

# USING LABORATORY FOLATE STATUS ASSESSMENT TO STRENGTHEN NTD PREVENTION

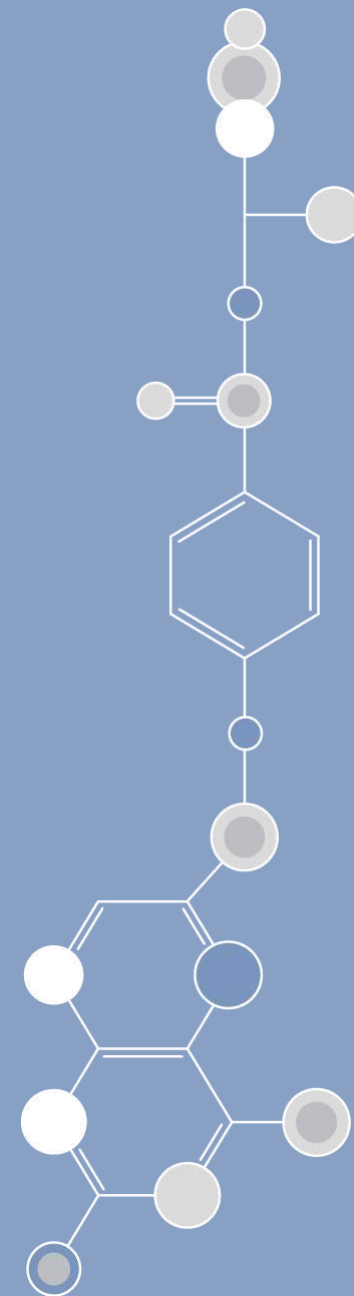
## INTERACTIVE WEBINAR

Join us on March 4th at 9 a.m. EST to learn about a regional laboratory training approach to improve folate status assessment to advance neural tube defect (NTD) prevention

**MARCH 4<sup>th</sup>** 2019 / **CLICK HERE TO REGISTER**  
<http://bit.ly/FolateTaskTeamWebinarMar4>  
**09:00AM – 10:30AM EST**



HOSTED BY THE  
**FOLATE TASK TEAM**



# The Folate Task Team



**Homero Martinez**  
MD, PhD  
Senior Technical Advisor  
Nutrition International

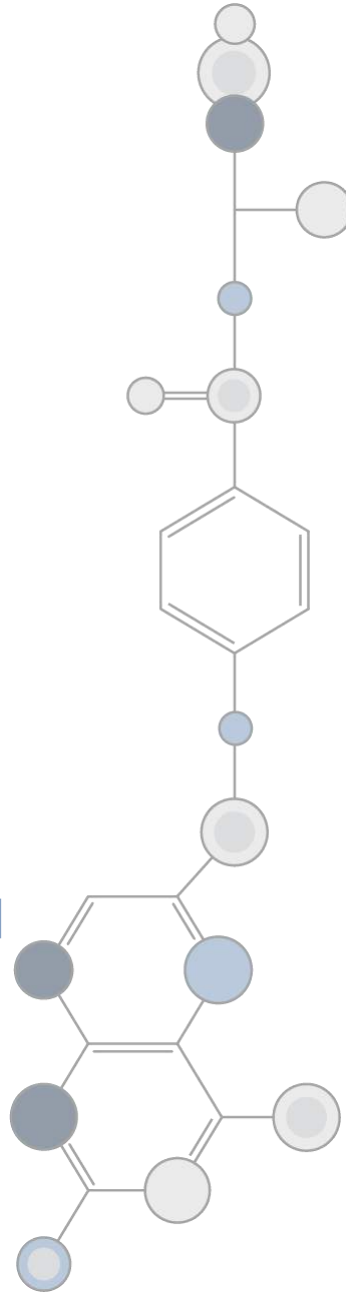


**Jessica Poulin**  
MSc  
Knowledge Translation Officer  
Nutrition International



**Alik Pappas Weakland**  
MPH, MSW  
Project Consultant  
Core Engagement

**FOLATE TASK** TEAM



# List of Speakers

Homero Martinez *MD, PhD*

*Senior Technical Advisor Nutrition International*

Christine Pfeiffer *BS, MS, PhD*

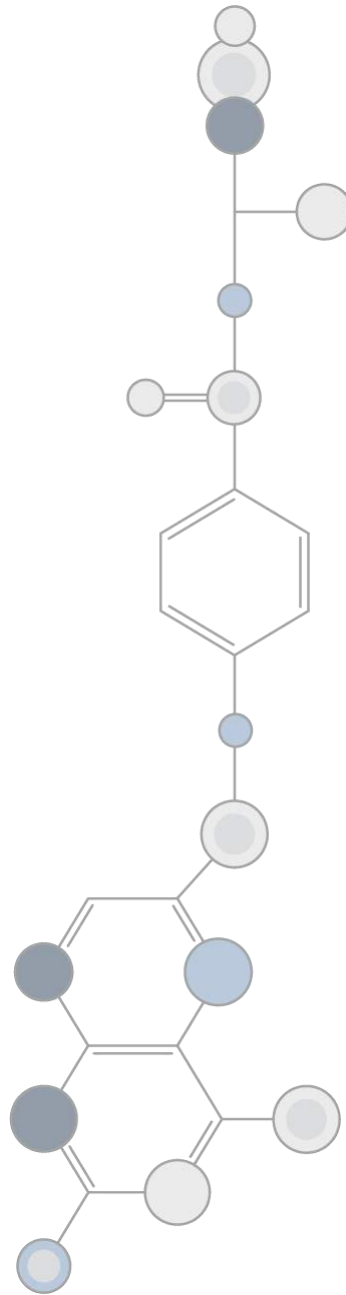
*Chief, Nutritional Biomarkers Branch, Division of  
Laboratory Sciences, CDC National Center for  
Environmental Health*

Renuka Jayatissa *MBBS, MSc, MD*

*Department Head, Nutrition Medical Research Institute, Sri  
Lanka*

Kehkashan Begum *MSc, Manager, Nutrition Research  
Laboratory, Karachi, Pakistan*

**FOLATE TASK TEAM**





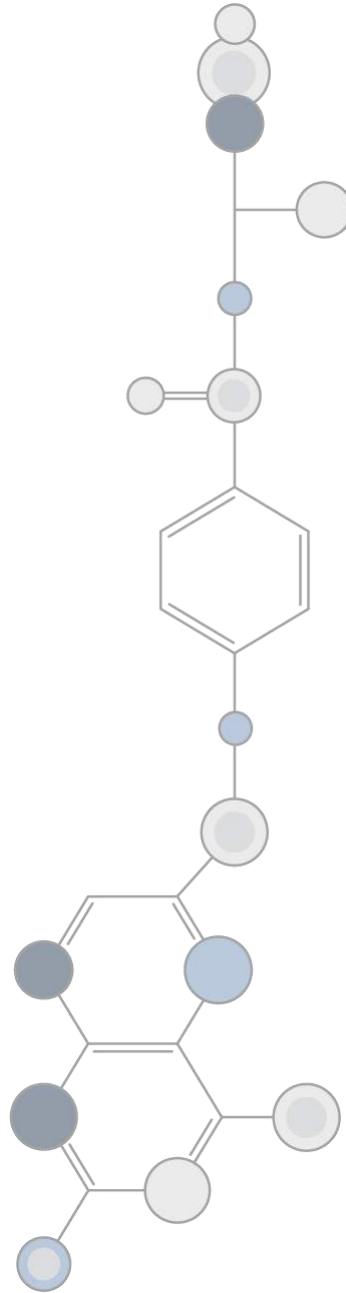
# Dr. Homero Martinez

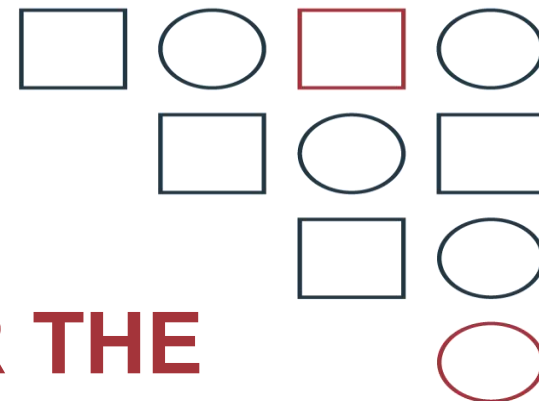
MD, PhD



Senior Technical Advisor  
Nutrition International

**FOLATE TASK** TEAM





**SUPPORTING A GLOBAL STRATEGY FOR THE  
CONTROL OF FOLATE DEFICIENCY AND FOLIC  
ACID RESPONSIVE NEURAL TUBE DEFECTS  
(ANENCEPHALY AND SPINA BIFIDA)**

**A grant by the  
Bill & Melinda Gates Foundation  
to Nutrition International**

# Background

- In 2016/2017, the Micronutrient Forum convened at NI a technical consultation on Folate Status in Women and NTD prevention.
- Main objectives of the consultation were:
  - ✓ To develop a roadmap for low- and middle-income countries to better inform and prioritize investments in NTD risk-reduction
  - ✓ To help guide implementation efforts in terms of feasibility of interventions and the potential for acceleration
  - ✓ To identify the knowledge gaps that remain including addressing any questions on safety and efficacy of folic acid interventions

# Two original contributions relevant for this work

- ✓ Rogers L, A.M. Cordero, C.M. Pfeiffer, D.G. Hausman, B.L. Tsang, L.M. De-Regil, et al. **Global folate status in women of reproductive age: a systematic review with emphasis on methodological issues.** Ann NY Acad Sci. 2018;1431(1):35-57.
- ✓ Pfeiffer CM, M. Zhang, S. Jabbar. **Framework for laboratory harmonization of folate measurements in low- and middle-income countries and regions.** Ann NY Acad Sci. 2018: 1414(1);96-108.

