEO & Co-founder | Pocket Naloxone Corp.



**Customer Request:**

Aphena Pharma Solutions Maryland, LLC (“Aphena”) is pleased to present Pocket Naloxone Corporation (“Customer”) the following proposal for manufacturing and packaging; engineering, validation activities, and commercial work for Pocket Naloxone – 2 applicator carton. Aphena will be performing these contract services at our Easton, MD facility on behalf of and as instructed by Pocket Naloxone Corp., as outlined in this proposal. Included in this proposal Aphena will include all activities to produce a commercial ready product in a cGMP 21 CFR Parts 210 & 211 environment.

**Scope of Work**

Aphena will perform the engineering, registration and validation activities for manufacturing and packaging Pocket Naloxone. Liquid fill is 0.15mL nominal, contained in a swab/applicator in a peelable pouch format, in anticipation of commercial requirements in 2022. Pocket Naloxone Corp. has set up a central lab to handle all testing requirements, with a separate lab handling leachable and extractable testing.

**Manufacturing Requirements**

Formulation Details:

Final Formulation	% w/w
Naloxone hydrochloride 60 mg/mL	5.900
Na <sub>2</sub> EDTA 0.05% see notes for change	0.049
pH 4.5	
BKC 0.10%	0.098
Citric Acid 10mM	0.189
NaCl 0.15%	0.148
Purified Water	93.616
	<b>100.00 %</b>

**Manufacturing process:**

Notes provided by customer:

Here is the GLP lab preparation during formulation development and in vitro testing.

Preparation: The solution was prepared at 6 mL scale by preparing a 10 times concentrated mixture of all excipients, which was then added to solid API, further diluted with purified water, and then adjusted to pH 4.5 using hydrochloride and sodium hydroxide.

Currently, small CMO is making the clinical supplies for the Fall human pk study.

**Packaging:**

Insert (1) swab into filled cap on rotary table. Form/fill/seal printed pouch with (1) finished applicator. Adhere P.I. (patient insert) with glue dot to individual pouches. Load two (2) finished pouches into carton. Serialize carton.

### Aphena Supplies:

- Naloxone blended solution - 60mg/mL
- Patient Insert (glue dot to sachet/pouch)
- IFC – Internal folding carton
- Shipper
- Shipper label

\*Quotation is subject to change based upon final approved specifications.

### Customer Supplies:

- API
- Caps
- Applicators
- Lab Testing

### Pricing: ( Table 1 )

	<u>Registration</u> No Cartoning	<u>Validation</u> 2 pouch per carton	<u>Commercial Unit –</u> 2 pouch per carton	<u>Note(s)</u>
<b>Primary Pkg. Description</b>	1 swab/applicator pouched	1 swab/applicator with PI Per Pouch	1 swab/applicator with PI Per Pouch	
<b>Secondary Pkg. Description</b>	No Carton	2 Pouches Per Carton	2 Pouches Per Carton	
<b>(Annual) Volume</b>			1,774,828 cartons	
<b>Units per Batch (cartons)</b>	6,000	59,000	295,805	
<b>Required Batches</b>	3	3	n/a	
<b>Price</b>	See Chart Below	\$ 3.00 / Carton	\$ 2.84 / carton	

### Tooling or Setup Cost: ( Table 2 )

Item	Total Price	Lead Time	Comments
Seal bars	\$ 2,460	10 weeks	
Pumps	\$ 3,540	12 weeks	
Rotary table fixtures	\$ 4,200		
Installation labor	\$ 9,600		Will require before Validation Batches
10 liter vessel	\$ 1,200		
Film/foil printing cylinders	\$ 2,900		*estimate, artwork dependent?
Patient Insert (plates)	\$ 250		*estimate, artwork dependent?
Carton plate & die charges	\$ 1,650		*estimate, artwork dependent?
Hot melt glue system	\$ 18,000		Nordson Hot Melt System for commercial
<b>TOTAL:</b>	<b>\$ 43,800</b>		Payable at Time of Startup

