



# 多重目標檢測

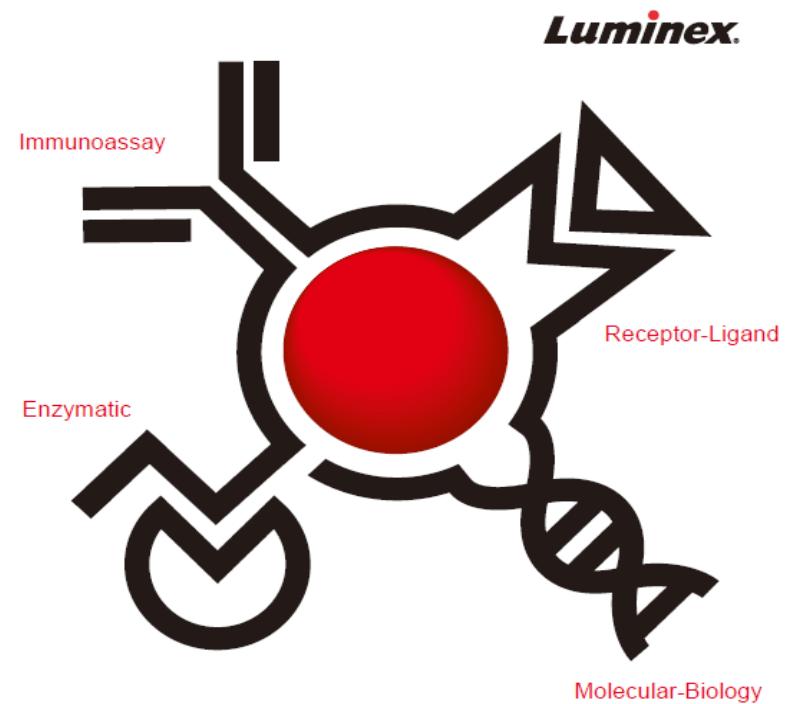
## The Luminex System

聖誠企業有限公司

鄭伊珊

# Outline

- Introduction of Luminex Corporation
- Luminex Technology
- Luminex Instrument
- Luminex Assay



# Quick Facts of Luminex Corporation

- Founded in 1995
- Headquartered in Austin, TX
- Serve both the Life Science Research & Diagnostics Markets
- Over 750 Employees
- Dedicated Sales + Support
- Significant Investment in R&D
- Publicly Traded Company (NASDAQ)

Madison  
Austin

Toronto

Amsterdam

Shanghai

Tokyo

Brisbane

**Luminex**

# Luminex: Customer Focused



## Clinical Diagnostics

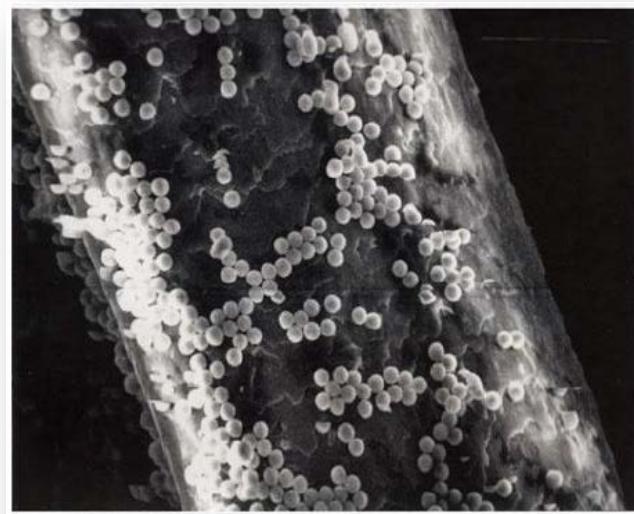
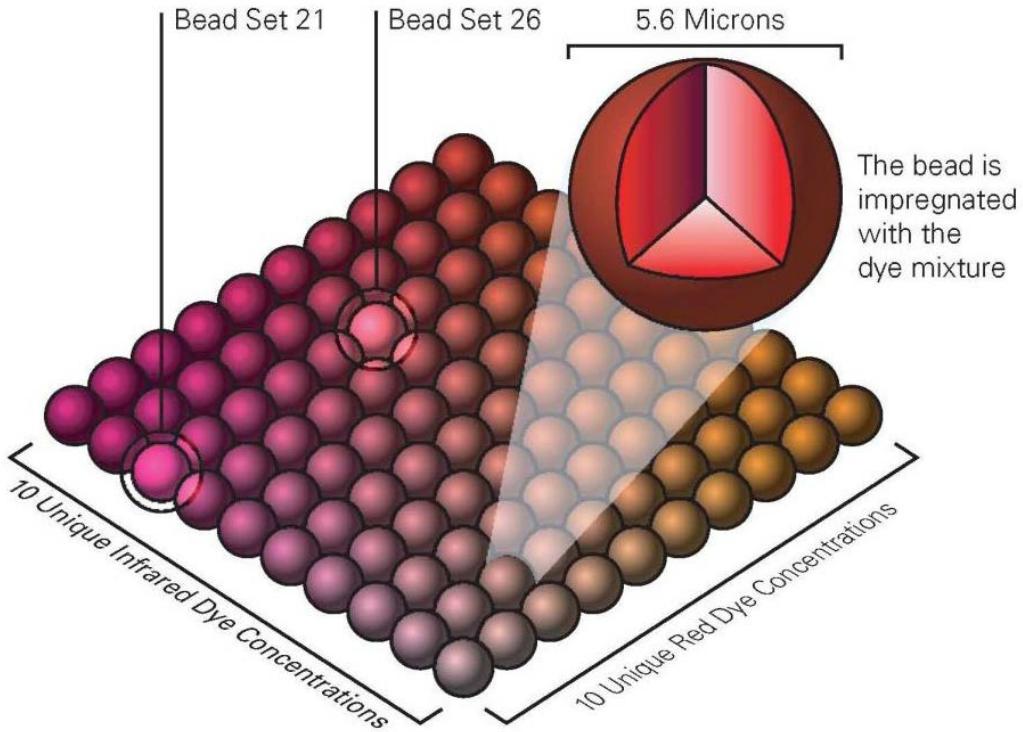
- Human Genetics
- Infectious Disease
- Pharmacogenetics
- Public Health
- Transplant
- Women's Health