# Main challenges to address

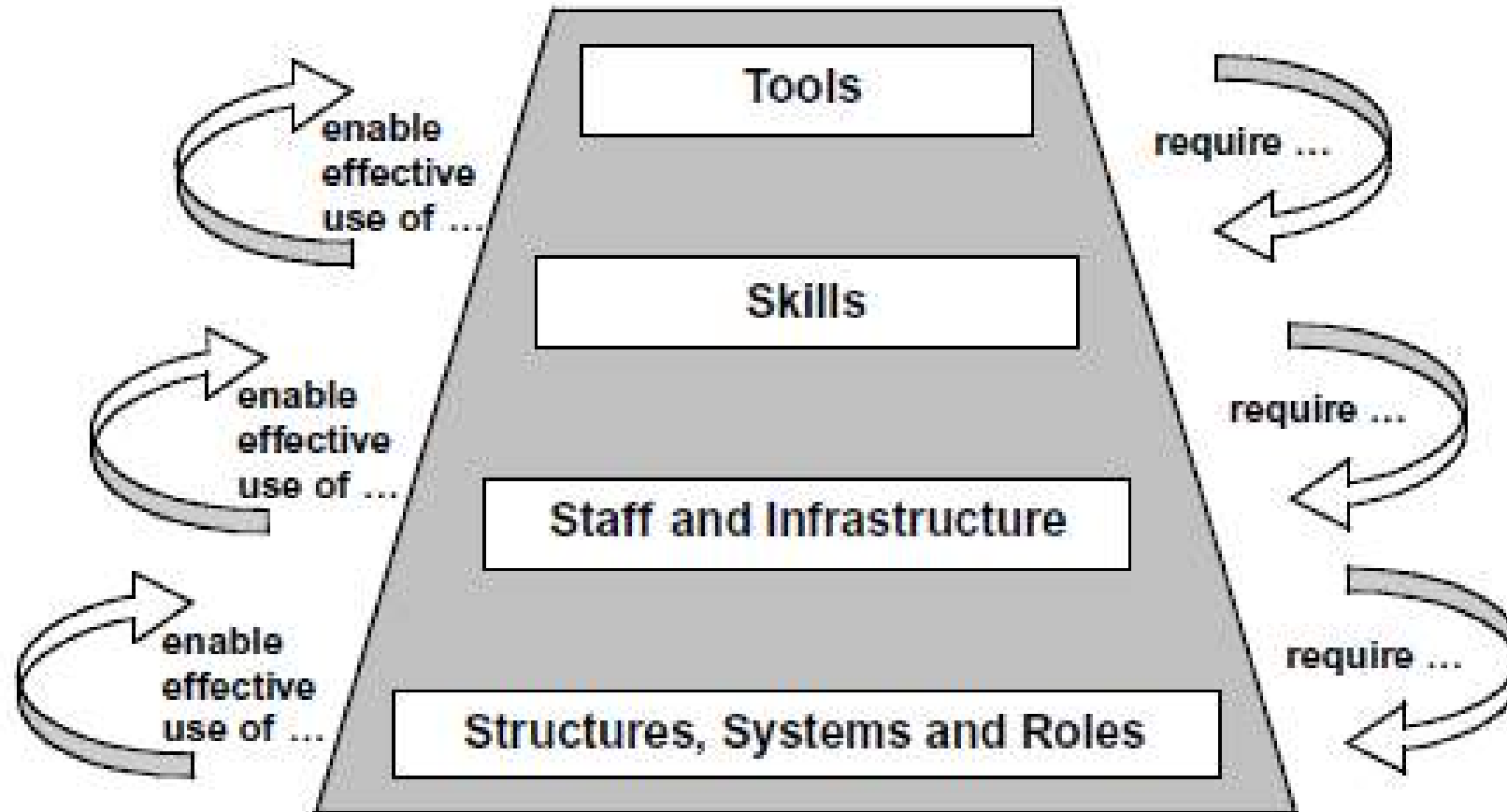
- ✓ Improving the folate status of women of reproductive age (WRA) before they are pregnant can help prevent the majority of folate-responsive NTDs
- ✓ However, several challenges remain, including:
  - Limited information on folate status in WRA, using a harmonized microbiological assay to measure red blood cell folate
  - Limited use and availability of laboratories properly trained in the recommended method to assess folate status



# To address and overcome these challenges, Nutrition International proposed to:

- Build capacity in selected LMIC to assess folate status, with a view to establish a future global network of regional laboratories
  - In collaboration with CDC-DLS, the project seeks to:
    - ✓ Identify 5 regional labs to send 2 trainees each to CDC-DLS
    - ✓ Provide these labs with equipment/reagents to conduct MBA to determine RBC folate
    - ✓ Produce a training video to shorten training time and provide long-lasting support
    - ✓ Set the basis for a future global network of regional lab

# A systemic capacity building approach



# Dr. Christine Pfeiffer

BS, MS, PhD

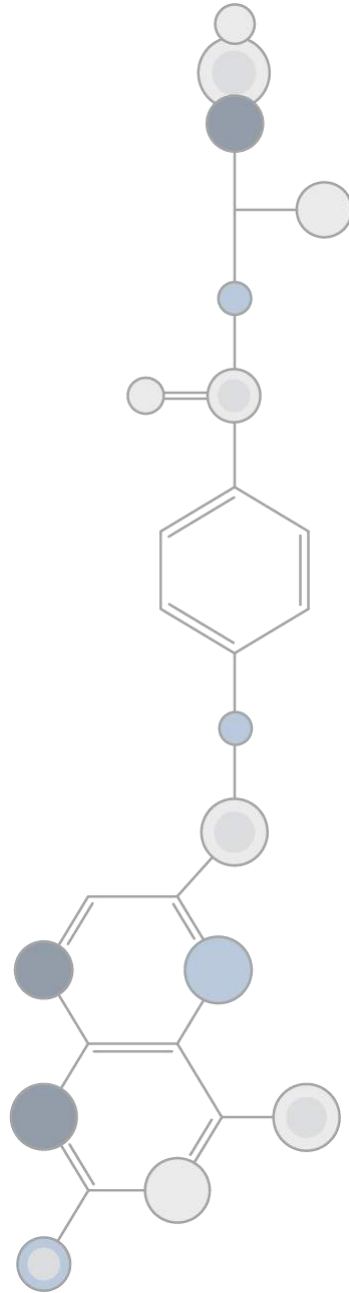


Chief, Nutritional Biomarkers Branch

Division of Laboratory Sciences

CDC National Center for Environmental Health

**FOLATE TASK** TEAM



# Using Laboratory Folate Status Assessment to Strengthen Neural Tube Defect Prevention: A Regional Training Approach

**Christine M Pfeiffer, PhD**

Chief, Nutritional Biomarkers Branch

## **Disclosure**

**Funding for this project has been provided by the Bill  
& Melinda Gates Foundation and Nutrition  
International, Canada to the CDC Foundation**

# Outline

- ❑ Why the folate microbiologic assay?
- ❑ Why a regional approach?
- ❑ Components of successful capacity building
- ❑ Project goal and objectives
- ❑ Training approach
- ❑ Laboratory engagement
- ❑ Progress
- ❑ Way forward

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES

Special Issue: *Folate Status in Women and Neural Tube Defect Risk Reduction*  
REVIEW

**Framework for laboratory harmonization of folate  
measurements in low- and middle-income countries  
and regions**

Christine M. Pfeiffer, Mindy Zhang, and Shameem Jabbar



## Good folate status is needed during periods of growth and development



## **Folate lab measurements face multiple analytical challenges**

### **Compound related**

**Several folate derivatives**

**Susceptibility to oxidation, decomposition, and interconversions**

**Folate derivatives have different affinities to folate binding protein**

**Low serum folate levels in serum and blood**

**Deconjugation of folate polyglutamates in RBCs**

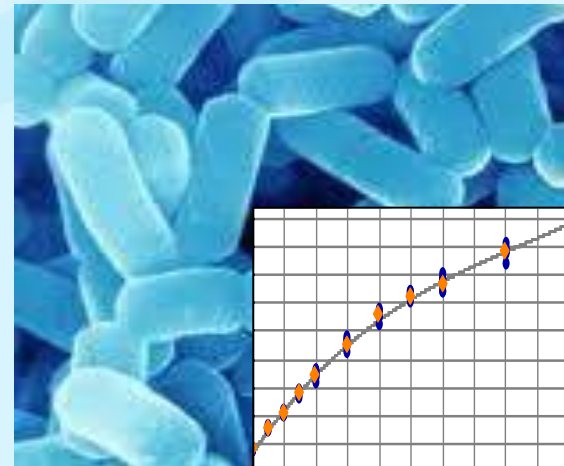
### **Sample collection related**

**Need well-controlled collection, processing, and storage conditions**

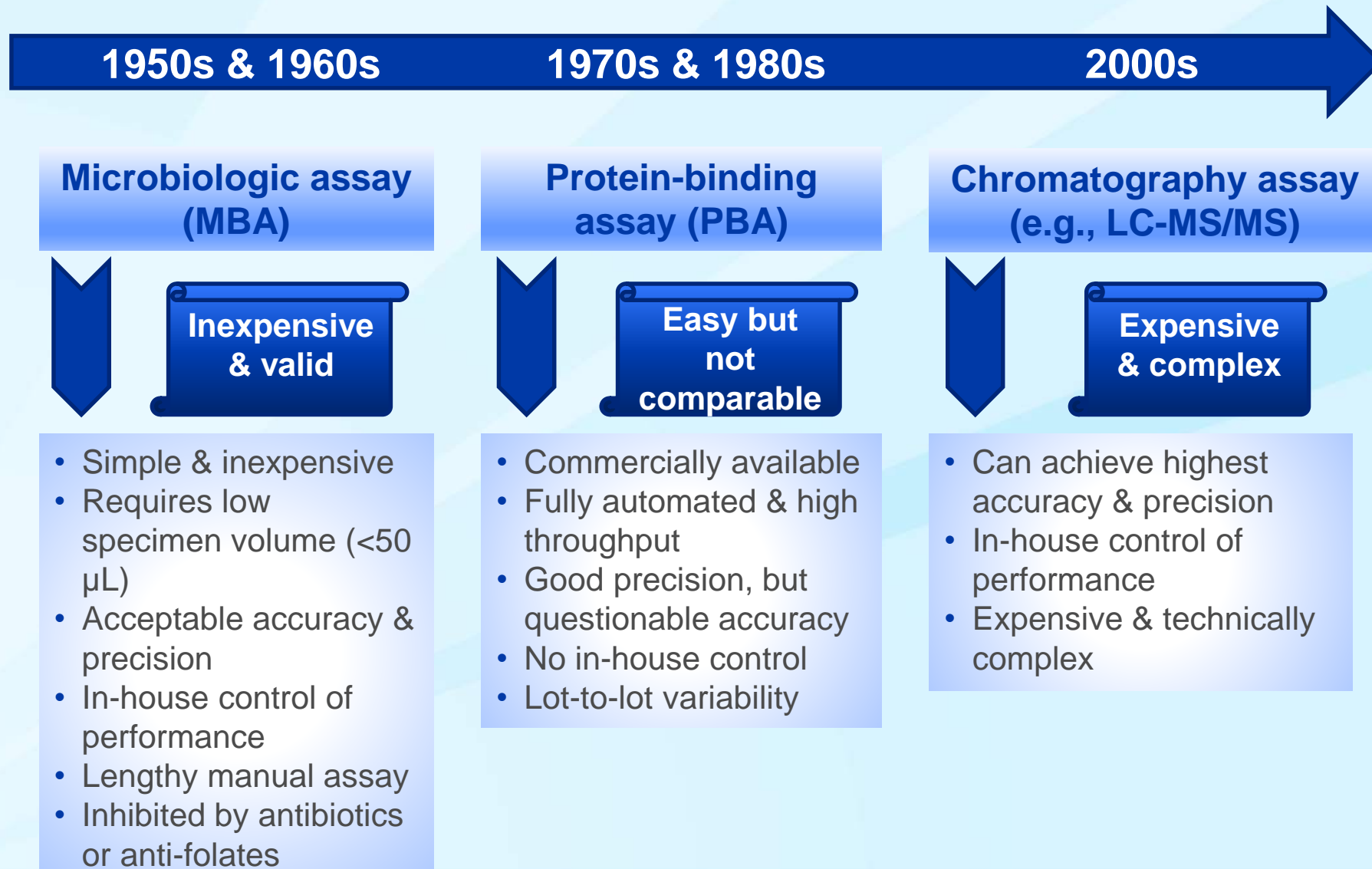
**Need to accurately generate whole blood hemolysate for RBC folate**

