

# HOW FEASIBLE IS A \$5 MOLECULAR TEST?

Advanced TB Diagnostics, Montreal, June 19, 2018

---

# CHALLENGES TO LOW COST NAT – TWO CHASMS



## DEVELOPMENT TO COMMERCIALIZATION

- Inadequate **business models**
- Poor understanding of clinician, patient & health systems behavior
- Insufficient **evaluation** in settings of intended use

## COMMERCIALIZATION TO ROLL-OUT

- Focus on supply over **demand**
- Weak **planning & budgeting**
- Weak **health systems**
- **User needs** are not fully met

# \$5 NAT - BARRIERS TO DEVELOPMENT



## DEVELOPMENT TO COMMERCIALIZATION

- Inadequate **business models**
- Poor understanding of clinician, patient & health systems behavior
- Insufficient **evaluation** in settings of intended use

## Recurring theme among TB NAT grant applicants

- ❑ Little to no knowledge of intended use setting
- ❑ Technocentric; seldom ask demand stakeholders what the real global health need is
- ❑ Usually do not adopt a comprehensive “end to end” (R&D through launch) strategy
- ❑ Emphasize “back-end” technology for amplification/detection of nucleic acids
  - Usually focus on simple sample types (e.g. swabs, low volume plasma)
- ❑ When asked, “how will you accommodate sputum testing”, the answers ...

# ANSWERS TO “HOW WILL YOU ACCOMMODATE SPUTUM TESTING?”

- ❑ We have great engineers. Don't worry, we'll figure it out
- ❑ Give me a million dollars; trust me

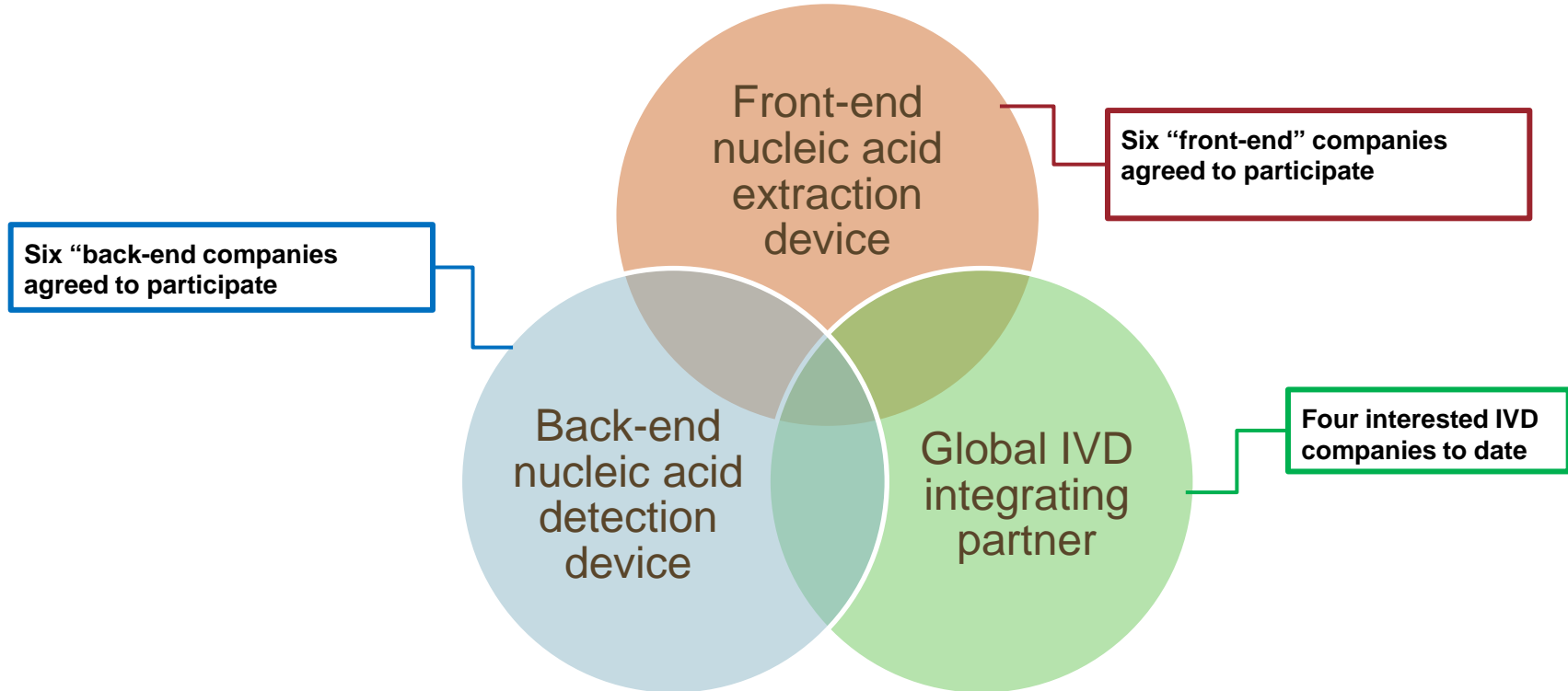
## True story - conversation with a CEO (after hours of discussion)