# xMAP® Technology

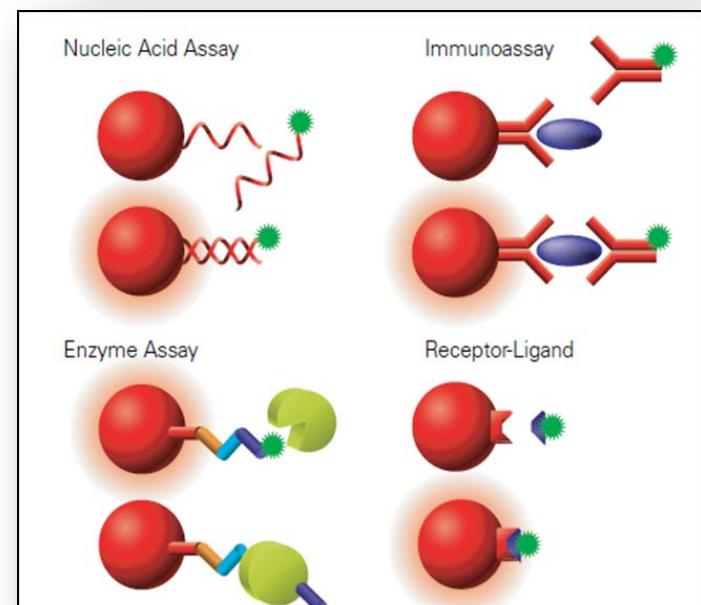
## Multiplexing

xMAP® = (x) Multiple Analyte Profiling

xTAG® = (x) Nucleotide anti-tag sequence T, A, G

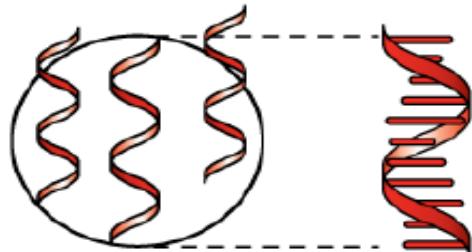


SEM photo of 3.4 micron particles on human hair, 1000x



# xTAG® 快速檢測流程

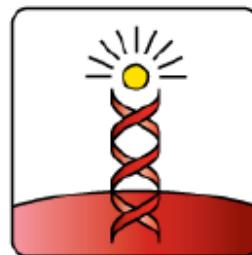
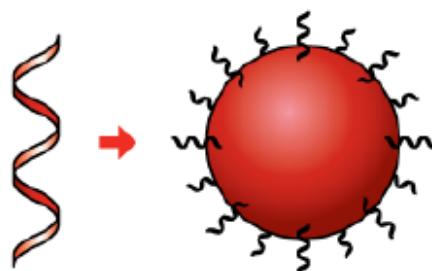
**Step 1:**  
Extraction and Purification



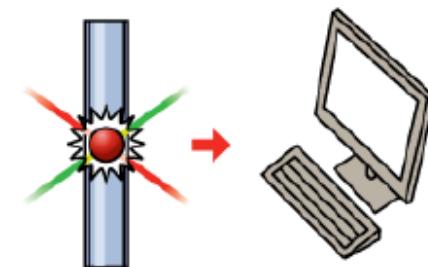
**Step 2:**  
Multiplex Amplification



**Step 3:**  
Bead Hybridization and detection



**Step 4:**  
Data Acquisition/Analysis



# xMAP vs. ELISA

10 proteins  
80 samples

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Number of plates required

Total time to result

Results per plate

Total sample used per panel

Internal controls possible?