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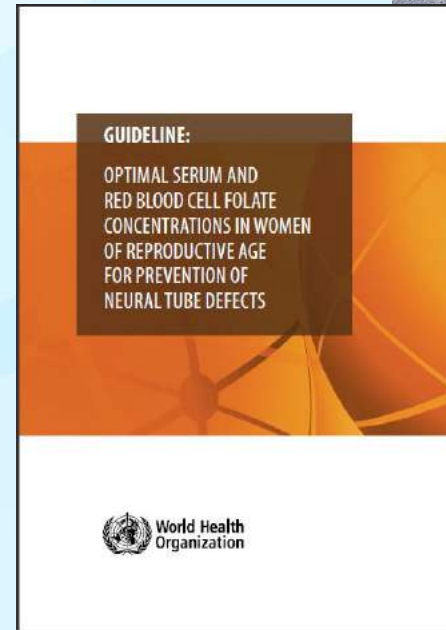


# Three major types of folate analytical methods

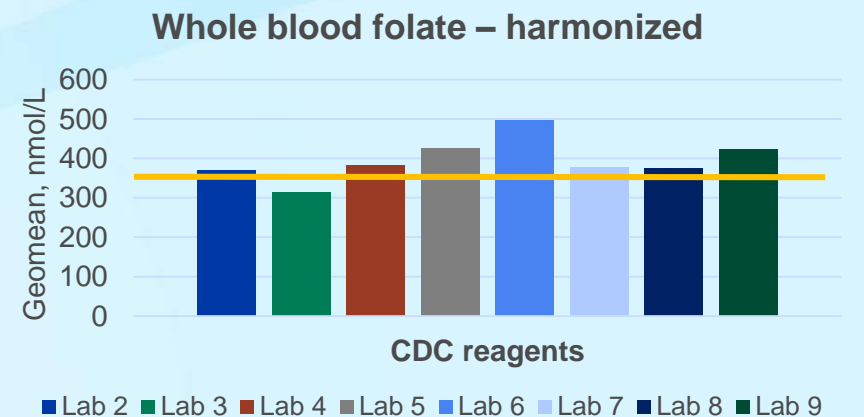
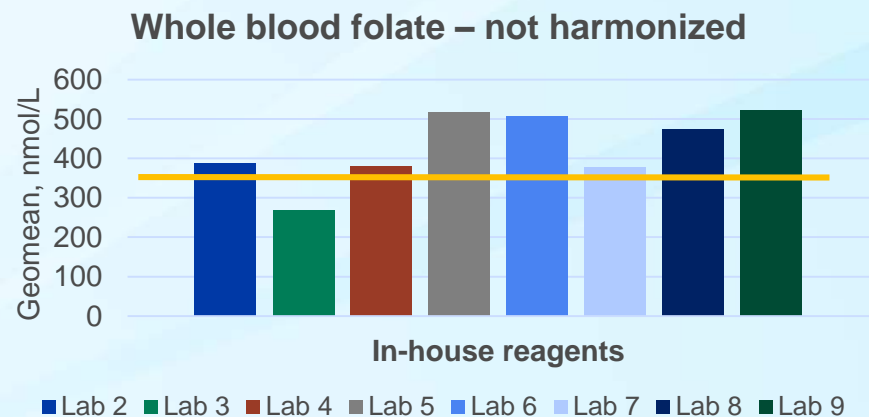
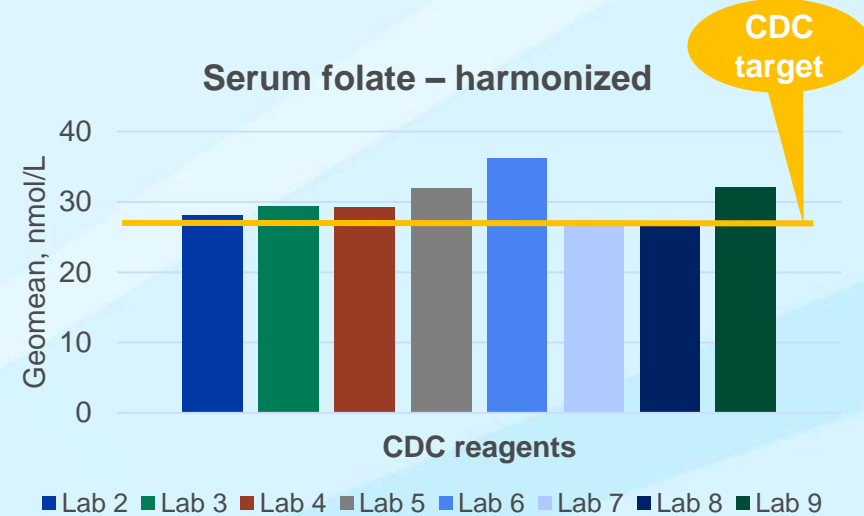
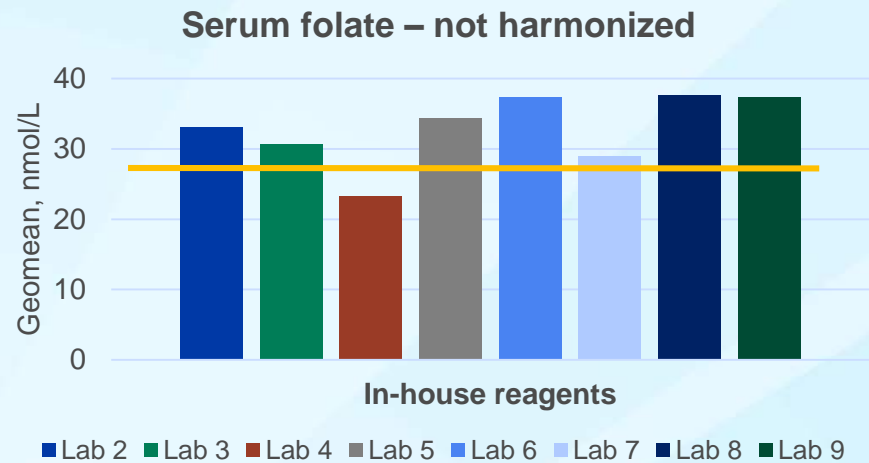


## MBA – practical choice for low-resource labs

- Assay used to derive cutoff values for folate deficiency (megaloblastic anemia) and insufficiency (risk of neural tube defects, NTDs)
- Assay recommended by WHO for population surveys



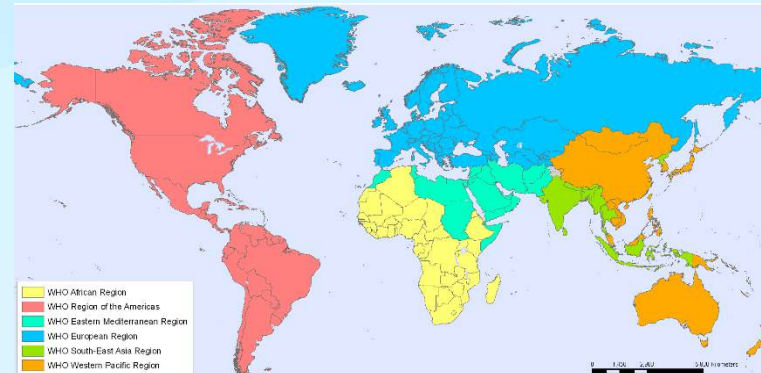
# Lab-to-lab variability improved with use of common critical reagents (microorganism and calibrator)





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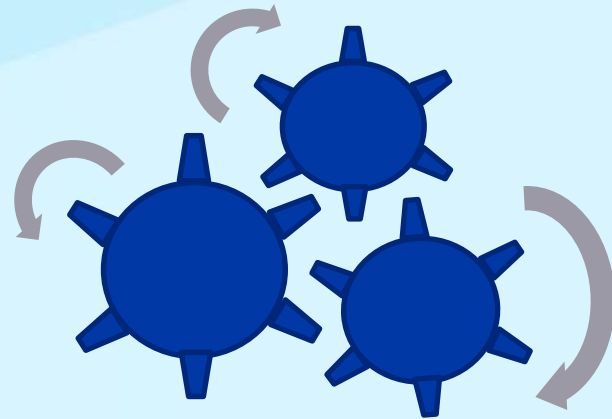


