ApoStream™ from Concept to Market

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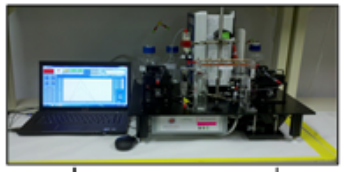
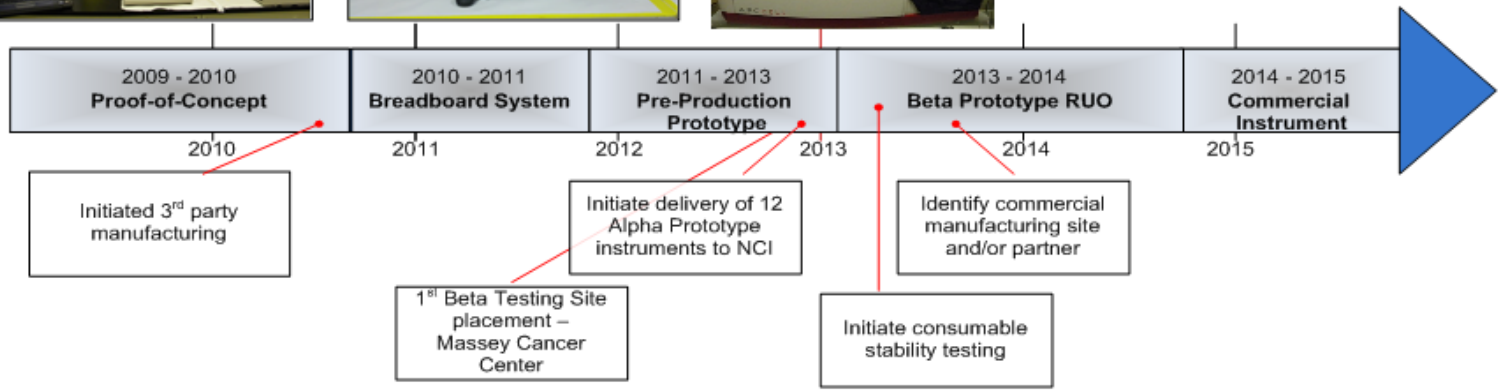
Introduction

- ApoStream™ is an antigen-independent dielectrophoretic (DEP) cell enrichment device that circumvents the need for specific antigen expression on the target cells' surface for isolation of rare circulating tumor cells (CTCs) and cancer stem cells from whole blood.
- ApoStream™ is being implemented as a Research Use Only device for the isolation and characterization of CTCs from cancer patients participating in clinical trials.
- ApoStream™ is being developed and designed in accordance with design controls per ISO 13485 and FDA Quality System Regulation (21 CFR 820).

ApoStream™ Development Path and Status





Instrument Development Stage	Status	Funding Source	Purpose
Proof of Concept	Completed	ApoCell	Demonstrate technology
Breadboard System	Completed - 2011	SAIC/NCI	Currently used to support development and clinical research studies. Engineering build
Alpha Prototype RUO	First units delivered Q4 2012	SAIC/NCI	First prototype that "looks like/works like" commercial instrument. Used to support development, clinical research studies, KOL programs, commercial sales. Engineering build
Beta Prototype RUO	Target start – Q3/Q4 2013	TBD	2nd prototype iteration that "looks like/works like/manufactured like" commercial instrument. To be registered as FDA Class 1 device. Used to support development, clinical studies, KOL programs, commercial sales. Pilot production
Commercial	Target start – 2014/2015	TBD	Commercial system for research, clinical studies, KOL programs. Qualified commercial production. May be used as part of FDA Class 3 diagnostic system