Dynamic Range

Lower limit of detection

## xMAP® Technology



3 hours

800

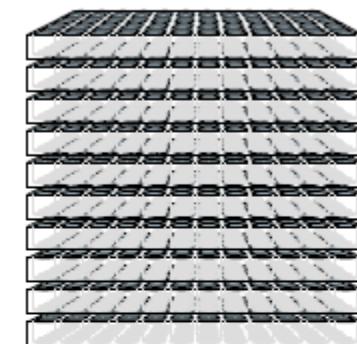
50 µl

YES

1-10,000 pg/ml

~1 pg/ml

## ELISA



10 hours

80

4 ml

NO

10-2500 pg/ml

~1 pg/ml

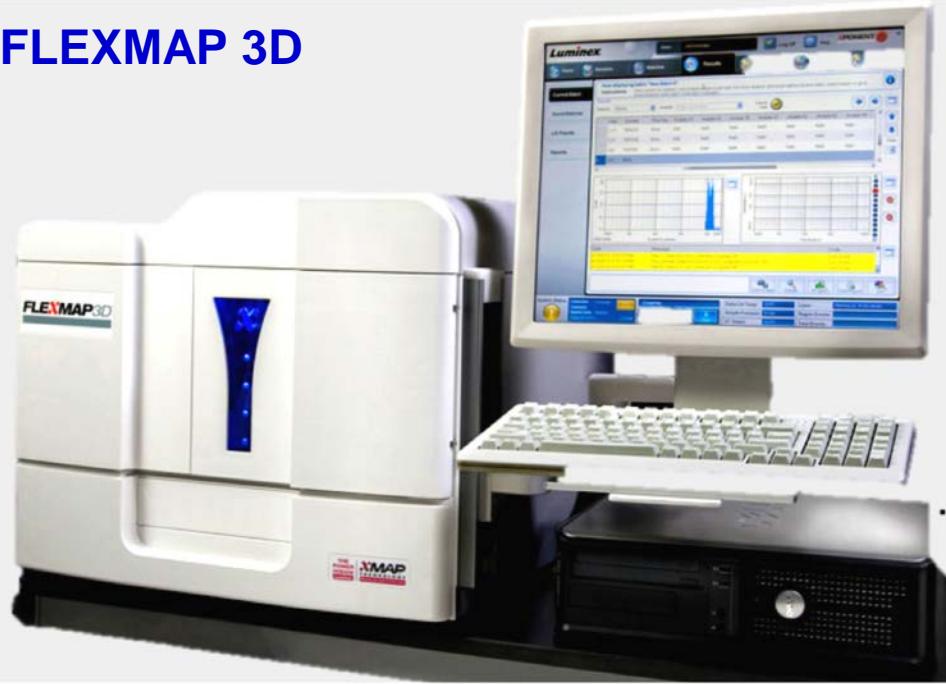
## MAGPIX



## Luminex 200



## FLEXMAP 3D



# The Right Solution for Customer Needs

MULTIPLEXING CAPABILITIES



Project ARIES  
*In development*

<5-Plex



MAGPIX®  
*Launched 2010*

FLEXIBLE PLATFORMS

50-Plex



LX 200™  
*Launched 2005*

100-Plex



FLEXMAP 3D®  
*Launched 2009*

500-Plex

SYSTEM THROUGHPUT

# Luminex Instruments

	MAGPIX®	Luminex® 200™	FLEXMAP 3D®
Software	xPONENT® 4.2	xPONENT® 3.1	xPONENT® 4.0
Optics	LED/CCD Camera	Flow Cytometry	Flow Cytometry
Bead Types	MagPlex® Beads only	All Bead Types	All Bead Types
Plex	50-plex	100-plex (80 MagPlex)	500-plex
Read Time	1 hr/96 wells	~45 min/96 wells	~20 min/96 wells ~75 min/384 wells
LOD Observed	~100 PE/Bead	~100 PE/Bead	~70 PE/Bead
Assay Kits	RVP Fv2, GPP, CYP2C19, CSF, BPP	RVP Fv2, GPP, CYP2C19, CSF, BPP, CYP2D6, SSA	No LUMINEX kit available



# Luminex Assay



## □ Infectious Disease Testing

- Respiratory Pathogens:  
**xTAG RVP Fast v2 (IVD)**
- Gastrointestinal Pathogen:  
**xTAG GPP (IVD)**
- Meningitis pathogens:  
xTAG CSF Viral Panel  
xTAG CSF Bacterial Panel
- Bloodstream Pathogen:  
**xTAG BPP**

## □ Pharmacogenetics

- **xTAG CYP2D6 Kit v3 (IVD)**
- **xTAG CYP2C19 Kit v3 (IVD)**
- **xTAG CYP2C9+VKORC1**

## □ Food Safety

- **xMAP Salmonella Serotyping**





# xTAG® CSF Pathogen Panel

*xTAG® CSF Bacterial Panel*

*xTAG® CSF Viral Panel*

**Luminex**

# xTAG® CSF Bacterial Panel

- Qualitative test
- Detection of DNA from 8 bacterial pathogens and 1 drug-resistance marker

Bacterial Targets	<i>Haemophilus influenzae</i>
	<i>Listeria monocytogenes</i>
	<i>Mycoplasma pneumoniae</i>
	<i>Neisseria meningitidis</i>
	<i>Streptococcus pneumoniae</i>
	<i>Streptococcus agalactiae</i> (Group B Strep)
	<i>Staphylococcus aureus</i>
Antibiotic Resistance Gene	mecA

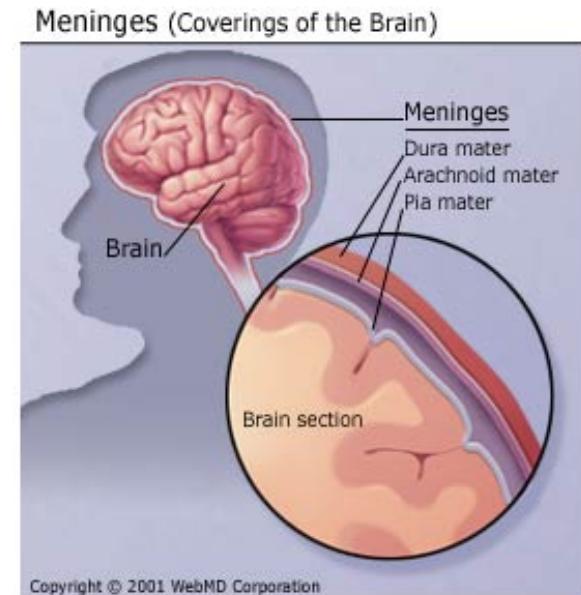
# xTAG® CSF Viral Panel

- Qualitative test
- Detection of nucleic acid from 7 viruses (both RNA and DNA)