## Each country has a limited need for blood folate measurements at the population level

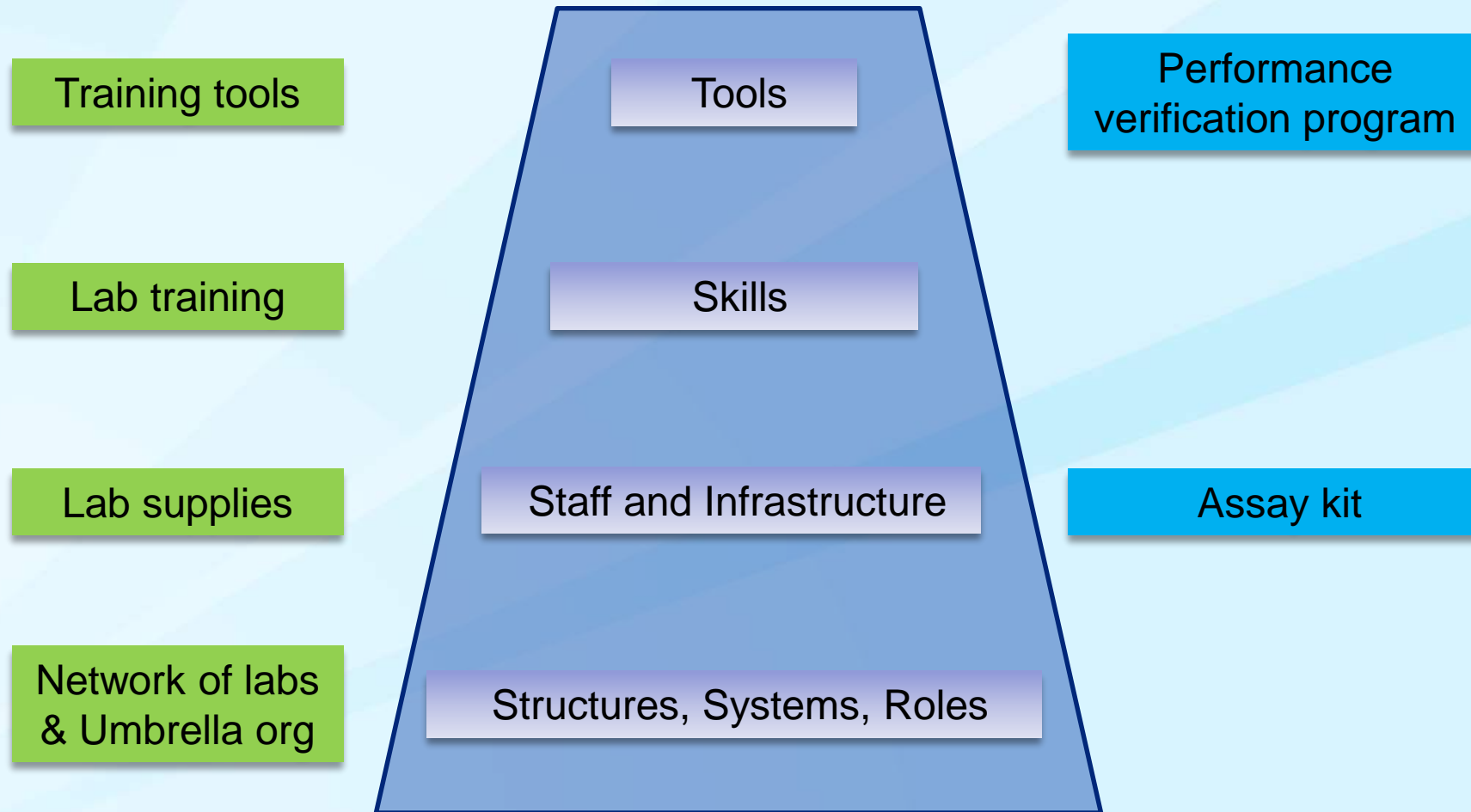
- Periodic nature of surveys (baseline, follow-up to assess impact, periodic monitoring)
- Routine lab can handle ~10,000 samples/year
- Interruptions of routine analysis may lead to problems when assay is restarted
- Efficient approach - **Network of regional resource laboratories:**
  - Proficient at conducting the MBA
  - Willing to perform fee-for-service work for other countries
  - Produce reliable folate data that can be compared across labs and over time

# Outline

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## Building and sustaining lab capacity entails more than just training



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## **Facilitate the development of regional resource labs to assess folate insufficiency and monitor prevention strategies globally**

- ❑ Train 6-12 laboratories worldwide (across WHO regions)
- ❑ Provide critical supplies to new resource laboratories
- ❑ Develop a training video for the folate MBA
- ❑ Develop comprehensive tool package (training manual, posters, SOPs)
- ❑ Provide start-up and/or survey assay kit containing critical reagents
- ❑ Set up performance verification program for testing laboratories
- ❑ Initiate steps to develop a network of resource laboratories
- ❑ Identify an umbrella organization to host the network



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CDC Training – 2018 Dec  
Sri Lanka & Tanzania

# Training planning and execution – expect the unexpected

## Logistical planning



- Identify trainees
- Invitation letters
- Trainee visa/passport
- CDC Guest Researcher approval
- CDC Security Clearance
- Travel arrangements

## Training execution



- Lab safety orientation
- Demonstrate/observe procedure
- Allow for repeat experiments
- Review instrument operation & maintenance
- Teach proper data review
- Discuss QC rules & QA program
- Provide start-up kit & some supplies

## Technical preparation



- Identify & fulfill supply needs
- Produce training video
- Generate training manual
- Develop training posters
- Assemble other training tools
- Prepare host lab for training

## Post-training follow-up



- Assist remotely with questions & troubleshooting
- Review & interpret trainee lab data
- Provide guidance on assay improvement
- Determine lab proficiency

## Traditional 2-week training format

Mon	Tue	Wed	Thu	Fri			Mon	Tue	Wed	Thu	Fri
	Run 1										
		Run 2									
							Run 3				
								Run 4			
									Run 5		

## New 5-day training format – video-assisted

Mon	Tue	Wed	Thu	Fri
Run 1				
	Run 2			
		Run 3		

Review folate MBA training video and other materials ahead of time

# Training components – Folate MBA step-by-step

## Prepare reagents



## Dilute samples



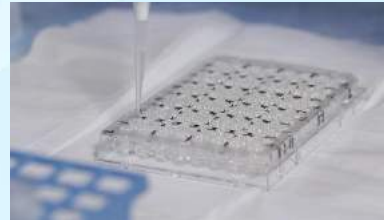
## Prepare 96-well plates



## Dilute calibrator & add to 96-well plate



## Add samples to 96-well plates



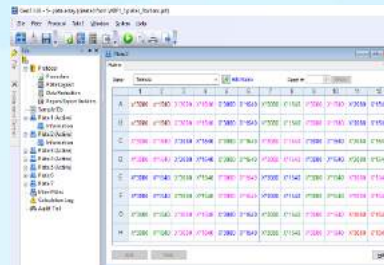
## Seal & incubate plates



## Read plates



## Review results



## Clean up & disposal



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Questionnaire for potential resource laboratories for folate microbiologic assay

Obtain permission to use a potential resource laboratory To be considered as a potential resource laboratory for folate assay, the following requirements should be met. Please respond based on the experience and characteristics of your laboratory and organization.

1. Proficiency to conduct the folate microbiologic assay

a. The laboratory personnel have been previously trained in the assay:  
By CDC? ☐ Yes ☐ No When? \_\_\_\_\_ Why? \_\_\_\_\_  
By other? ☐ Yes ☐ No When? \_\_\_\_\_ Why? \_\_\_\_\_  
Other (describe): \_\_\_\_\_

b. The laboratory has been conducting the assay for an extended period of time.  
Yes ☐ No ☐  
How long? \_\_\_\_\_  
Frequency? \_\_\_\_\_  
How many samples? \_\_\_\_\_ per month or \_\_\_\_\_ per year  
Please indicate any surveys or publications reporting lab-generated folate assay data:  
\_\_\_\_\_

c. Laboratory personnel will gain proficiency through training program participation.  
a. CDC H-Abeta training Yes ☐ No ☐  
b. Folate H-Abeta training video Yes ☐ No ☐  
c. Folate H-Abeta training manual Yes ☐ No ☐

2. Previous collaboration with CDC program

a. The laboratory participated in the CDC RoundRobin international folate microbiologic assay comparison study (Zhang et al. 2018).  
Yes ☐ No ☐

# Selection criteria for trainee labs to ensure successful technology transfer

## INSTITUTION

### Requirements to ensure successful assay implementation in country laboratories

- Laboratory conducts public health related work
- Supportive management
  - Provide laboratory space
  - Continuity in personnel
- Equipment & supplies available or readily procurable
- Quality assurance program in place

## TRAINEE

### Requirements to ensure efficient training

- Proficiency written & spoken English
- Bachelor of Science degree
  - Advanced degree (MS or PhD) desirable
  - Research experience highly desirable
- Experience with biological specimens and pipettes
- Ability to work with MS Office
- Good interpersonal & organizational skills



## Needs assessment of trainee labs

### Developed detailed folate MBA supply checklist:

- Essential chemicals, supplies and equipment – 37 item list @ \$23K US
- “Helpful” chemicals, supplies and equipment – 12 item list @ \$16K US

**Folate Microbiologic Assay -- Essential (tier I) chemicals, supplies, and equipment**

Chemicals	Unit price	Units needed	Total price	Comment
Folic acid casei medium (Himedia M543, 100 g). No alternative available as of 2018.	\$130	3	\$390	One bottle sufficient for 9 runs with 5-6 plates/run (~700 samples) or 12 runs with 2-4 plates/run; <b>purchase 3 bottles to set up assay and have some extra for a small study</b>
L-Sodium ascorbate, 99% purity (Ex: Fisher Item # AC352685000, 500 g). Alternate brand can be used.	\$113	1	\$113	One bottle lasts for several years; need only 2.5 g/run
Tween-80 (Ex: Fisher Item # T054625G, 25 g). Brand can be substituted.	\$16	1	\$16	One bottle lasts for several years; need only 60 <del>ul</del> for 200 mL medium
Ethyl alcohol, 100%, USP (Ex: Fisher Item# 07-678-005, 500 mL). Alternate brand can be used.	\$43	1	\$43	Used to clean pipettes
Bleach or alternate disinfectant				Added to leftover medium to deactivate non-pathogenic bacteria
Disinfectant hand soap - can be purchased from household store				Used to wash hands after lab work
<b>SUM</b>	<b>\$302</b>		<b>\$562</b>	

# Capacity assessment of potential network labs

Developed 7-part Lab Readiness Questionnaire to provide objective parameters for decision-making

1. Proficiency in conduct of folate MBA
2. Previous collaboration with CDC preferred
3. Participation in folate MBA harmonization efforts
4. Capacity and willingness to analyze samples from other countries
5. Skilled technical staff and stable workforce
6. Appropriate laboratory resources and infrastructure
7. Supportive organization and management

Round one – fall 2018:

- Contacted 18 labs from 17 countries
- 15 potential; 1 logistical issues; 2 no response

Round two – early 2019: Ongoing inquiry

The image shows two overlapping copies of a questionnaire titled "Questionnaire for potential resource laboratories for folate microbiologic assay". The questionnaire is designed to assess the capacity and readiness of laboratories for folate microbiologic assay (MBA). It includes sections for laboratory information, proficiency in folate MBA, previous collaboration with CDC, participation in folate MBA harmonization efforts, capacity and willingness to analyze samples from other countries, and supportive organization and management. The questionnaire is a 7-part form, with each part containing specific questions and checkboxes for "Yes", "No", or "Maybe".

**Questionnaire for potential resource laboratories for folate microbiologic assay**  
Resource laboratory for folate assay assessment, the following requirements should be met. Please respond based on the experience and characteristics of your laboratory and organization.

