Aptamer-Bioconjugate Drug Delivery Device

Fourth Year Design Proposal

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Consultant – Professor Juewen Liu

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Customer Requirements

Primary :

- Cancer specific targeted drug delivery

Secondary:

- Optimize selectivity of delivery device
- Show dose/response characteristics

Tertiary:

- Show stability under different operating conditions

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Expected Design Issues

- Characterizing efficacy
- Compatibility of individually successful systems
- Being aware of FDA requirements
  - Current Good Manufacturing Processes
- Cost of device development and testing
- IP management of drug and aptamer

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Contingencies

If unable to achieve conjugation of aptamer:

- Conjugate to high Z material (TiO_2, Fe) for use as imaging aid/ radiation sensitizer
- Switch to different aptamer also shown to be successful
  - Breast cancer - Osteopontin
  - Colorectal cancer - Beta-Catenin
  - Generic cancer (Human Epidermal Growth -3, Sialyl-Lewis x, Nucleolin, etc.)

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The Proposal

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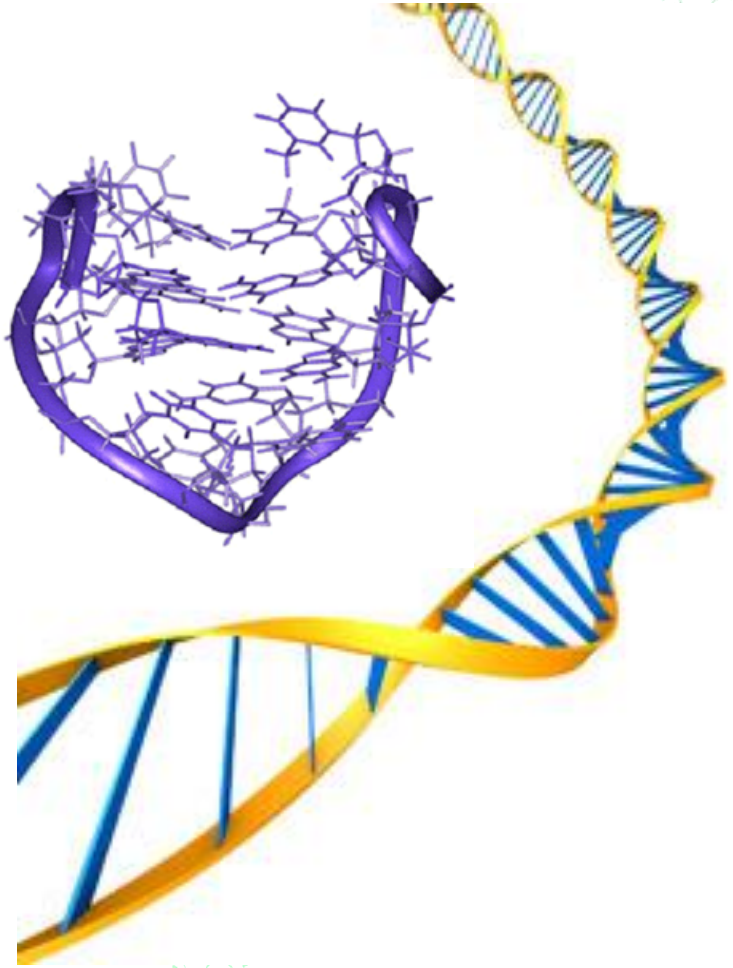
Aptamers

- ssDNA/RNA oligomers of 20-70 nucleic units
- Take tertiary structure to specifically bind to targeted cell surface
- Matched to target by Selective Evolution of Ligands by Exponential Enrichment (SELEX) process
- Our choice: sgc4 DNA aptamer which binds to leukemia cells
- Poor biological lifetime if non-conjugated



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EcoSphere®

- EcoSphere® is a product of EcoSynthetix
- Cross-linked starch nanoparticle (~120 nm)
- Tested in drug delivery systems (Duke University)
  - Proven to be non-toxic (biological components)
  - Can carry drug for delivery applications
  - Long biological half-life
  - Size advantage