<b>Viral Targets</b>	Enterovirus
	Human parechovirus
	Human herpes virus 1 / Herpes simplex virus 1
	Human herpes virus 2 / Herpes simplex virus 2
	Human herpes virus 3 / Varicella zoster virus
	Human herpes virus 4 / Epstein-Barr virus
	Human herpes virus 5 / Cytomegalovirus

# xTAG® CSF Pathogen Panel

- 用於引起腦炎、腦膜炎的細菌及病毒的多重檢測
- 臨床醫生對病毒性感染和細菌性感染進行鑑別診斷
- 採取針對性的治療方案，減少抗生素的濫用





# xTAG® RVP Fast v2

*Respiratory Viral Panel Fast v2*

**Luminex**

IVD

# xTAG®RVP Fast v2

## 18種呼吸道病毒基因檢測試劑

Virus	Subtype
Influenza A	H1
	H3
	2009 H1N1
Influenza B	
Respiratory Syncytial Virus	
Parainfluenza Virus	Parainfluenza 1
	Parainfluenza 2
	Parainfluenza 3
	Parainfluenza 4
Human Metapneumovirus	
Rhinovirus	
Human Bocavirus	
Corona Virus	NL63
	229E
	OC43
	HKU1
Adenovirus	

# 關於呼吸道病毒

- 兒童呼吸道感染裡病毒排名
  - ✓ 1.RSV 60%
  - ✓ 2.流感 30%
  - ✓ 3. PIF 副流感病毒
- RSV：住院病人較多，多為較小的兒童
- 流感：門診病人較多，多為較大的兒童
- PIF 症狀會較嚴重，會與RSV症狀相似
- RSV 培養時間需達21天

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## **Impact of Human Metapneumovirus in Childhood: Comparison With Respiratory Syncytial Virus and Influenza Viruses**

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Samantha Bosis,<sup>1</sup> Susanna Esposito,<sup>1</sup> Hubert G.M. Nieters,<sup>2</sup> Piero Crovari,<sup>3</sup>  
Albert D.M.E. Osterhaus,<sup>2</sup> and Nicola Principi<sup>1\*</sup>

“The households of the hMPV- and the influenza positive children had significantly more illnesses, needed significantly more medical visits.”

J Med Virol. 2005 Jan;75(1):101-4.

## RATE AND INFLUENCE OF RESPIRATORY VIRUS CO-INFECTION ON PANDEMIC (H1N1) INFLUENZA DISEASE

Frank P. Esper, M.D.<sup>1,2</sup>, Timothy Spahlinger<sup>3</sup>, and Lan Zhou, M.D., Ph.D.<sup>3</sup>

“Many patients with influenza have more than one viral agent with co-infection frequencies reported as high as 20%.”

J Infect. 2011 Oct;63(4):260-6.

“The frequency of respiratory virus co-infections varies widely in the literature but is often reported between 10–20% and in one report as high as 60% .”

J Infect. 2011 Oct;63(4):260-6.

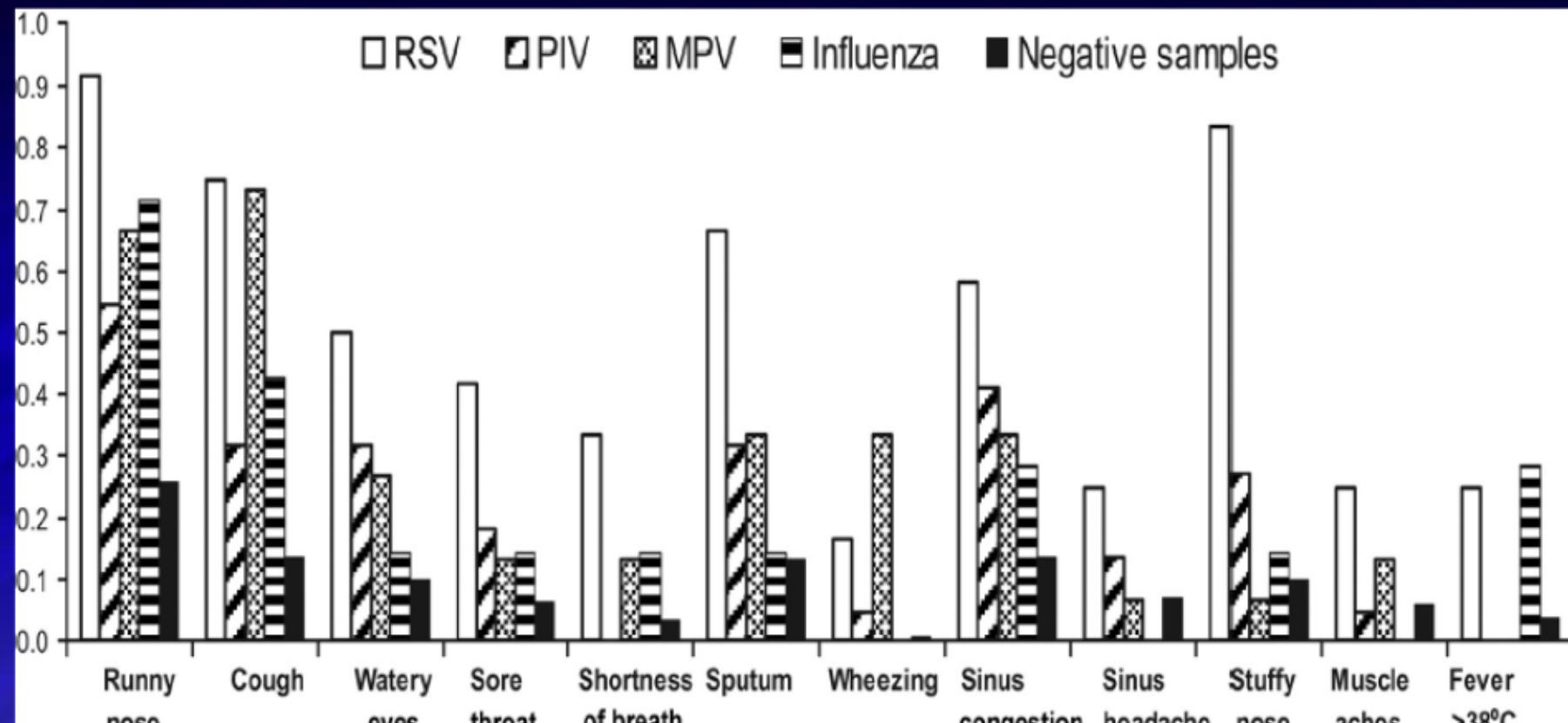
## Single Versus Dual Respiratory Virus Infections in Hospitalized Infants: Impact on Clinical Course of Disease and Interferon- $\gamma$ Response

