

**Sender:** Kale Kalidas </O=CARTER-WALLACE/OU=CRANMAIL/CN=RECIPIENTS/CN=KKALE>  
**Sent:** Tuesday, March 21, 2006 5:12:02 PM  
**Recipient:** D'Addio Alex <ADAddio@medpointepharma.com>  
**Cc:** Balwani Gul <GBalwani@medpointepharma.com>  
**Subject:** Astelin – Flonase Combination Product Feasibility Assessment Plan.  
**Attachments:** Astelin-Flonase Combination Product Feasibility Assessment plan.doc

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Alex,

Please review attached draft document. If you like we can discuss this plan today afternoon. If it is OK with you I will like to attend Interphex in NY city tomorrow.

Kalidas



# Astelin – Flonase Combination Product: Feasibility Assessment Plan.

## Background

**Table 1: Formulations comparison**

Product	Flonase	Astelin Improved Taste
Active Compound	Fluticasone propionate	Azelastine Hydrochloride
Active concentration per spray	50 microgram	137 microgram
Polymers	Micro-crystalline cellulose and carboxymethyl-cellulose sodium,	Hydroxypropyl methylcellulose
Sweetener, Osmolarity	Dextrose	Sucralose NF Sorbitol
Preservative	0.02% benzyalkonium chloride & 0.25% phenylethyl alcohol	0.025% benzyalkonium chloride
Surfactant	Polysorbate 80	
Chelating agent		EDTA
Buffer		Sodium Citrate, dihydrate
Water	q.s.	q.s.
pH	5-7	6.0-6.9
Appearance	Suspension	Clear, colorless liquid

## Plan A:

1. Filter or centrifuge Flonase product and determine the solubility of Azelastine Hydrochloride in the filtrate or centrifugate.
2. If Azelastine Hydrochloride is sufficiently soluble then add required amount of Azelastine Hydrochloride powder to the Flonase suspension.
3. If Azelastine Hydrochloride is not sufficiently soluble, modify the formulation or process so that Azelastine Hydrochloride is completely in solution.
4. Identify suitable spray pump head for existing Astelin bottle to attain similar spray pattern and droplet size distribution of Flonase spray.
5. Determine accelerated stability of the product stored in the Flonase amber colored glass bottle and commercial Astelin container closure system.

## **Plan B**

1. Identify a water soluble corticosteroid compatible with Azelastine Hydrochloride
2. Include it in the existing Astelin Improved Taste formulation.
3. Determine accelerated stability of the formulation
4. Determine accelerated stability of the product packaged in the commercial Astelin container closure system.

## **Plan C**

1. Increase the solubility of Fluticasone propionate by various solubility enhancement technologies.
2. Develop a solution formulation suitable for nasal delivery containing Fluticasone propionate and Azelastine Hydrochloride
3. Determine accelerated stability of the formulation
4. Determine accelerated stability of the product packaged in the commercial Astelin container closure system.