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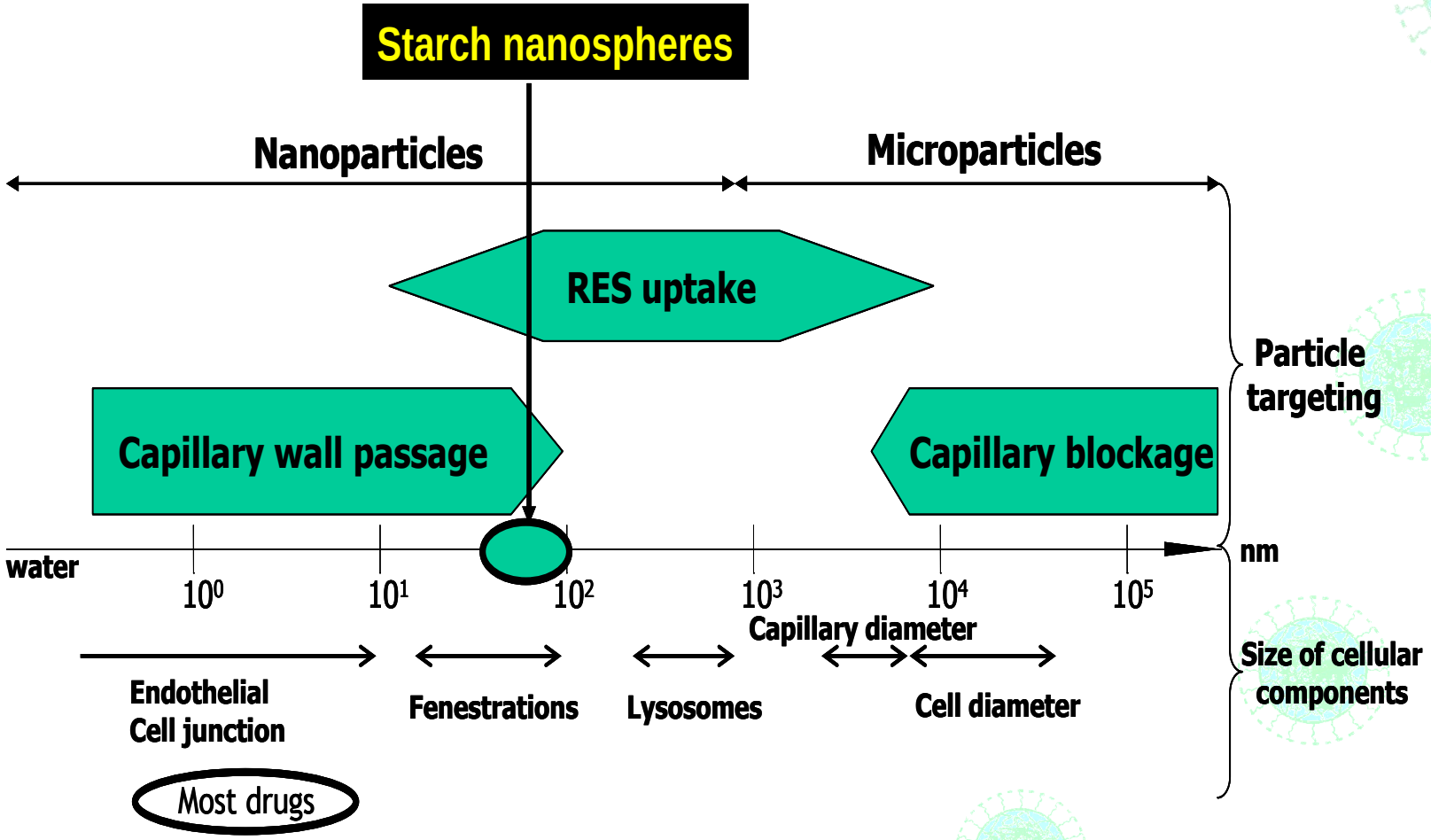