Aberle, Judith H. MD\*; Aberle, Stephan W. MD\*; Pracher, Elisabeth MD‡; Hutter, Hans-Peter MD†; Kundi, Michael MD†; Popow-Kraupp, Therese MD\*

“Dual infections with rhinovirus and RSV was associated with a more severe clinical course than other co-infection combinations.”

Pediatr Infect Dis J. 2005 Jul; 24(7):605–610.

# Same syndromes, different causes

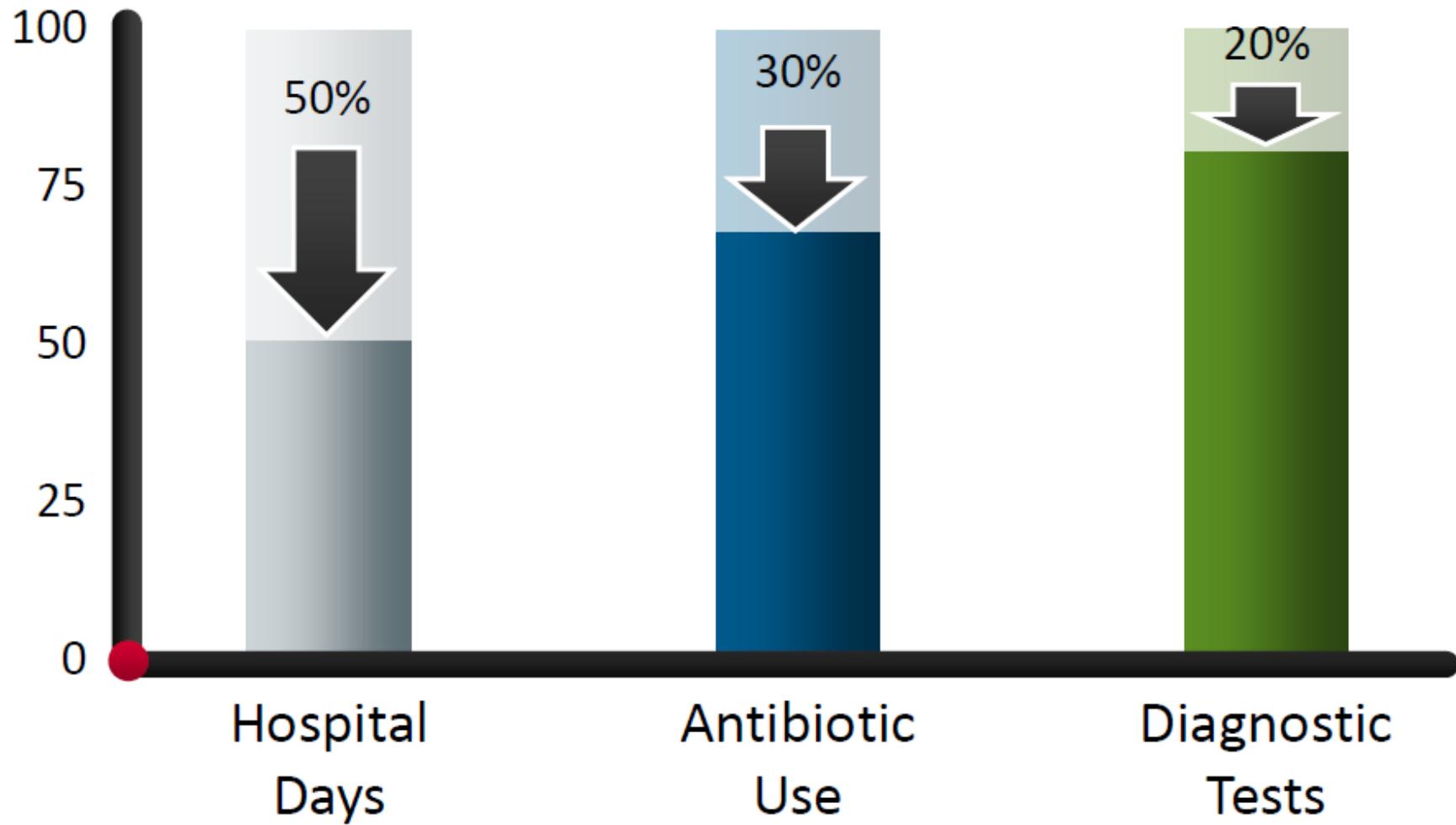


Diagnostic uncertainty due to overlapping clinical presentations requires laboratory diagnosis!