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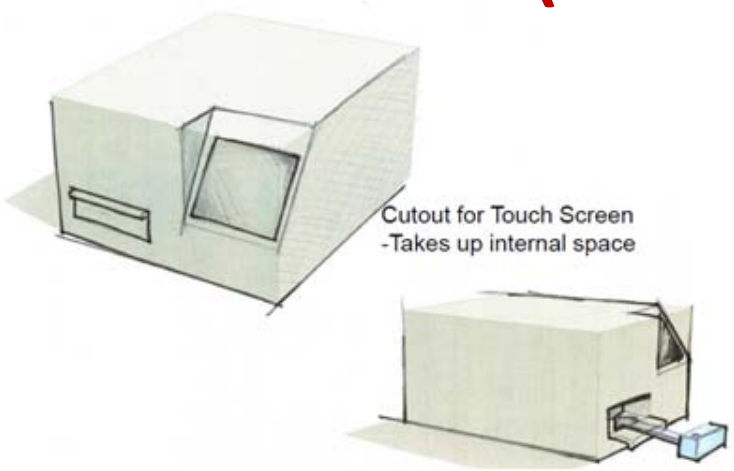
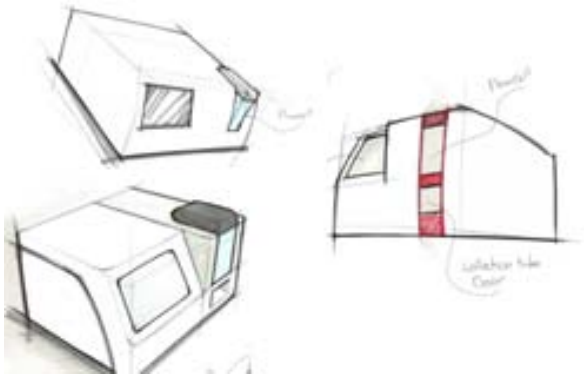
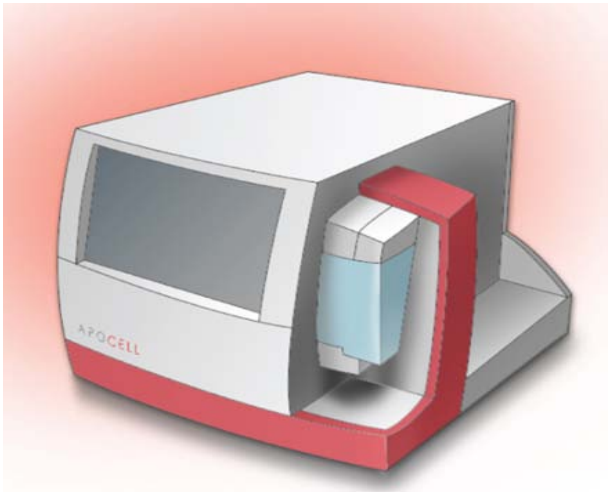
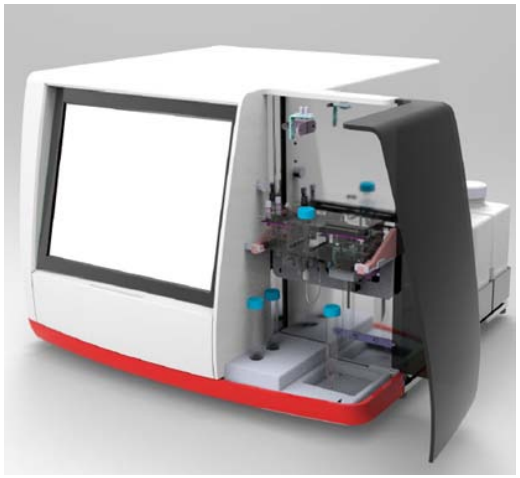
Prototype Design Evolution (Industrial Design)