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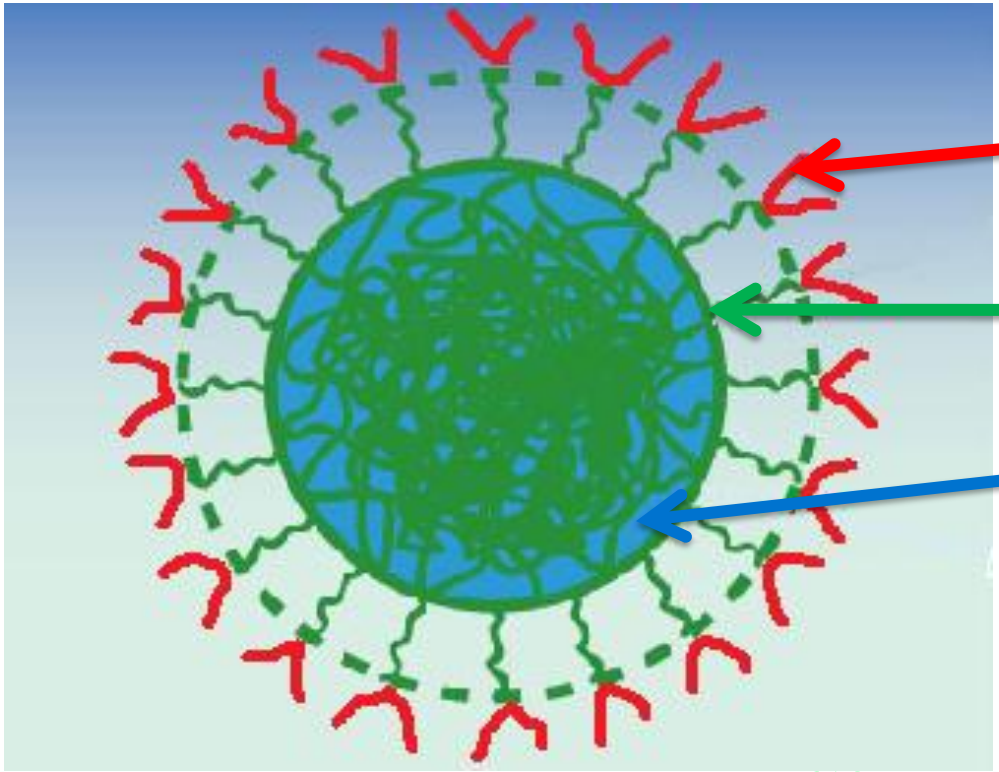
Schematic - Device



Red Lines
Aptamers (~ 6nm)

Green Circle
EcoSphere® (~ 120 nm)

Blue Filling
Drug

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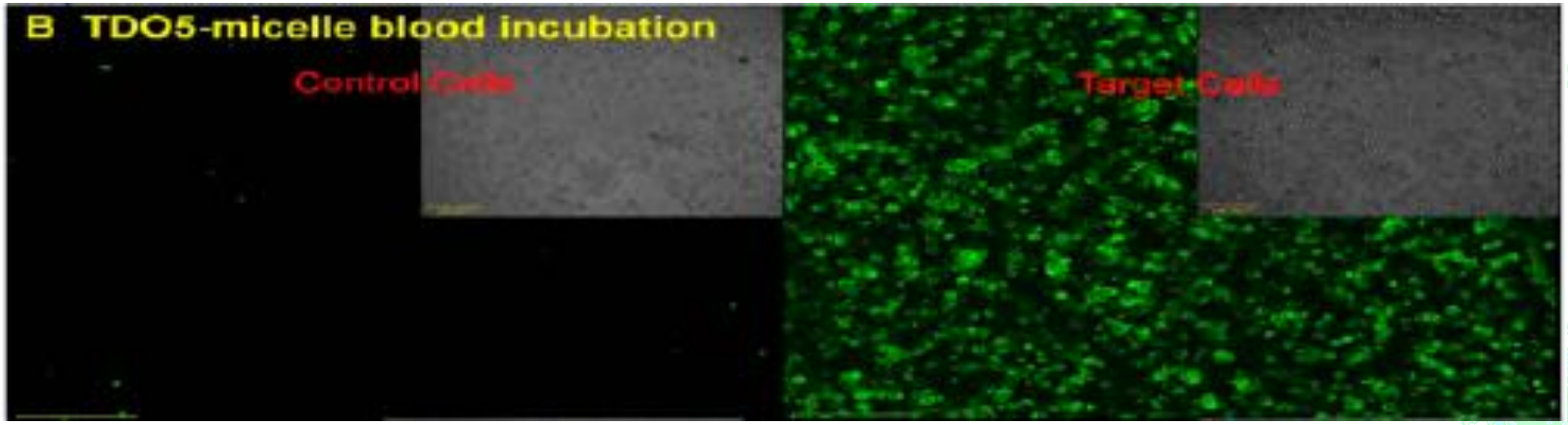
Design Verification

- Cell culture experiments with fluorescence microscopy



Control refers to non-cancer cells
Target refers to cancer cells

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Materials Budget

	Quantity	Price (CAD)	Supplier
Aptamer	1 µg	$151.28	IDT
Doxorubicin	100 mg	$360.00	Selleck Chemicals
Ecosphere	Unspecified	Supplied	EcoSynthetix
TEMPO	25 g	$265.00	Sigma-Aldrich
NaBr	100 g	$50.10	Sigma-Aldrich
NaClO (Store @2-8 C)	250 mL	$40.80	Sigma-Aldrich
HCl (Bioreagent)	300 mL	$76.50	Sigma-Aldrich
EDC	5 g	$151.00	Sigma-Aldrich
NHS	25 g	$53.90	Sigma-Aldrich
MATERIALS SUBTOTAL		**$1148.58**	