# 為什麼選擇Luminex RVP Fast v2

- 臨床敏感性總體超過92%，特異性超過97%
- 同時檢測18種呼吸道病毒及亞型
  - 提高臨床陽性檢出率
  - 覆蓋多數流行的呼吸道病毒，包括2009H1N1
  - 可測合併感染(co-infection)
  - 廣泛的檢測有助於識別病原體
- 速度快(~5 hr,含萃取)、高通量(同時檢測96 tests)
- 臨床意義：
  - 提供適當的診斷工具，高效並針對性地治療患者
  - 減少不必要的抗生素，降低抗藥菌株的出現

# After using Luminex RVP Fast v2...





# xTAG® GPP

*Gastrointestinal Pathogen Panel*

**Luminex**

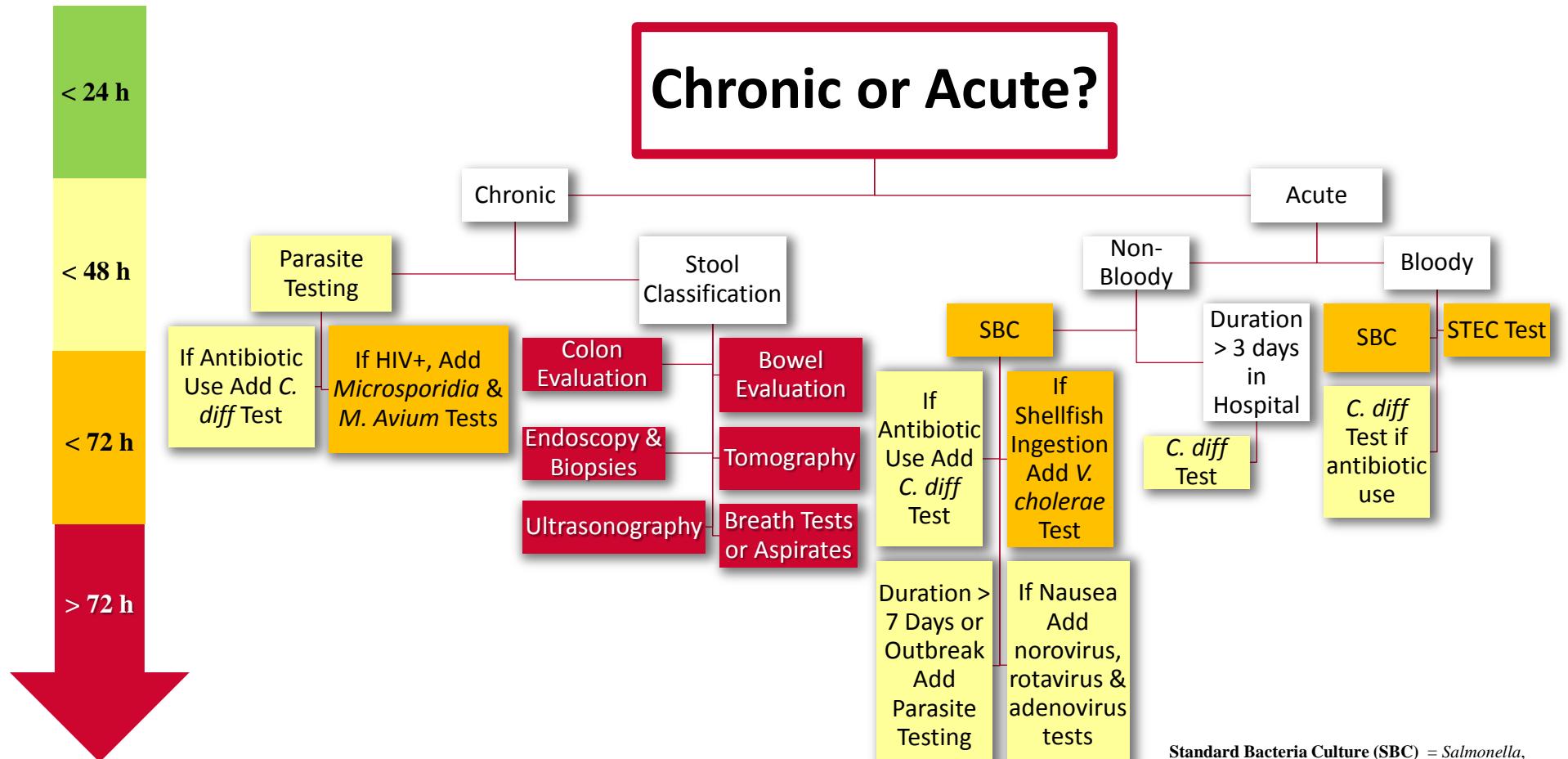
IVD

# 腹瀉的危害

- WHO統計每年約有20億腹瀉病患，**180萬人**死亡
- 腹瀉是5歲以下兒童第二大致死原因及導致營養不良的第一大原因
- 嚴重腹瀉可導致脫水，可能危及生命
  - ✓ 幼兒
  - ✓ 老人
  - ✓ 營養不良的人
  - ✓ 免疫受損的人