- ❑ JG: Let me get this straight, even though you have
  - Never engaged demand stakeholders outside of the US, and
  - never worked with sputum, and
  - you don't have any nucleic acid extraction technologies (i.e. a back-end innovator), and
  - you have no TB clinicians advising you on TB Dx,
  - **you want BMGF to fund you to develop a technological approach for nucleic acid extraction from sputum?**
- ❑ **CEO: Yes**

# GETTING TO LOW COST NAT – TRYING TO SOLVE SAMPLE PREP – BMGF (FORMER) PROPOSAL FOR “DREAM TEAMS”

- ❑ The crux of low cost NAT is sample prep; little POC innovation going on for technologies capable of handling sputum; lots of innovation in detecting nucleic acid
- ❑ May 2016 - BMGF invited 40 institutions (big company, small company innovators, academic innovators, regulators, venture funds, global health NGOs, etc.) to solve this
- ❑ BMGF planned to solicit grant applications from consortia; must join forces - no single institution has everything needed
- ❑ Required consortium must have a large company in the grant application for integration into NAT
- ❑ A successful low cost sample extraction technology could become the preferred method for any “back-end” NAT detection method (open business model)
- ❑ **Bottom line – large companies were not interested; BMGF abandoned program**
- ❑ Plan B derisk front-end & back-end tech companies in head-to-head challenge & approach IVD companies interested in commercializing these innovations

# GETTING TO \$5 NAT PLAN B: FRONT-END AND BACK END CHALLENGE GRANTS - THREE “MUST HAVES”



# ASSESSING FRONT- AND BACK-END TECHNOLOGIES

		Before storage		
		<b>Stool</b>		
Panel	Levels	Other ID	Sal (DNA)	MS2 (RNA)
Stool	High Sal/Low MS2	ST1	22.7	34.2
	Neg	ST2	--	--
	High Sal	ST3	23.2	--
	High MS2	ST4	--	16.3
	Low Sal	ST5	32.9	--
	Low MS2	ST6	--	32.1
	Low Sal/ High MS2	ST7	33.0	15.9
	Neg	ST8	--	--
	Med Sal	ST9	27.9	--
	Med MS2	ST10	--	24.2

		Before storage		
		<b>Whole Blood</b>		
Panel	Levels	Other ID	Spn (DNA)	MS2 (RNA)
Blood	High Spn/ Low MS2	BL1	20.9	32.3
	Neg	BL2	--	--
	High Spn	BL3	20.8	--
	High MS2	BL4	--	19.7
	Low Spn	BL5	33.3	--
	Low MS2	BL6	--	33.5
	Low Spn/ High MS2	BL7	33.0	20.7
	Neg	BL8	--	--
	Med Spn	BL9	28.4	--
	Med MS2	BL10	--	24.9

		Before storage		
		<b>Sputum</b>		
Panel	Levels	Other ID	Mtb (DNA)	FluA (RNA)
Sputum	High Mtb/ Low Flu A	SP1	16.8	33.4
	Neg	SP2	--	--
	High Mtb	SP3	17.1	--
	High Flu A	SP4	--	19.6
	Low Mtb	SP5	33.9	--
	Low Flu A	SP6	0.0	32.7
	Low Mtb/ High Flu A	SP7	35.9	19.6
	Neg	SP8	--	--
	Med Mtb	SP9	26.4	--
	Med Flu A	SP10	--	26.5