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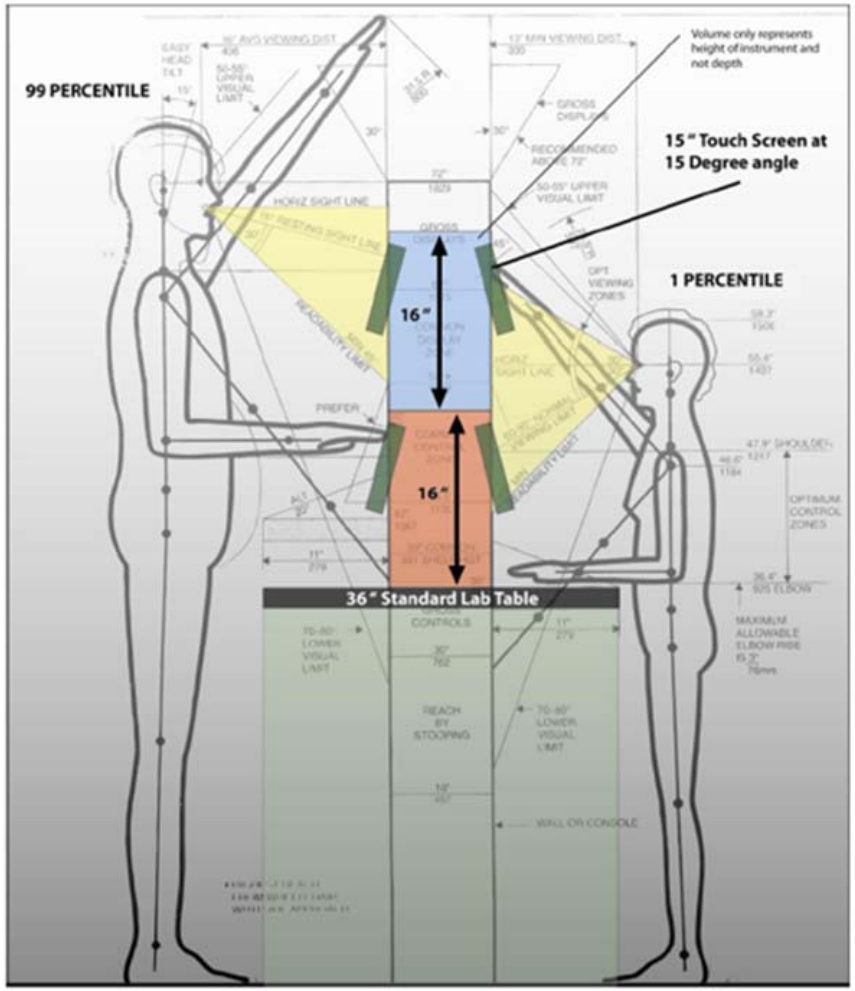
Design Process

- Design inputs
  - Technical specifications
  - Human factors engineering
  - Cognitive task analyses
  - Customer requirements (e.g. stackable design)
  - Process analysis
  - Risk analysis
- Design outputs:
  - Sample loading from front
  - Consumables accessible from side
  - 24” x 19” x 16” (w x d x h)
  - 15” color, touchscreen display with tilt capability
  - Software: GUI and ICP
  - Fluid schematics, electronics, mechanical design



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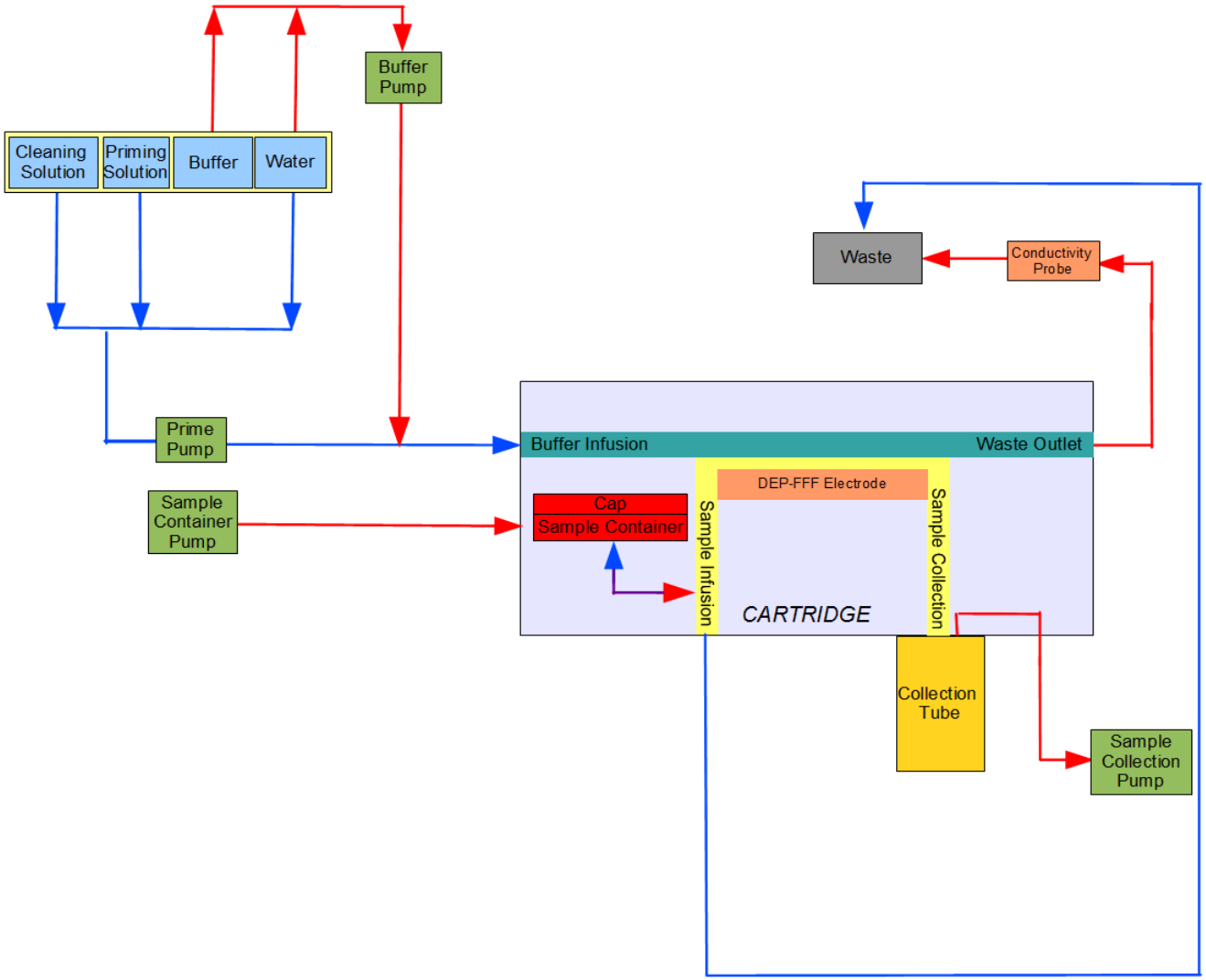
Device Schematic