**1. Proficiency in conduct of the folate microbiologic assay**

a. The laboratory personnel have been previously trained in the assay:  
By CDC? ☐ Yes ☐ No ☐ When?  Why?   
By other (describe):

b. The laboratory has been conducting the assay for an extended period of time.  
Yes ☐ No ☐  
How long?   
Frequency?   
How many samples?  per month  per year   
Please indicate key surveys or publications regarding lab-generated folate MBA data:

**2. Previous collaboration with CDC preferred**

a. The laboratory participated in the CDC Round-Robin International Folate Microbiologic Assay comparison study (Zhang et al, 2018).  
Yes ☐ No ☐

b. Proficiency (continued)  
i. CDC in-house training Yes ☐ No ☐  
ii. CDC QA/QC program(s) Yes ☐ No ☐  
iii. Folate MBA training module Yes ☐ No ☐  
iv. Folate MBA training manual Yes ☐ No ☐

c. Please describe briefly your quality assurance program and sources of your QC materials:

**3. Participation in folate microbiologic assay harmonization efforts**

a. The laboratory recognizes the importance of generating comparable folate concentrations across laboratories and over time.  
Yes ☐ No ☐

b. The laboratory recognizes the value of using common key reagents (e.g., quality control materials, microorganism, incubator) and agrees to use such reagents if available as part of a user-fee program.  
Yes ☐ No ☐

c. The laboratory agrees to participate regularly in a certification program to document proficiency in the folate MBA, if available as part of a user-fee program.  
Yes ☐ No ☐

**4. Capacity and willingness to analyze samples from other countries**

a. The laboratory is willing to receive and analyze survey samples from other countries.  
Yes ☐ No ☐ Maybe ☐  
\*\*Briefly outline any circumstances/limitations related to your answer:

# Outline

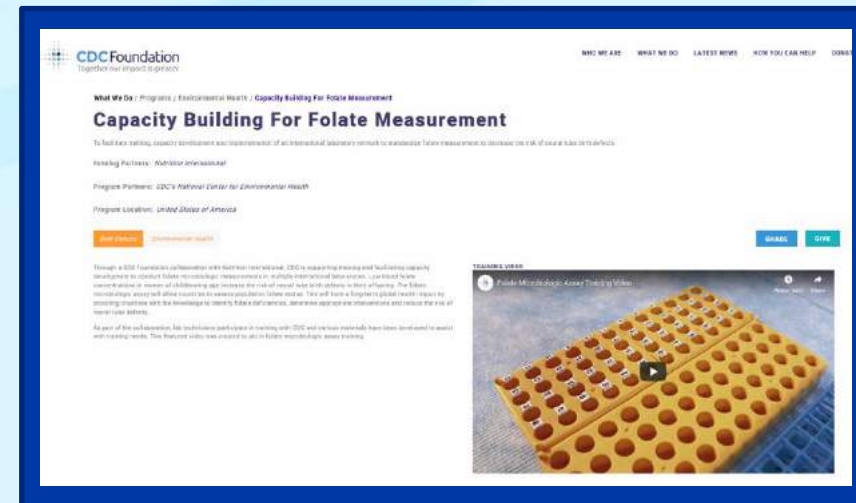
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CDC Training – 2018 Dec  
Sri Lanka & Tanzania

# Training video development took nearly 4 months

- Select video production company
- Pre-production (~6 weeks)
  - Script preparation and visualization
  - Voice-over recording
  - Scout and prep shooting location
- Production (1 day)
  - Ten hour in-lab shoot
- Post-production (~8 weeks)
  - Editing, review and revision
  - Graphics addition
- Web hosting – CDC Foundation



# **Folate Microbiologic Assay Training Video**



# Training aids increase the efficiency & effectiveness of the folate MBA training



**Folate Microbiologic Assay Training Poster**

**Part 1: Prepare Reagents**

- 

The frozen assay kit contains (a) microorganism (*L. reuteri*), (b) calibrator stock solution (5-methyltetrahydrofolate), (c) 2 levels of quality control materials, and (d) three reagents (ascorbic acid, chloramphenicol, and manganese sulfate) required for the growth medium preparation.
- 

Not provided with the kit are the following items: growth medium, Tween-80, sodium ascorbate, and deionized water.
- 

Two reagents need to be prepared freshly for each run: 0.5% sodium ascorbate and growth medium containing the microorganism.
- 

**Sodium ascorbate solution preparation:** To prepare a 0.5% solution, add 2.5 g of sodium ascorbate to a 500-ml beaker. Add 500 mL of deionized water, mix well. Cover the beaker with foil.
- 

**Medium preparation - Step 1:** To prepare 200 mL of growth medium, add 14.1 g of Folic Acid Casei Medium to a 500-ml beaker. Add 200 mL of deionized water, mix well. Cover the beaker with foil.
- 

**Medium preparation - Step 2:** Heat the solution to boil and keep boiling for 3 min. Cool down to room temperature.
- 

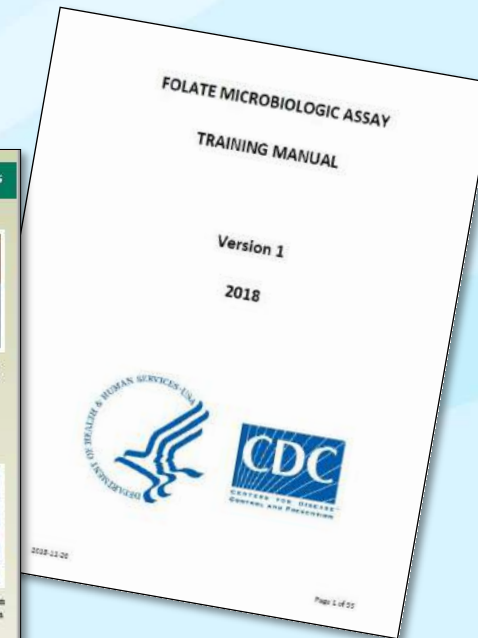
**Medium preparation - Step 3:** Add one vial each of chloramphenicol, ascorbic acid, and manganese sulfate stock solution, and 60 µL of Tween-80. Mix well for a few minutes.
- 

**Medium preparation - Step 4:** Thaw one vial of frozen microorganism and add 700 µL (or amount specified in assay kit) of the inoculum to the medium. Stir gently and cover the beaker with foil.

 Centers for Disease Control and Prevention  
National Center for Environmental Health

**Division of Laboratory Sciences**  
[www.cdc.gov/nceh/dls/nbb.html](http://www.cdc.gov/nceh/dls/nbb.html)

CDC Foundation | Nutrition International | BBS & Melinda Gates Foundation



## Recently trained 5 countries from 4 WHO regions

WHO Region	Country trained	Year of training
Western Pacific	Philippines	2019 January
Western Pacific	Viet Nam	2019 January
Eastern Mediterranean	Pakistan	2019 January
South-East Asia	Sri Lanka	2018 December
Africa	Tanzania	2018 December
Americas	Chile	2017 May
South-East Asia	India (2 labs)	2016 September
Africa	Ethiopia	2015 August
Western Pacific	China	2013 August
Eastern Mediterranean	Iraq*	2010 November
Americas	USA**	2010 April
Eastern Mediterranean	Jordan	2009 August
Americas	Venezuela**	2008 May
Europe	Uzbekistan**	2007 April

\* Lab not available due to logistical issues

\*\* Lab no longer available

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CDC Training – 2019 Jan  
Pakistan, Philippines & Viet Nam



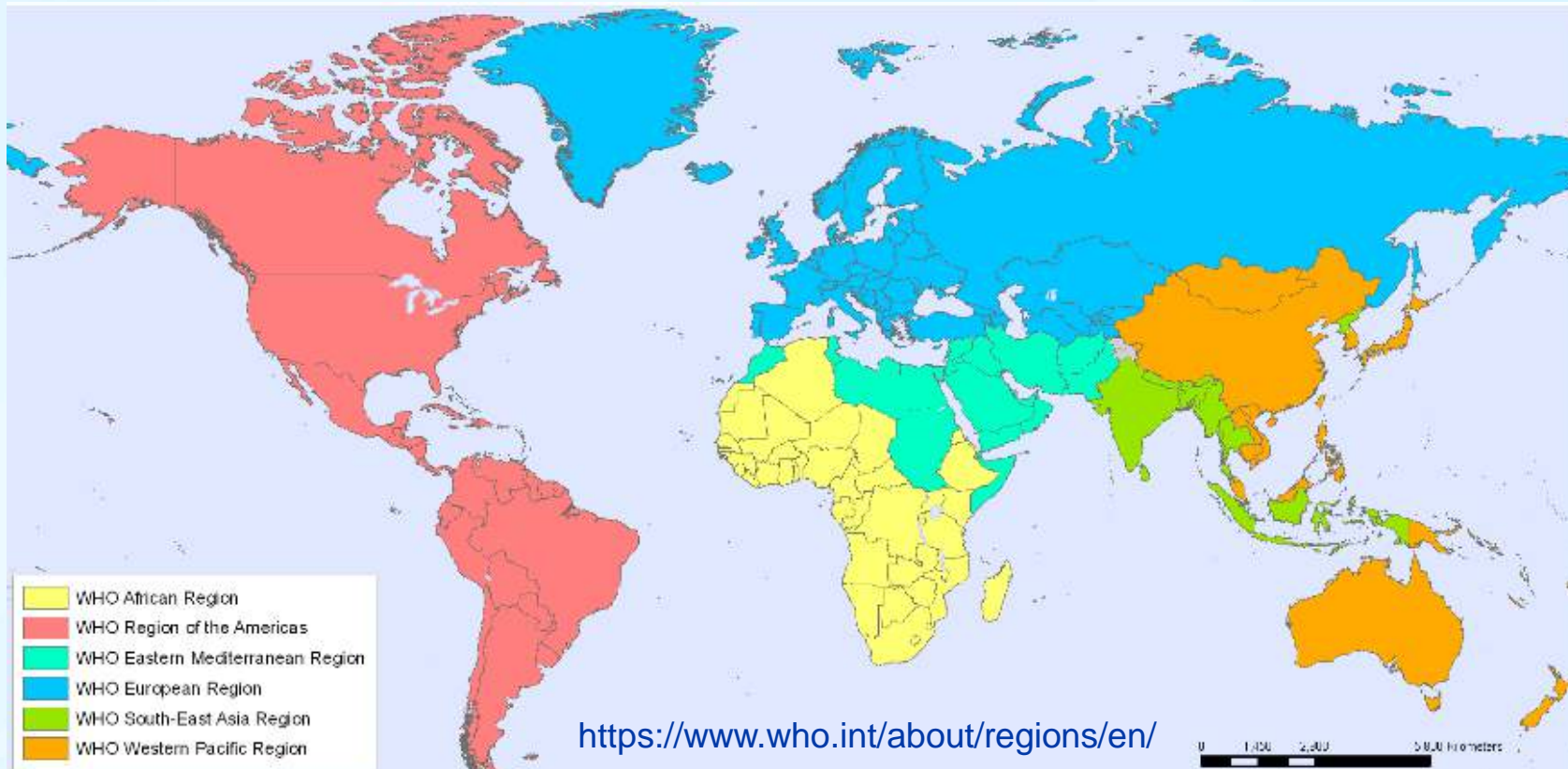
## Put skills into practice



Once newly trained lab technicians can demonstrate proficiency, they need to put their skills into practice to maintain proficiency.

That means, analyzing samples, and more samples...