**Lab – One-time charges: ( Table 3 )**

Item	Price	Lead Time	Comments
Method Transfer for BKC and EDTA	TBD		Development performed by outside lab
Method Transfer for Assay*: Naloxone (Identification, Content Uniformity) – CLM 1056	\$ 6,000	6	
Method Transfer for Assay*: Impurities – CLM 1046	\$ 6,000	4	
Method Transfer* for in vitro release assay – CLM 1079	\$ 6,000	4	
Micro BCC validation – USP<60> Suitability	\$ 2,500	6	Outsourced to 3 <sup>rd</sup> party lab
Micro Suitability USP <61> <62> Suitability	\$ 3,660	4	
<b>Total:</b>	<b>\$ 24,160</b>		

**\*Note: To qualify as a method transfer the development lab must support the transfer with full involvement and cooperation to include all validation documentation, joint testing, equipment details, etc.**

**Non-GMP Engineering Trial – Per Trial Run ( Table 4 )**

Item	Fees	Batch size	Unit of Measure	Total Price	Comments
Risk Assessment FMEA	\$ 3,500				Only if requested
Engineering & Cleaning Study – Manufacturing	\$ 6,720	2.60	Gallons	\$ 11,975	Includes one day of blending
Engineering & Cleaning Study – Packaging	\$ 6,720	5,000	Pouches	\$ 16,535	Includes one day of packaging
<b>Total:</b>				<b>\$ 28,510</b>	

**Note: Pricing above does not include Bulk Lab testing.**

**Registration Batch Production – One-time charges ( Table 5 )**

Item	Doc. Fees	Batch Size	Total Price	Comments
Risk Assessment FMEA	\$ 3,500		\$ 3,500	Fee only if a Report is required
Registration/submission (1 Batch) – Mfg & Packaging	\$ 12,100	12,000 Pouches	\$ 55,300	Includes Finish Goods Testing
Registration/submission (2 Batch) – Mfg & Packaging		12,000 Pouches	\$ 43,200	Includes Finish Goods Testing
Registration/submission (3 Batch) – Mfg & Packaging		12,000 Pouches	\$ 43,200	Includes Finish Goods Testing
Cleaning Validation – MFG & Pkg	\$ 9,800		\$ 9,800	
<b>Total:</b>			<b>\$ 155,000</b>	Does not include Risk Assessment

**Note: Registration blends are billed at the minimum price above, the yield could be off based on stability samples and heightened quality testing.**

**Validation Batches – 3 Production Runs – Saleable Units ( Table 6 )**

Description	Fees / Documents	Batch Size	Unit of Measure	Estimated Total Price	Comments
Validation – Mfg & Pkg. Batch 1 ( Only Pkg 20% of Batch )	\$ 6,000	25 gallons 59,000 Cartons	Cartons	\$ 188,000	Only Packaging 20% of blend for validation
Validation – Mfg & Pkg. Batch 2 ( Only Pkg 20% of Batch )		25 gallons / 59,000 Cartons	Cartons	\$ 182,000	Only Packaging 20% of blend for validation
Validation – Mfg & Pkg. Batch 3 ( Only Pkg 20% of Batch )		25 gallons / 59,000 Cartons	Cartons	\$ 182,000	Only Packaging 20% of blend for validation
<b>Total</b>				<b>\$ 552,000</b>	

**Note: Validation blends are billed at the minimum price above, the yield could be off based on stability samples and heightened quality testing.**

**Stability Program: - Two orientations 1 vertical, 1 horizontal ( Table 7 )**

STABILITY PROGRAM		
2 Orientations (vertical & horizontal), 3 conditions (25C, 30C, & 40C), each batch		
DESCRIPTION	PRICE PER PULL POINT	COMMENTS
Stability Protocol fee	\$2,400	Price per Required Stability Study
<b>T0</b>	\$0	Includes Storage
<b>1M</b>	\$0	Includes Storage
<b>2M</b>	\$0	Includes Storage
<b>3M+Micro</b>	\$ 11,467	Includes Storage
<b>6M+Micro</b>	\$ 11,467	Includes Storage
<b>9M+Micro</b>	\$ 10,857	Includes Storage
<b>12M</b>	\$ 3,822	Includes Storage
<b>18M+Micro</b>	\$ 9,954	Includes Storage
<b>24M</b>	\$ 2,919	Includes Storage
<b>36M</b>	\$ 2,919	Includes Storage
<b>Total Stability Estimate PER BATCH*</b>	<b>\$55,805*</b>	