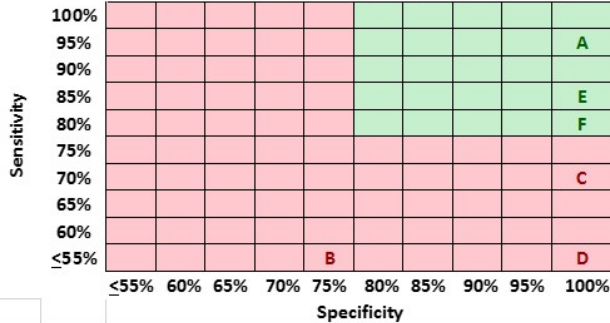
- ❑ Sputum, whole blood, stool spiked (or not) with DNA and/or RNA pathogens
  - M tuberculosis, S typhimurium, S pneumoniae, MS2 phage, Influenza A
- ❑ All samples sent blinded in triplicate
  - Spiked matrices for front-end sample prep; Qiagen extraction as reference method
  - Purified NA from same pathogens (in background human DNA) for back-end amplification/detection
- ❑ CDC/PATH reference method PCR
- ❑ Sensitivity & specificity assessed; technologies ranked; **workflow & COGs assessed as well**

# ASSESSING FRONT- AND BACK-END TECHNOLOGIES

## Phase 1: Front End Sample Prep (2017)

Sputum, Stool, & Whole Blood Spiked with DNA/RNA Pathogens

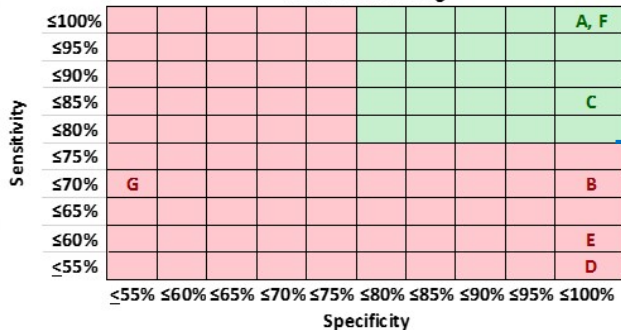
### All Pooled Ranking



## Phase 2: Back End Nucleic Acid Detection (2017)

DNA/RNA Pathogen nucleic acid in human DNA background

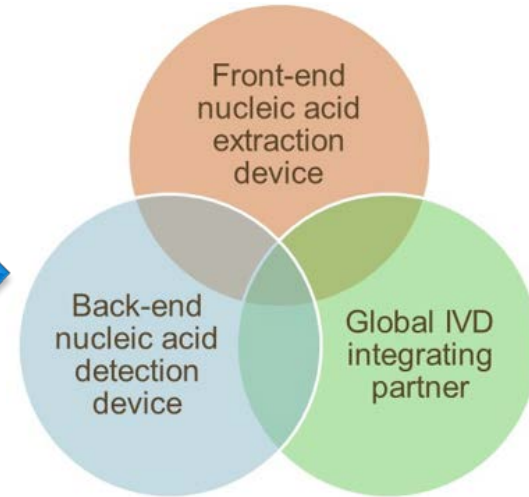
### All Pooled Ranking



2018 – Q1 2019

Best pairs filtered through

- 1) Dx accuracy using frozen & fresh sputum samples
- 2) Workflow potential
- 3) COGs potential (credible to get to \$5 pricing)





## \$5 NAT - BARRIERS TO ROLL OUT – COGS/PRICING



### COMMERCIALIZATION TO ROLL-OUT

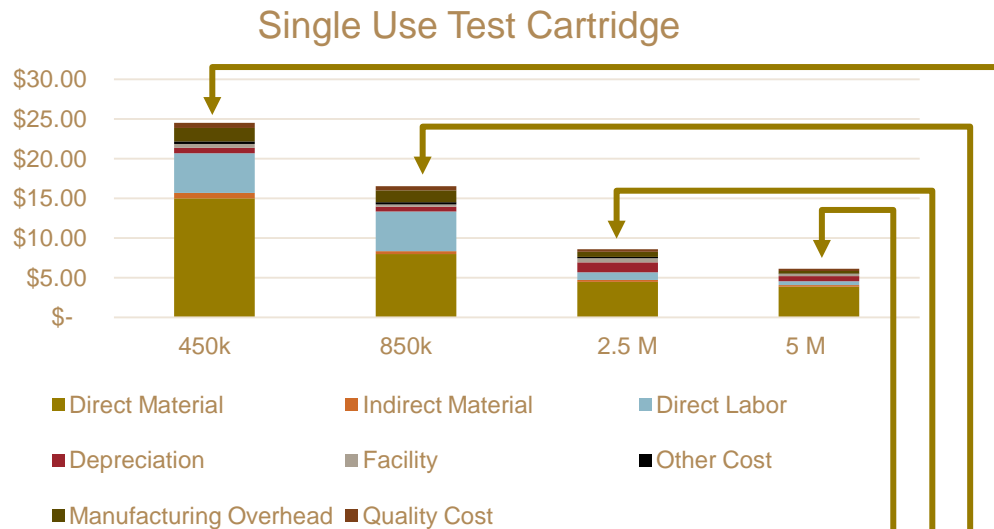
- Focus on supply over demand
- Weak planning & budgeting
- Weak health systems
- User needs are not fully met