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HR & Equipment Budget

	Price (CAD)	Supplier
Human Resources & Intellectual Property		
Consulting with Ecosynthetix	Supplied	EcoSynthetix
(Provisional Patent Filing Costs	$4500	Gowlings)
Equipment		
Fetal Bovine Serum	$310.00	ATCC®
T-ALL cell line	$265.00	ATCC®
Confocal Microscope (5 hours + hour training)	$475	UW Biology
Cell Culture Equipment and Lab Space	Supplied	Consultant
Penicillin G sodium salt (Bioreagent, 100MU)	$120.50	Sigma-Aldrich
HR & Equipment SUBTOTAL (not including patent costs – Industrial Sponsor)	**$1170.50**	

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Budget Overview

	Price (CAD)
MATERIALS SUBTOTAL	$1148.58
HR & Equipment SUBTOTAL	$1170.50
30% Shipping and Handling plus Taxes (not on microscope)	$659.57
30% Contingency Factor (After S&H plus taxes)	$893.60
Total Projected Budget	$3872.25

External Sources of Funding: Industrial Sponsorship, Engage Grant, NSERC Grant

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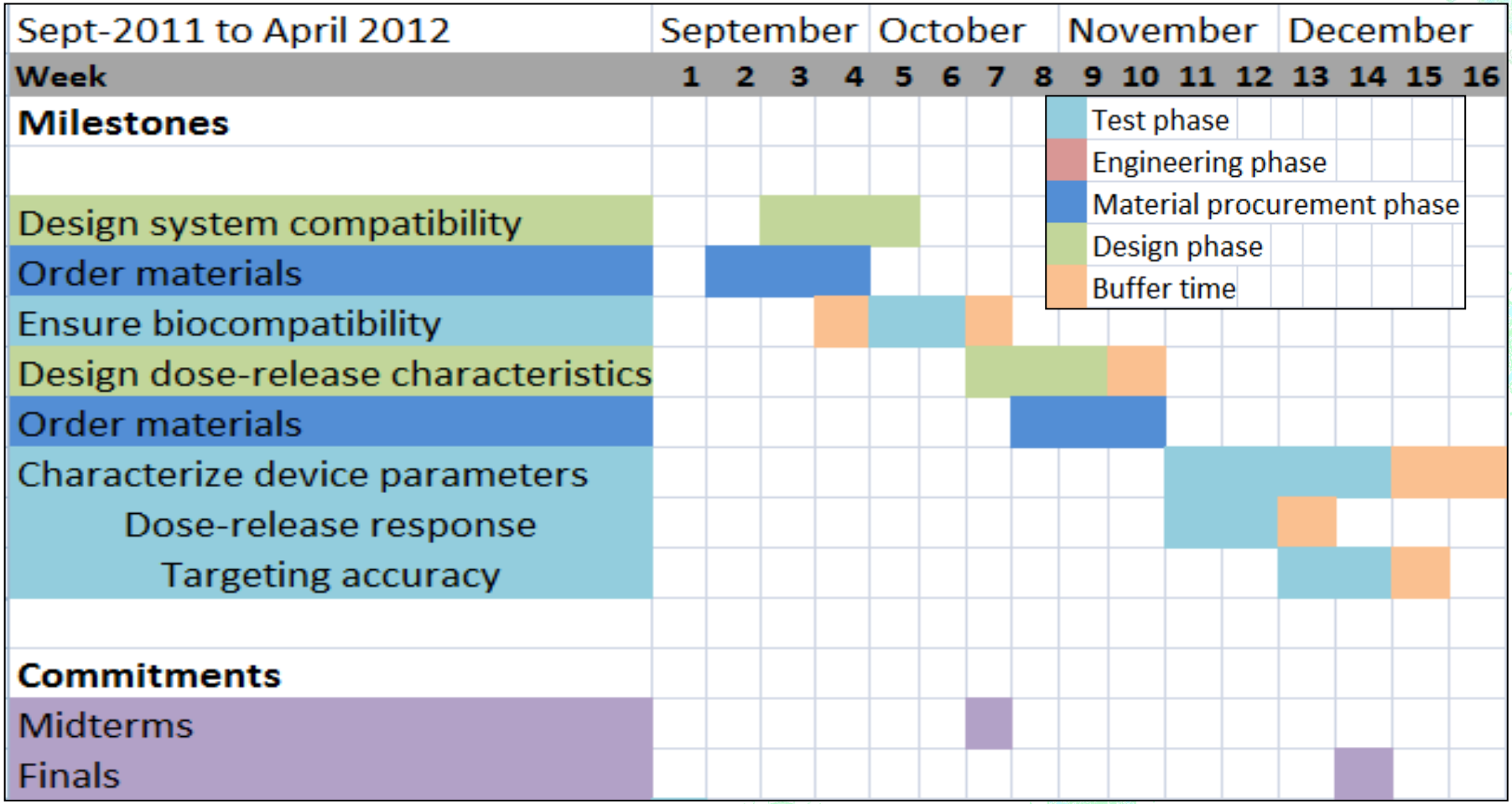
Timeline