**Build global network of ~12 resource laboratories  
proficient in the folate MBA  
across 6 WHO regions**



***Selection of resource laboratories based on assay performance and capacity***

## New proposed project components to enhance and expand the reach and impact of this project

- ❑ Collaborate with the future umbrella organization that will host the network to guide resource labs to self-sustainability
- ❑ Train additional laboratories in order to achieve required balance and representation in each WHO region
- ❑ Explore the potential to expand the scope of the resource laboratories to other micronutrients



CDC Training – 2019 Jan  
Pakistan, Philippines & Viet Nam



CDC Training – 2018 Dec  
Sri Lanka & Tanzania



# Acknowledgments

**CDC Global Micronutrient Team at Nutritional Biomarkers Branch  
CDC Foundation**

**Collaborators at Nutrition International, Folate Task Team  
Colleagues at CDC Birth Defects and Chronic Centers**



# Questions?

**For more information please contact Centers for Disease Control and Prevention**

1600 Clifton Road NE, Atlanta, GA 30333

Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

Visit: [www.cdc.gov](http://www.cdc.gov) | Contact CDC at: 1-800-CDC-INFO or [www.cdc.gov/info](http://www.cdc.gov/info)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

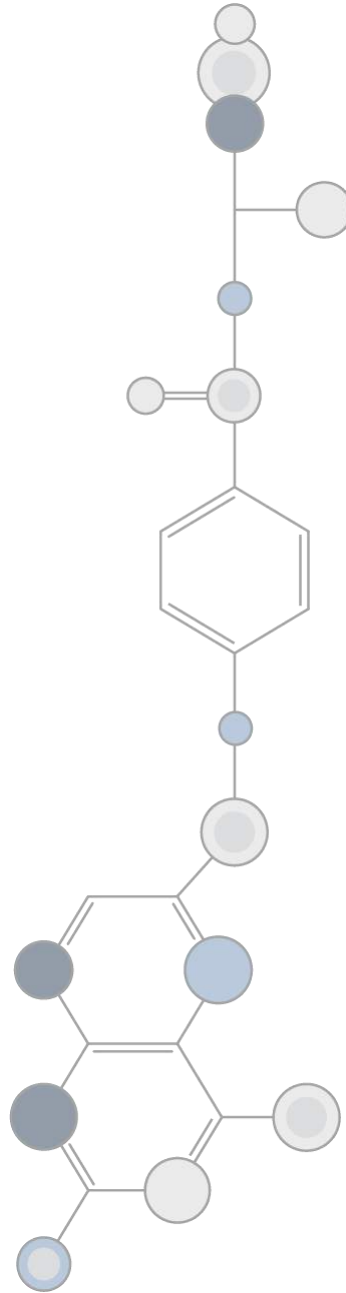
# Dr. Renuka Jayatissa

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**FOLATE TASK** TEAM



# Using Laboratory Folate Status Assessment to Strengthen NTD Prevention – Sri Lankan Experience

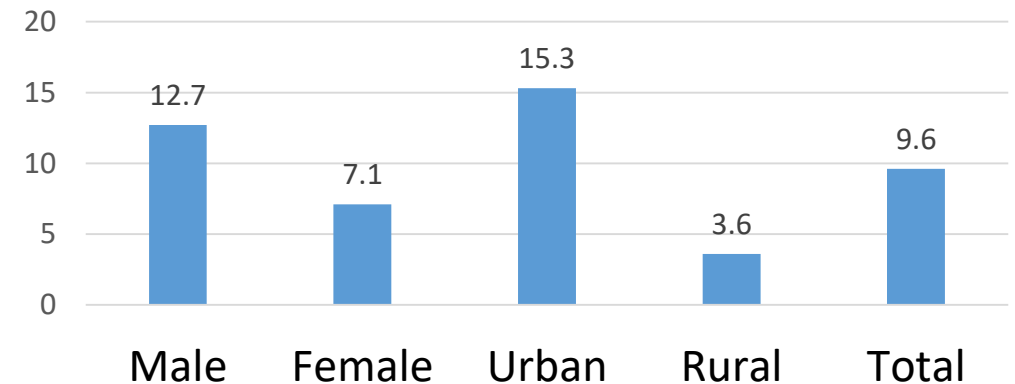
Dr. Renuka Jayatissa  
Head, Department of Nutrition  
Medical Research Institute  
Ministry of Health  
Sri Lanka



# Why Sri Lanka need to assess folate status?

- Prevalence of folate deficiency in adults – 9.6%.
- Incidence of NTD - 1.2/1000 live births; 4000 per year (FHB 2015, Birth defects surveillance).
- Pre natal folic acid supplementation coverage - 48% with varied duration of the supplementation (MRI 2015).
- Iron deficiency anaemia of pregnant women - 10% due to many supplementation programmes.
- But the rate of anaemia is 30% over last 20 years (MRI 2015).
- Need folic acid contribution to explore etiology.

**Figure 1: Prevalence of folic acid deficiency (<3ng/ml) in Sri Lankan adult 30-60 years (Source: MRI 2012)**



# National recommendation on folic acid

- A national level study on folate deficiency and insufficiency among the general population and women of reproductive ages
- Need baseline folate data for future evaluation of folate interventions.
- Challenge was our laboratory was not equipped and trained.

[MINISTRY OF HEALTH NUTRITION AND INDEGENOUS MEDICINE]

## Report of the expert panel appointed to provide recommendations on rice fortification with folic acid

Final Version

1<sup>st</sup> August 2016

# CDC Training opportunity for Sri Lanka

- Food Fortification Initiative, Nutrition International and CDC provided the training opportunity for Sri Lanka in December 2018.
- Our laboratory had basic supplies and well-trained permanent lab staff recruited by the MoH
- WFP Colombo, CDC and Nutrition International supported with other supplies.



# Process of training

- Comprehensive and step by step – one of the best
- Individual attention and friendly atmosphere
- Provide sufficient time to repeat and re-repeat to improve the competency
- Whole process help us to streamline other test in our lab



# Current status

First shipment of  
supplies received  
in end February

Second shipment  
expected in mid  
March

Establish the test  
in April and need  
further technical  
support from CDC

Blood collection  
of national  
micronutrient  
survey in May

# Way forward

- Complete analysis of blood samples of National micronutrient survey to disseminate data in December 2019.
- Estimate cost per test to establish regional hub
- Challenges
  - Availability of appropriate calibration materials
  - Access to agents who can provide supplies
- Future support
  - CDC – Provision of external QC and calibration materials
  - Nutrition International – Link with other countries to share experience



Thank you





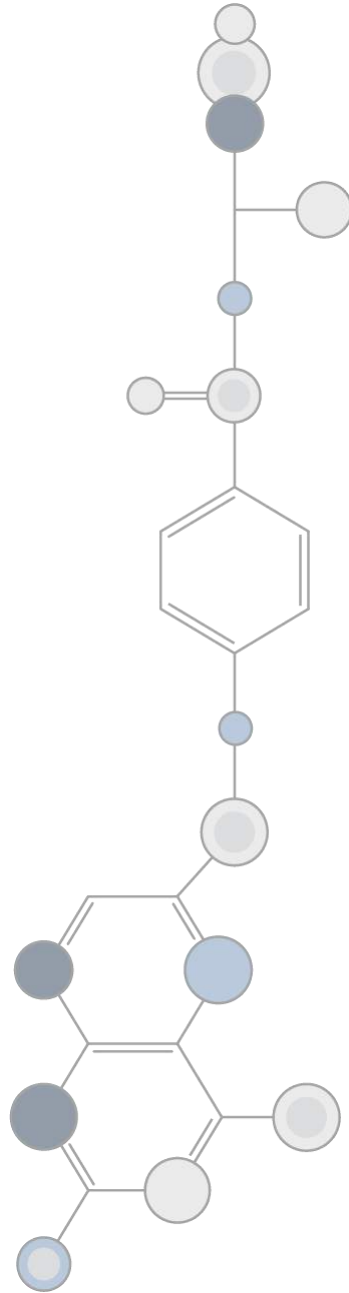
# Kehkashan Begum

MSc



Manager, Nutrition Research Laboratory  
Aga Khan University, Karachi

**FOLATE TASK** TEAM





# **USING LABORATORY FOLATE STATUS ASSESSMENT TO STRENGTHEN NTD PREVENTION.**

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KEHKASHAN BEGUM

COUNTRY: PAKISTAN

OCCUPATION: DESIGNATED AS MANAGER IN  
NUTRITION RESEARCH LABORATORY AT AGA KHAN  
UNIVERSITY BASED IN KARACHI, PAKISTAN.

# VENUE:

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- Held at CDC Chamblee campus, Atlanta, Georgia.
- 5 days training program (from 27<sup>th</sup> Jan 2019 to 1<sup>st</sup> Feb 2019)
- Trainers: Christine M Pfeiffer, Mindy Zhang, Shameem Jabbar.
- 3 countries participated (Pakistan, Vietnam & Philippines)
- Sponsored by Nutrition International and Global Affairs Canada
- Organized by Folate Task Team, Nutrition International, Canada.





# OBJECTIVE:


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Pakistan's need to access folate deficiency.

To get expertise on quantifying folate using a globally recommended method.

Future Vision



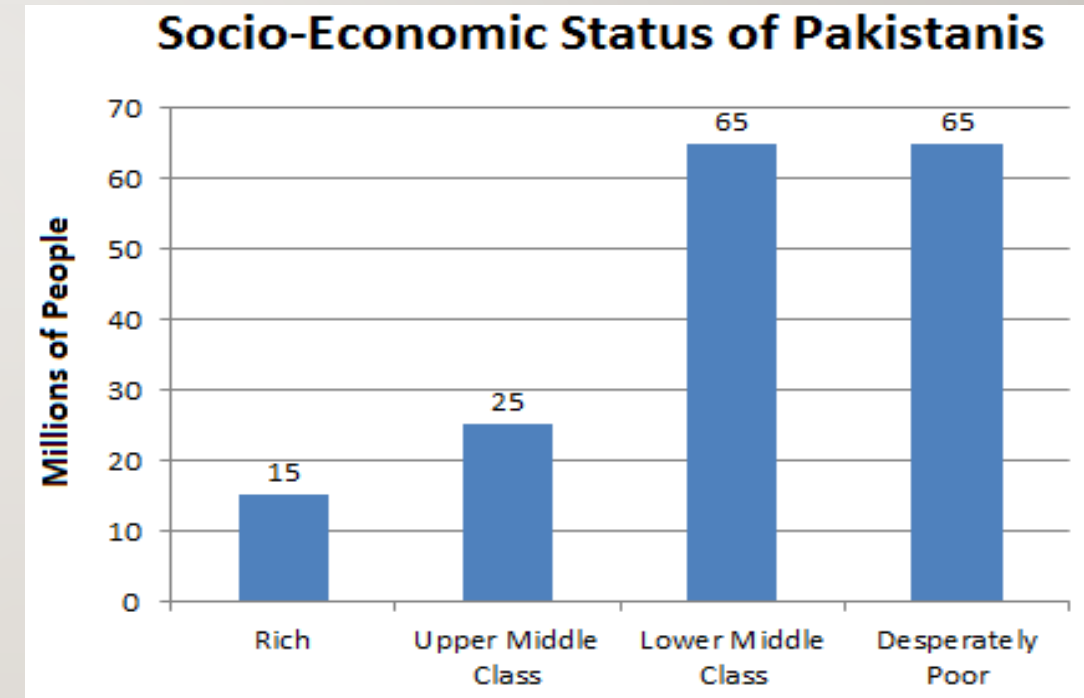
# Pakistan's Need To Access Folate Deficiency.