# DIAGNOSTIC ALGORITHM

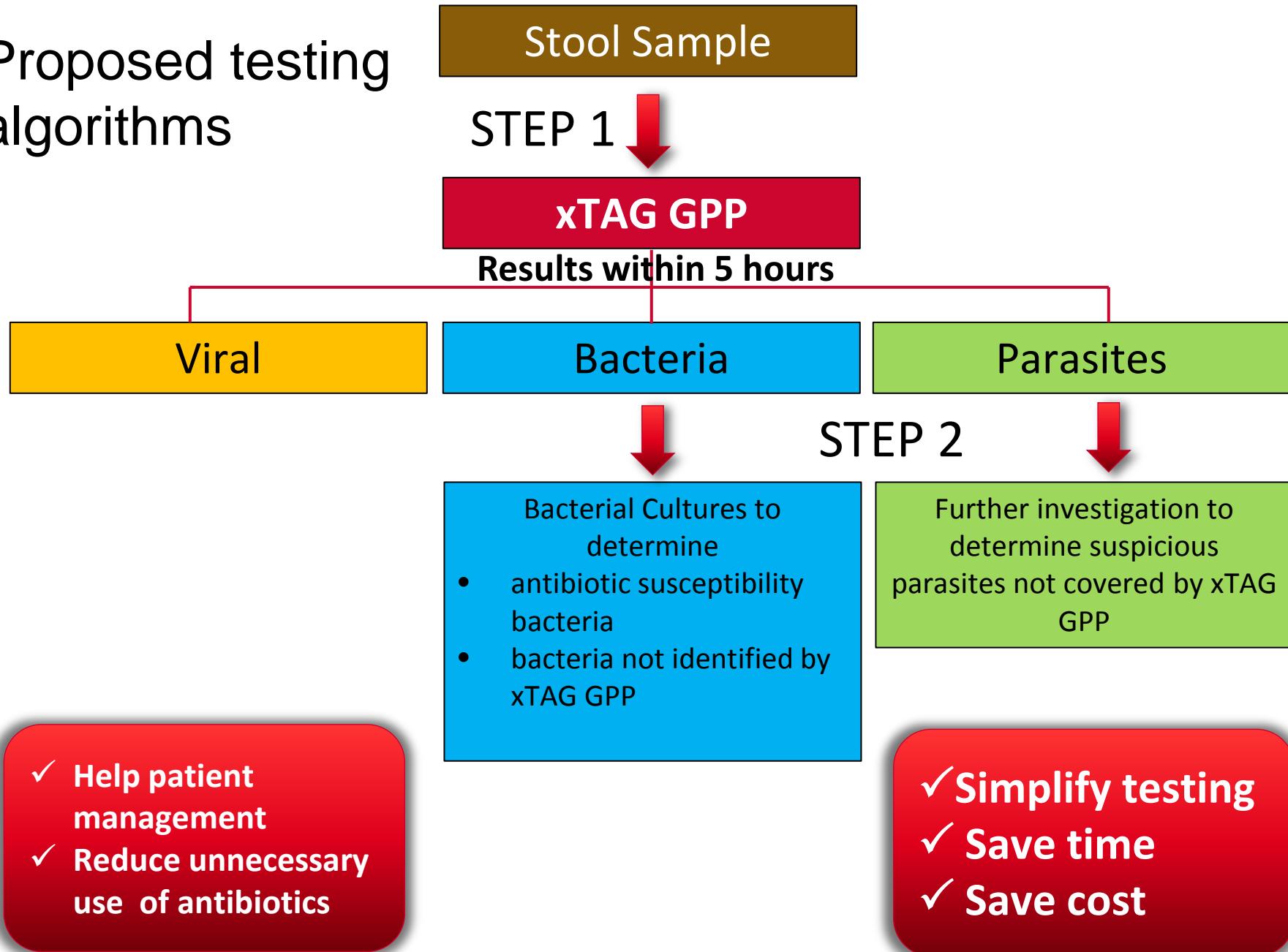


Evaluating the patient with diarrhea: a case-based approach. Swester, S. Mayo Clin Proc. Jun;87(6):596-602  
 Practice Guidelines for the Management of Infectious Diarrhea. Pickering et al. Clin Infect Dis. 2001 Feb 1;32(3):331-51  
 Infectious diarrhea: when to test and when to treat. Farina, D. Hatchette, T. CMAJ, 183(3) 339-344. 2011.

# The evolution of GI diagnosis



# Proposed testing algorithms



## 15種腹瀉病原體基因檢測試劑

- 腸道病原體檢測(bacteria, virus, parasite)共15種 (~5hr)
- xTAG GPP Test for...