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Graphical User Interface

Run Tab

- User Inputs
  a. User Name
  b. Sample ID
  c. Sample folder
  d. Flow Chamber ID

- DEP Channel Parameters
  a. Frequency
  b. Voltage
  c. Conductivity
  d. Temperature

- Sensor Indicators
  a. Door
  b. Flow Chamber
  c. Collection Tube

- Progress Indicators
  a. Sample Run time
  b. Cumulative Run Time

Graphical User Interface

Fluidics Tab

- Pump Status and Flow Rate
  a. Buffer Pump
  b. Container Pump
  c. Collection Pump
  d. Prime Pump

- Valve Indicators
  a. Buffer Infusion
  b. Sample Container
  c. Prime
  d. Sample collection

- Fluid Level Indicators
  a. Water
  b. Buffer
  c. Priming Solution
  d. Cleaning Solution

- Lot Numbers
  a. Elution Buffer
  b. Sample Buffer
  c. Pretreatment Buffer

Risk Analysis

- Risk analysis conducted in accordance with ISO14971

Potential Hazard					Risk Reduction Approach				
Category	**Hazard Description**	**S**	**O**	**R#**	**- Mitigation**	**Reference**	**S**	**O**	**R#**
Inadequate service and maintenance	System does not operate or perform as intended	4	3	12	- Life testing - Defined maintenance and service intervals - User instruction - Prompt service through software		4	2	8
USE BY UNSKILLED OR UNTRAINED PERSONNEL									
Use by inappropriate personnel	Damage to system, improper data, User injury	4	4	16	- Laboratory use only - System user login - User instruction		4	2	8
REASONABLY FORESEEABLE MISUSE									
Misuse of system	System damage or incorrect data output	4	4	16	- User instruction - Scheduled maintenance		4	2	8
	Reuse of flow chamber/disposables	4	4	20	- User instruction - Labeling - Barcoding of disposables - Automated chamber cleaning is part of protocol		4	2	8
	Short cut process	3	4	12	- User instruction - Software specification - System warning		3	3	9
	Flow chamber removed from system	2	4	8	- Flow chamber/collection tube/door sensor - User instruction - System warning		2	1	2
	Door opened during process	4	5	20	- Door sensor		4	2	8