# SOCIO-ECONOMIC STATUS OF PAKISTAN

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- PAKISTAN is an economic mess. It is well behind other large Asian countries
- In low-income and middle-income countries, anaemia is a major public health problem. (1)

World Health Organization (WHO) and United Nations Children's Fund (UNICEF). Focusing on anaemia: towards an integrated approach for effective anaemia control. 2004



# FOLATE DEFICIENCY IN PAKISTAN

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In Pakistan, anaemia, and vitamin B12 and folate deficiencies are a severe public health concern among WRA

**Table 2** Prevalence of micronutrient deficiencies in women of reproductive age

Micronutrient deficiencies	%	SE	95% CI		n
			Lower	Upper	
Anaemia	50.4	0.5	49.4	51.5	10787
Folate deficiency	50.8	0.6	49.7	51.9	8371
Vitamin B <sub>12</sub> deficiency	52.4	0.6	51.3	53.5	8400

Prevalence and possible factors associated with anaemia, and vitamin B12 and folate deficiencies in women of reproductive age in Pakistan: analysis of national-level secondary survey data NNS 2011 data:



# PREVALENCE OF NEURAL TUBE BIRTH DEFECTS IN PAKISTAN.

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Forty-six patients with neural tube defects were seen among 3310 deliveries during a study period in Peshawar (KPK Province), Pakistan.

Incidence of NTDs in our study was 13.90 per 1000 deliveries where as in UK, USA, Denmark and Oman it is around 1-5 per 1000 deliveries.

INCIDENCE AND RISK FACTORS FOR NEURAL TUBE DEFECTS IN PESHAWAR Sania Tanveer Khattak\*, Tabassum Naheed\*\*, Shahnaz Akhtar\*\*, Tanveer Jamal\*\* \*Department of Gynae/Obs, Saidu Medical College, Swat and \*\*Postgraduate Medical Institute, Lady Reading Hospital, Peshawar, Pakistan

# NEURAL TUBE DEFECTS & FOLATE DEFICIENCY IN PAKISTAN.

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- A study was conducted in tertiary care hospital of Karachi catering to lower socioeconomic background. Maternal factor related to neural tube defects in same study showed >80% mothers had not taken folic acid during pregnancy.

Table-4: Effect of intake of Folic Acid on neural tube defects.

Folic acid intake	Neural tube defect	Normal pregnancy	Total
Yes	1	500	501
No	45	2810	2855

Raza MZ, Sheikh A, Ahmed SS, Ali S, Naqvi SM. Risk factors associated with birth defects at a tertiary care center in Pakistan. Italian journal of pediatrics. 2012;38:68



To Get Expertise On  
Quantifying Folate Using  
A Globally  
Recommended Method.

# NEED OF LABORATORY HARMONIZATION:

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- I. For Laboratory correlation: (For Quality control purpose)

This could be achieved by:

Getting an opportunity to learn proper PPEs and specific laboratory working environment required for assuring good quality results.

Assuring the Lab proficiency by looking at the advanced equipment being used in well-developed labs.

Observing the standard pre analytical, analytical and post-analytical procedures.

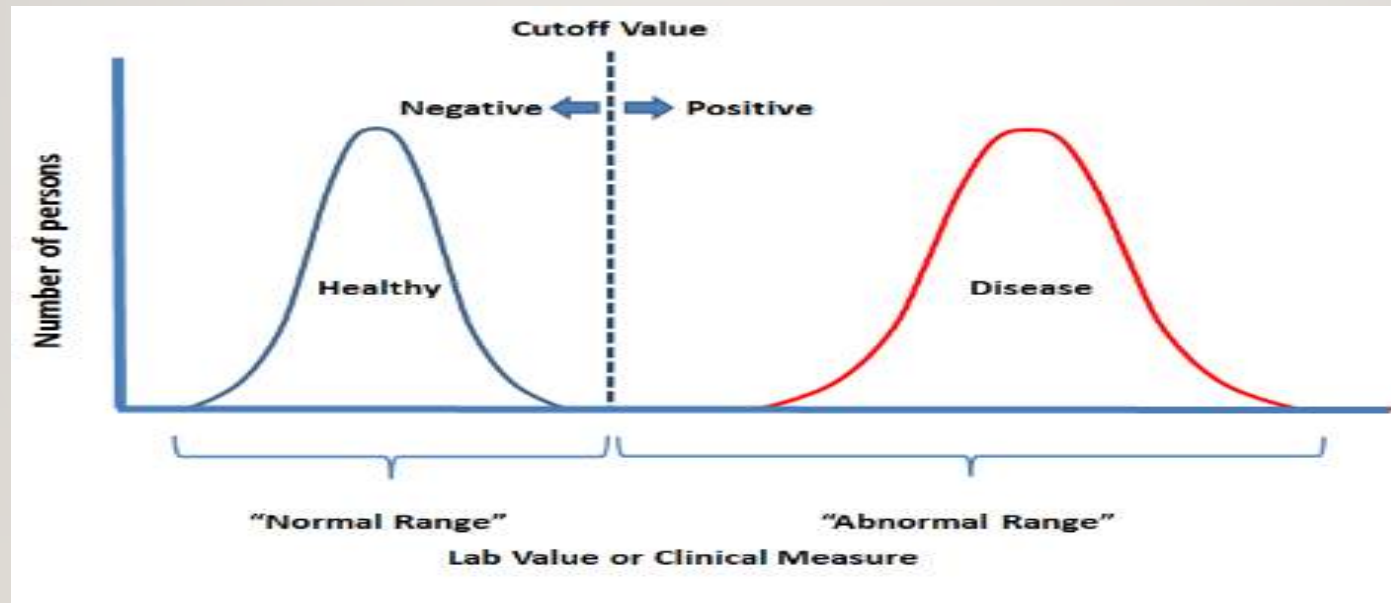




## 2. VALID AND ACCURATE FOLATE DEFICIENCY ASSESSMENT ACROSS PAKISTAN.

To establish a generalizable cut-off value for folate deficiency assessment.

As of Pakistan's socioeconomic condition, a cost-effective and reliable technique is required for surveying such a highly populated region.



### 3. ADVANCEMENT OF NUTRITION RESEARCH LAB

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- The Aga Khan Hospital serves as the main contributor in the government of Pakistan's health related projects and surveys.
- Aga Khan is the only CAP accredited hospital in Pakistan and also one of the top most biological & biomedical research institute of Pakistan.
- Our laboratories' quality and SOPs serve as a benchmark for other labs all over the Pakistan.





# Experience Of Training At CDC.



- Training was provided by highly skilled and innovative researchers.
- Lab was well-equipped and had co-operative and friendly environment.
- Brain storming sessions to achieve informative technical expertise.
- Got opportunity to have hands on experience to perform the assay & QC.







- Came across with the modified and improved techniques of performing microplate assays.
- CDC helped with providing the supplies useful for quick and easy performance of the assay.
- Step by step practical demonstration.





# Future Vision

- To become a reference lab in Pakistan for assessing RBC folate.
- To train laboratories on regional basis to individually perform this assay.
- To set a quality control foundation in Pakistan for other laboratories in Pakistan to periodically check the assay performance quality.
- To be able to have a robust folate status in the population of Pakistan and get a way forward for the required intervention for a healthy Pakistan.