Viruses (3)	Bacteria and bacterial toxins (9)
Adenovirus 40/41	<i>Salmonella</i>
Rotavirus A	<i>Shigella</i>
Norovirus GI/GII	<i>Campylobacter</i>
	<i>Escherichia coli</i> O157
Parasites (3)	<i>Yersinia enterocolitica</i>
<i>Giardia lamblia</i>	<i>Vibrio cholerae</i>
<i>Cryptosporidium</i>	<i>Clostridium difficile</i> toxin A/B
<i>Entamoeba histolytica</i>	Enterotoxigenic <i>E. coli</i> (ETEC) LT/ST
	Shiga-like Toxin producing <i>E. coli</i> (STEC) stx 1/stx 2

# 為什麼選擇Luminex GPP

- 一天內可同時檢測15種細菌及毒素、病毒和寄生蟲等腹瀉病原體
- 一次檢測可覆蓋 > 90% 腹瀉病原體
- 可測合併感染(co-infection)
- 臨床意義：
  - ✓ 提高腹瀉病原體的診斷能力，便於病人管理
  - ✓ 可根據病因合理進行治療，減少抗生素的使用
  - ✓ 快速對患者進行正確的初始治療，以獲得更好的治療結果，尤其針對兒童、老年人和免疫功能低下的患者
  - ✓ 降低醫療費用，減少住院時間

# 腹瀉檢測方法比較

方法	檢測	時間	備註
培養	單種細菌或病毒	2-3天	<i>Campylobacter spp.</i> 培養困難，病毒及寄生蟲不常用此方法檢測
鏡檢	寄生蟲	>3天	主觀性強，經驗要求高，陽性率低
EIA(快篩) ELISA	每次檢測單種病原體	20-30分鐘 2-3小時	主要用於 <i>Rotavirus A</i>
Real-time PCR	每次檢測1-3種病原體	3-5小時	In-house method， 缺乏標準及驗證
xTAG GPP	單管同時檢測15種病原體	5小時	IVD試劑

## **Microbiological Diagnosis of Severe Diarrhea in Kidney Transplant Recipients by Use of Multiplex PCR Assays**

Coste JF, Vuillet V, Moustapha B, et al.

“Significantly improved the detection of single and multiple enteric infections by comparison to classical techniques and could quickly become the key element in the management of severe acute diarrhea in transplant recipients.”

## **Rapid screening method for multiple gastroenteric pathogens also detects novel enterohemorrhagic Escherichia coli O104:H4**

Malecki M, Schildgen V, Kamm M, Mattner F, Schildgen O.

“Useful to prescreen patients suffering from the new EHEC strain.”

“Patients can be monitored more closely by the clinicians and test results associated to the clinical course of hemolytic-uremic syndrome.”

## **Molecular revolution entering GI diagnostic testing**

Dunbar SA.

“Due to the multiplexing capabilities and short turnaround time, these new molecular methods have the potential to revolutionize patient diagnosis and treatment for diarrheal disease.”

“Using a single comprehensive molecular assay aids laboratories and physicians in screening out both suspected, and more importantly, unsuspected causes of diarrhea to get ahead of potential outbreak scenarios. “

## Gastroenteritis and 'doing more with less.'

McEwan R.

“Negative results have a predictive value >99%, allowing for rapid and accurate sorting of infectious and non-infectious cases and critically reducing the need for expensive infection control measures.”

“A new economic study estimated that the test could reduce the costs of managing these patients by as much as 45%.”

# GPP經典案例

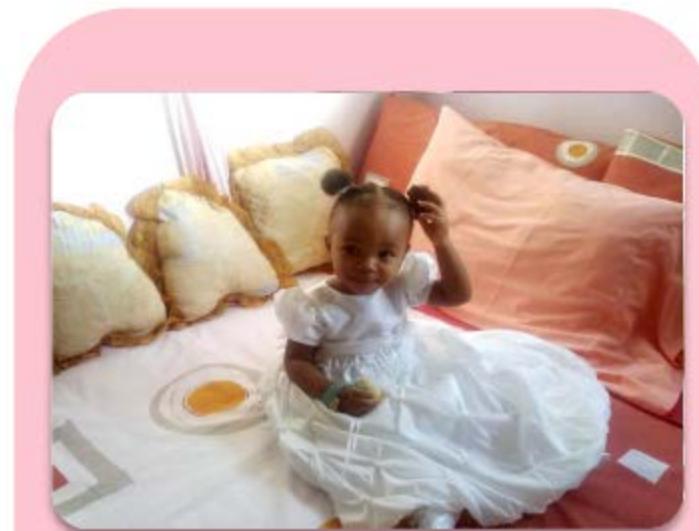
- Haitian (海地) , 新生兒 , 4周 , 嚴重腹瀉 , 體重下降
- 實驗室培養 : *Salmonella* spp., *E. coli*, *Vibrio cholerae* 均為陰性
- 懷疑水受污染 , 服用Amoxicillin , 預計幾天內會好轉
- 2個月後未見好轉。在兩家不同的實驗室檢測 , 依然陰性
- ‘致病原因持續成謎 .....’



# GPP經典案例

- 3個月後，情況加重，GHESKIO實驗室建議用xTAG® GPP檢測
- 幾個小時後，*C. difficile*陽性，此菌在Haitian(尤其是兒童)並不常見
- 由於懷疑結果，該醫生重新檢測，結果相同。改採 Metronidazole治療
- 一周內嘔吐和腹瀉停止，狀況好轉

**“for me, the Luminex test saved the life of my baby”.**



*Baby Liz Angel Abraham today  
at home in Haiti (11 months)*

# Multiplexing—流程優化

多個實驗方法

(*Microbiology, Virology,  
Molecular*)

多種方法

(*culture, EIA, microscopy, PCR*)

時間長短不一

*Results trickle in across 1-4 days*

OR

xTAG® GPP

1 次檢測15種病原體  
5個小時

提高效率、節  
省時間及人力

# Thank you!