Excerpt from risk analysis

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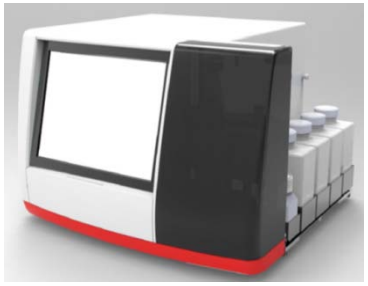
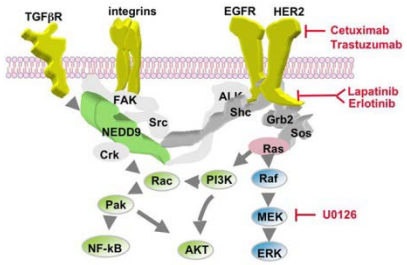
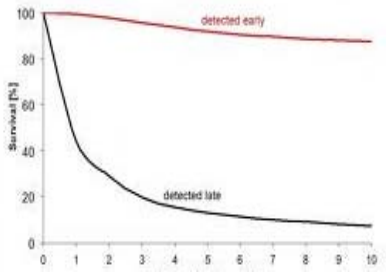
Long-Term Goal: Clinical Utility
ApoStream™ for Personalized Cancer Therapy

Cancer Patients	Diagnostic Test	Personalized Therapy	Improved Survival



ApoStream™ POC





Patients directed for less invasive testing of disease → ***Molecular testing of circulating tumor cells*** → ***Directed therapy to patients' specific cancer type for increased chance for survival***

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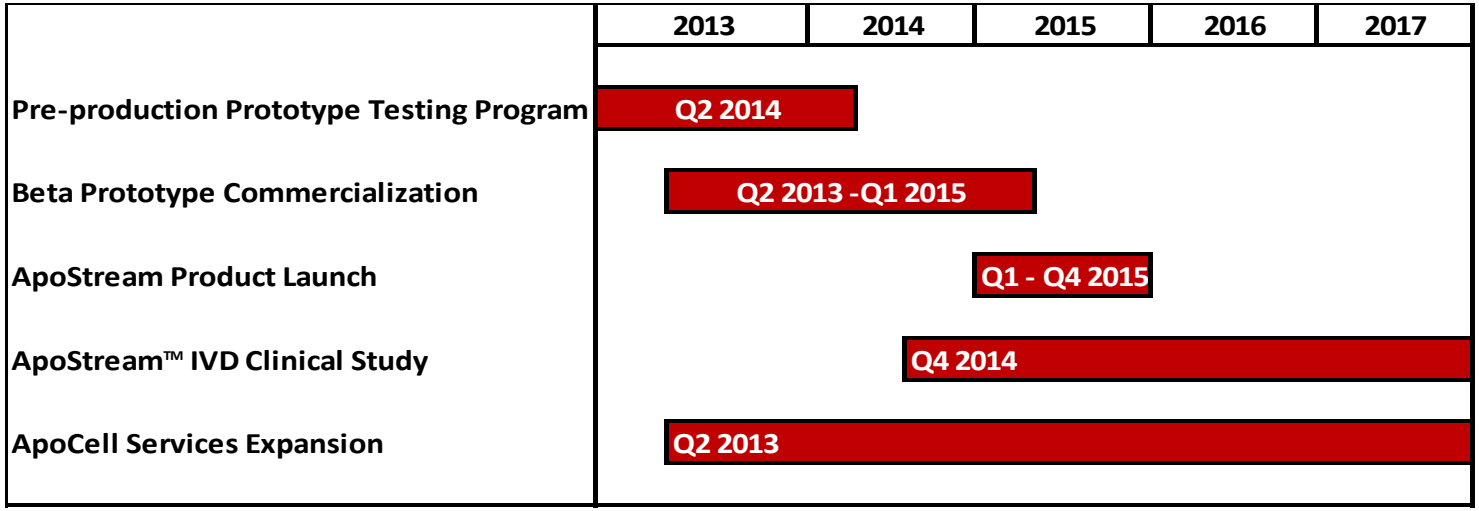
ApoStream™ Commercialization Timeline



- **ApoStream™ Pre-Production Investigational Use Only (RUO) system**
  - Engineering build
  - Academic research market and internal service work
  - Beta testing program

- **ApoStream™ Beta-Prototype Investigational Use Only (RUO)**
  - Pilot production build
  - Basis for diagnostic assay development
  - FDA class I clearance (subsequent filing)
  - CE mark in accordance with IVDD (subsequent filing)

- **ApoStream™ In Vitro Diagnostic Device (IVD)**
  - Clinical market, validated device (production manufactured)
  - Provider of clinical diagnostic assays
  - FDA class II clearance (510(k))
  - CE mark in accordance with IVDD

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