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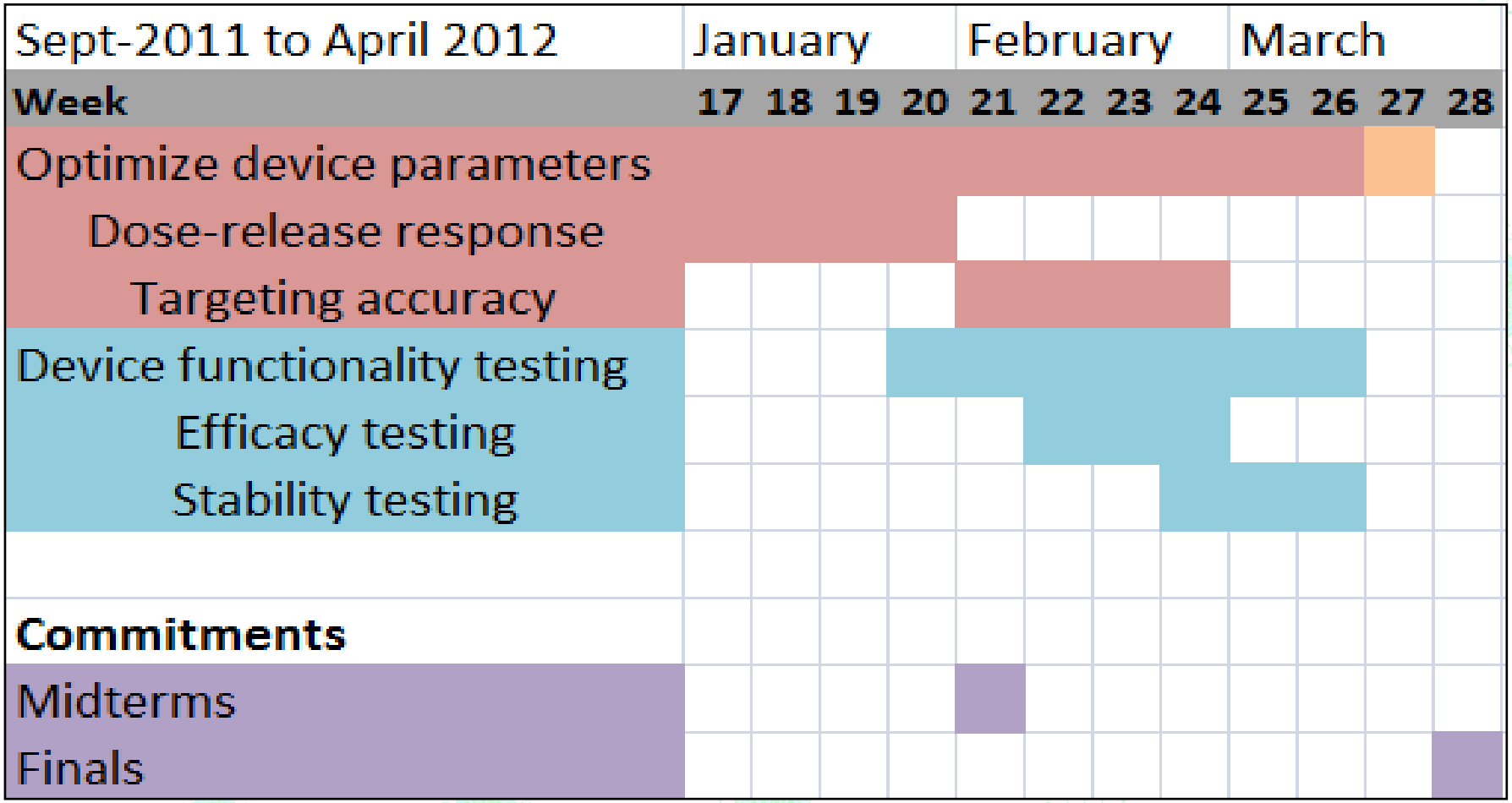

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Sources of Information

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Questions?

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