**\*NOTE: BKC ASSAY & EDTA ASSAY need to be developed therefore stability pricing is not complete.**

**Ongoing Charges (Estimates): ( Table 8 )**

Item Description	Price	Comment
Lab materials for testing	TBD	
Finished goods testing per batch	\$ 10,593	Two methods need to be developed cannot finalize. Not complete.
Bulk Hold Study	\$ 17,894	
Bulk release testing per batch	\$ 10,593	Release testing cost is built into Commercial Unit Price
Raw material testing	\$ 36,234	With approving Aphena's Citric Acid & Sodium Chloride
Disposable costs hazardous waste	\$ 2,500	This is an estimated price

**Cleaning Methods**

Aphena will perform an equipment cleaning assessment, which includes a review of the equipment train that will be used to manufacture and package the product.

**API, Spec Generation, and Raw Material Testing**

All testing to be performed by outside labs and Aphena cGMP laboratories.

**Engineering & Feasibility Services**

Documentation required for the manufacturing of a feasibility or engineering batch will not undergo Quality Assurance ("QA") review.

Aphena will manufacture one (1) feasibility / Engineering batch. This batch will be used to confirm critical process parameters, analytical performance and to perform a packaging line trial. If parameters or materials have not been identified Aphena will work with Customer through a 3<sup>rd</sup> party testing lab to determine these items. If the engineering batch fails during the blending or packaging process for any reason Aphena will work with the Customer to identify the root cause before the process has to repeated.

**Stability Details – n/a**

Aphena will prepare a stability protocol based on the requirements from the Customers to conduct a stability study to monitor.

**Storage**

Additional \$75 charge per pallet/per month may apply if Products are not shipped within 30 days from product release to customer, subject to space availability.

**Serialization Setup**

IF REQUIRED: A one-time serialization set up fee of \$6,500 will be charged for the initial client set-up for DSCSA compliance. An additional serialization set up fee will be charged for each product SKU. The unit price for serialization will be included in the commercial price.

Initial & Date                     <sup>DS</sup>  
Initial & Date                      12/19/2020

Serialization Initial Setup will consist of the following activities:

- Serialization Initial Client Set up meeting
- Client Spec / Labeling Template Review
- RF Xcel Initial configuration
- Client company master data & templates configuration
- Serialization SKU Set up in RX Xcel and Optel
- Product Master Data Set up
- Serial Numbers Transfer Verification
- Serialization Process Verification Run

### **Payment/Deposits**

- Pricing is based on information available to Aphena and indicated components and may be adjusted based on final batch, bulk quantities, lab testing and/or changes to product specifications.
- Project acceptance subject to Aphena approval of product MSDS and Credit Check
- Pricing is FOB, 7978 Industrial Park Drive Easton, MD
- Valid for 90 days from the date of this letter.
- Payment Terms: Net 30 days
- Deposit:
  - Aphena will require a **\$75,000** deposit to start the project and show customers commitment

### **Commitment Term**

- Supplier Agreement Commitment: Both companies agree to enter into a supplier agreement within 30 days of receiving the required deposit to start the project. For Aphena to achieve the commercial pricing we must invest \$900,000 in capital for a higher speed automated line for this pouch and filling design. Aphena is willing to make this investment with a 4-year agreement with Pocket Naloxone and committed volume of 4,500,000 cartons over 4 years. Both Parties understand and agree that the 4-year Agreement is contingent on FDA approval of the Pocket Naloxone Corp. Product submitted for such approval.

Best Regards,

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