Of course I know what a “cog” is!



# \$5 NAT - BARRIERS TO ROLL OUT – COST OF GOODS SOLD (COGS)

	Single Use Disposable Test Cartridge			
Units/Year	450k	850k	2.5 M	5 M
Direct Material	15.00	8.00	4.50	3.90
Indirect Material	0.70	0.37	0.21	0.18
Direct Labor	5.00	5.00	1.00	0.50
Depreciation	0.67	0.59	1.25	0.63
Facility	0.50	0.29	0.53	0.27
Other Cost	0.31	0.29	0.14	0.07
Manufacturing Overhead	1.68	1.48	0.64	0.32
Quality Cost	0.64	0.51	0.34	0.27
<b>Cost per Test</b>	<b>24.50</b>	<b>16.54</b>	<b>8.62</b>	<b>6.14</b>



Guess where you are at launch!

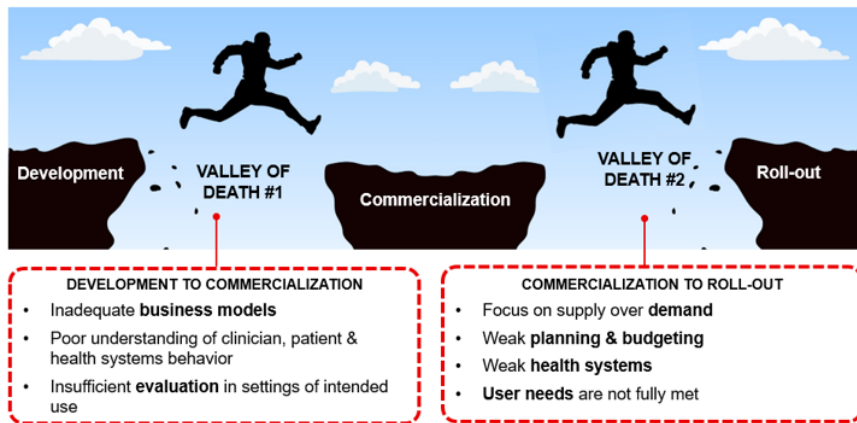
# \$5 NAT - BARRIERS TO ROLL OUT - COGS

## Lessons learned

- ❑ Design for low cost manufacturability of consumable & instrument (if required)
- ❑ Simplify, simplify, simplify...
  - Do you really need 5 enzymes?
  - Can you get by with fewer parts?
- ❑ Develop modular manufacturing schemes to accommodate uncertainty in volume forecasting
- ❑ Automate assembly & QC (100% inspection)
- ❑ **COGs at launch with low volumes preclude low pricing without a financial/market solution (stay tuned for “Do we need a GAVI for diagnostics?” session at 3:30 pm today)**

# GETTING TO \$5 NAT – CROSSING THE TWO CHASMS

Innovators face two “valleys of death” in the product development lifecycle



## 10 key drivers of scale & impact\*

1. Technology: **good**
2. Support from: **product champions, with one lead agency**
3. Global policies: **strong endorsement**
4. Countries: **adopt & include** in their national policies
5. Donors: **supportive** (often requires a global policy)
6. Cost: **affordable** in low-resource settings
7. Strategy: **supply and demand** must be built simultaneously
8. Implementation: **prioritize areas** where they can make a difference
9. Human aspect: **behavioural** and cultural issues are factored in
10. Ecosystem: Tech is part of larger **solution** to patients and systems