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# THANKS



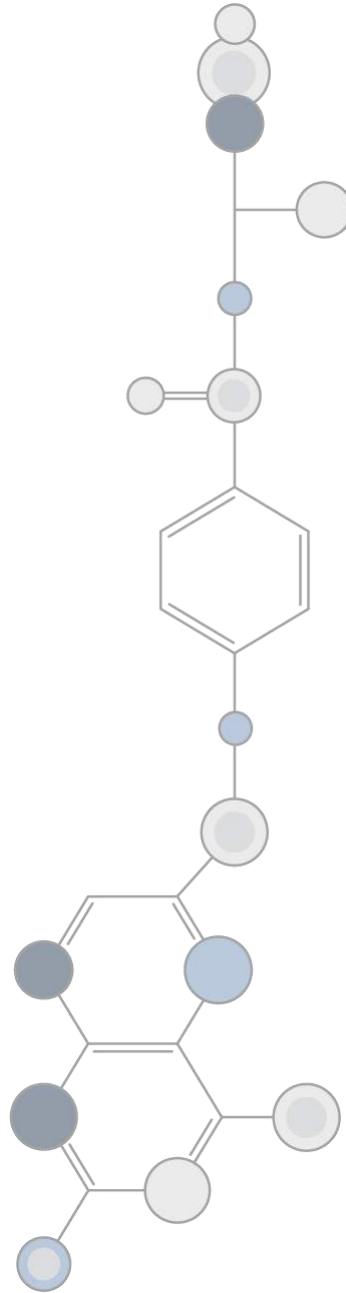
# Dr. Homero Martinez

MD, PhD



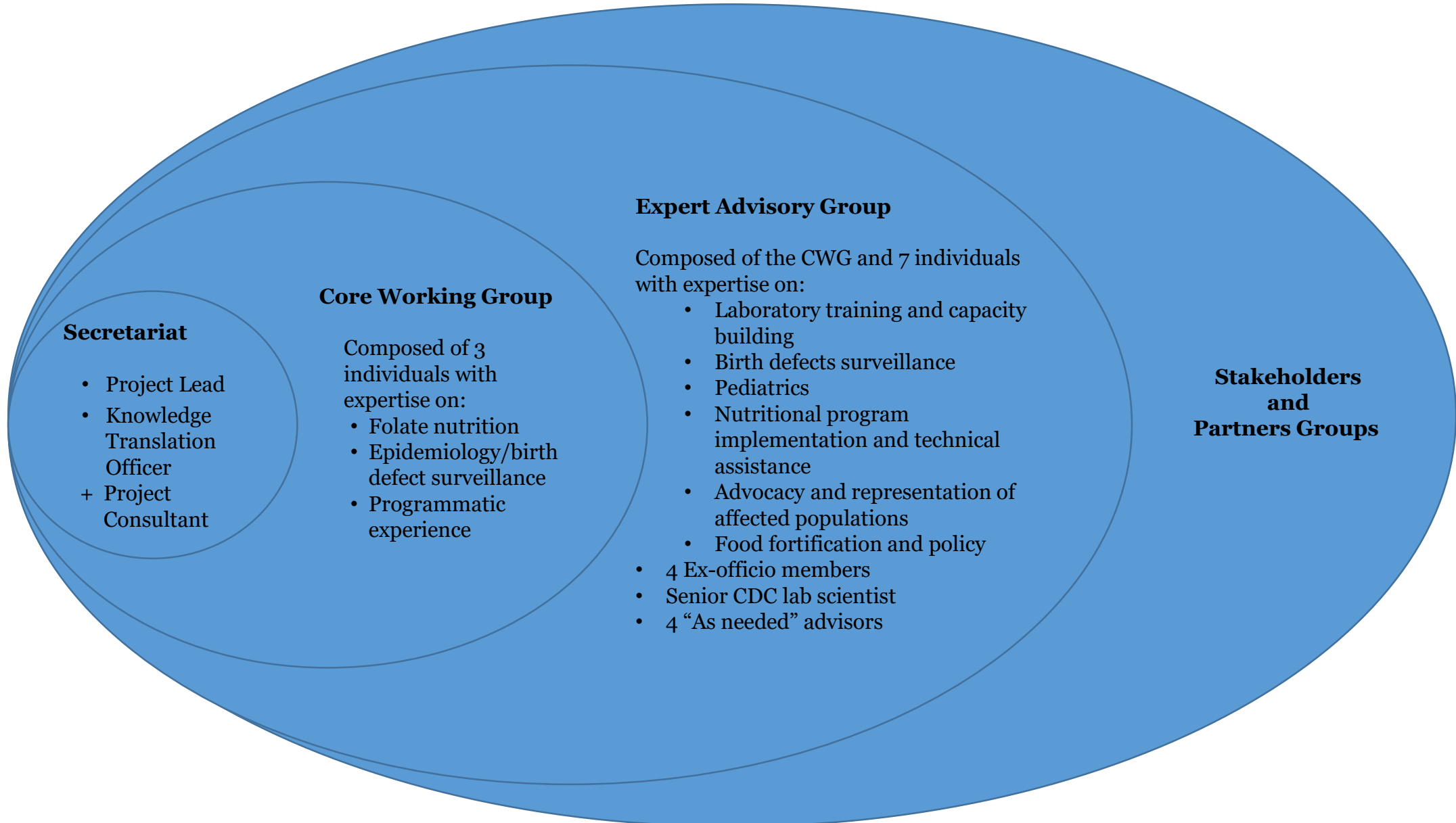
Senior Technical Advisor  
Nutrition International

**FOLATE TASK** TEAM





# Folate Task Team



FOLATE TASK  
TEAMGENDER EQUALITY AND  
NUTRITION

INITIATIVES &gt;

THEMES &gt;

PROGRAMS &gt;

MICRONUTRIENTS &gt;

## Nutrition Folate Task Team

A global nutrition Task Team for the control of folate insufficiency and folic acid responsive neural tube defects.

*The work of the Folate Task Team is being supported by a grant from the Bill & Melinda Gates Foundation.*

Through Nutrition Technical Assistance Mechanism (NTEAM)'s Folate Task Team project, Nutrition International is helping to lay the groundwork for implementing a global strategy for the control of folate insufficiency and prevention of related neural tube defects.

Maternal folate insufficiency in the first 28 days of pregnancy is a major cause of neural tube defects. The most common forms of these defects include spina bifida and anencephaly, which are important causes of elective pregnancy terminations, stillbirths, early neonatal deaths, or long-term disabilities. Improving maternal folate status through folic acid fortification or supplementation can dramatically reduce the number of affected births and significantly contribute to reducing neonatal and child mortality.

## ADVANCING THE ROADMAP FOR ACTION

### Supporting a global strategy for folate

A recent technical consultation convened by the Micronutrient Forum – whose Secretariat was hosted by Nutrition International between 2011 – 2017 – led to the development of a *Roadmap for Action* to advance and accelerate neural tube defects prevention globally. To advance the recommendations featured in this roadmap, Nutrition International has assembled a Folate Task Team, which will coordinate activities for the advancement of the implementation agenda to

## NEWS



More support needed by countries to maximize the benefits of mandatory food fortification

## FIELD STORIES

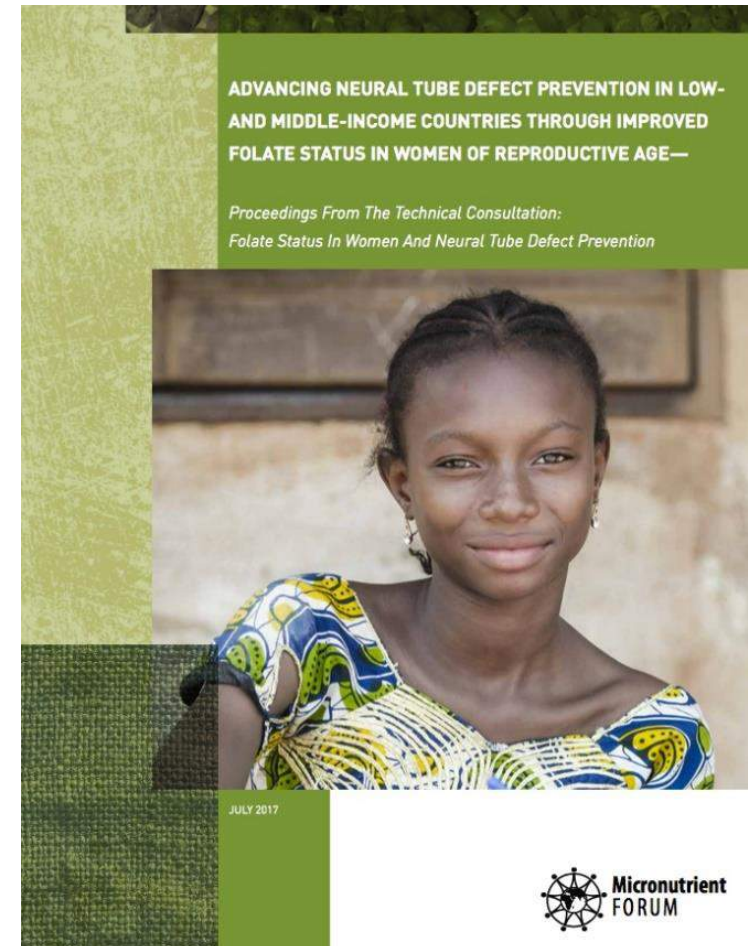




# Technical Consultation: Folate status in Women and Neural Tube Defect Prevention

## Resources

- <http://micronutrientforum.org/folate-consultation/>
- [http://micronutrientforum.org/content/user\\_files/2017/10/2017-07FolateTechnicalConsultation-FinalReport.pdf](http://micronutrientforum.org/content/user_files/2017/10/2017-07FolateTechnicalConsultation-FinalReport.pdf)  
**ISBN: 978-0-9959892-1-4**
- <https://www.nutritionintl.org/what-we-do/nteam/team-folate/>
- [hmartinez@NUTRITIONINTL.ORG](mailto:hmartinez@NUTRITIONINTL.ORG)





## Volume 1414, Issue 1

### Folate Status in Women and Neural Tube Defect Risk Reduction

Pages: 1-136

February 2018

GO TO SECTION

#### ISSUE INFORMATION

##### Issue Information

Pages: 1-3 | First Published: 13 March 2018

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- Martinez H, A. Weakland, L.B. Bailey, L.D. Botto, L.M. De-Regil, K. Brown. Improving maternal folate status to prevent infant neural tube defects: working group conclusions and a framework for action. Ann NY Acad Sci. 2018: 1414(1);5-19.
- Kancherla V., R.E. Black. A historical perspective and challenges in estimation of global prevalence of neural tube defects. Ann NY Acad Sci. 2018: 1414(1);20-30.
- Blencowe H, V. Kancherla, A. Moorthie, M.W. Darlison., B. Modell. Estimates of global and regional prevalence of neural tube defects for the year 2015: a systematic analysis. Ann NY Acad Sci. 2. 2018: 1414(1);31-46.
- Garrett G., L.B. Bailey. A public health approach for preventing neural tube defects: fortification and innovations. Ann NY Acad Sci. 2018: 1414(1);47-58.
- Stover P, M. Field. Safety of folic acid. Ann NY Acad Sci. 2018: 1414(1);59-71.
- Hoddinott J. The investment case for folic acid fortification in developing countries. Ann NY Acad Sci. 2018: 1414(1);72-81.
- Bailey LB, D.B. Hausman. Folate status of women of reproductive age as basis of NTD risk assessment. Ann NY Acad Sci. 2018: 1414(1);82-95.
- Pfeiffer CM, M. Zhang, S. Jabbar. Framework for laboratory harmonization of folate measurements in low- and middle-income countries and regions. Ann NY Acad Sci. 2018: 1414(1);96-108.
- Molloy A. Should vitamin B12 be considered in assessing risk of neural tube defects. Ann NY Acad Sci. 2018: 1414(1);109-125.
- Botto LD, P. Mastroiacovo. Triple surveillance: a strategy to accelerate neural tube defect prevention. Ann NY Acad Sci. 2018: 1414(1);126-136.
- Rogers L, A.M. Cordero, C.M. Pfeiffer, D.G. Hausman, B.L. Tsang, L.M. De-Regil, et al. Global folate status in women of reproductive age: a systematic review with emphasis on methodological issues. Ann NY Acad Sci. 2018;1431(1):35-57. doi: 10.1111/nyas.13963



## FOLATE TASK TEAM

### IMPROVING FOLATE STATUS IN WOMEN OF REPRODUCTIVE AGE TO PREVENT NEURAL TUBE DEFECTS

KNOWLEDGE  
BRIEF



## FOLATE TASK TEAM

### THE IMPORTANCE OF FOLIC ACID FOOD FORTIFICATION TO PREVENT NEURAL TUBE DEFECTS

ADVOCACY BRIEF



## FOLATE TASK TEAM

### SUPPLY CHAIN ANALYSES TO ASSESS THE FEASIBILITY OF NATIONAL FOOD FORTIFICATION PROGRAMS

KNOWLEDGE  
BRIEF





# FOLATE MICROBIOLOGIC ASSAY TRAINING VIDEO

Through a Folate Task Team collaboration with the CDC Foundation, CDC is supporting training and facilitating capacity development to conduct folate microbiologic measurements in multiple international laboratories. Low blood folate concentrations in women of childbearing age increase the risk of neural tube birth defects in their offspring. The folate microbiologic assay will allow countries to assess population folate status. This will have a long-term global health impact by providing countries with the knowledge to identify folate insufficiency, determine appropriate interventions and reduce the risk of neural tube defects.

As part of the collaboration, lab technicians participate in training with CDC and various materials have been developed to assist with training needs. This featured video was created to aid in folate microbiologic assay training.

<https://www.cdcfoundation.org/programs/capacity-building-folate-measurement>

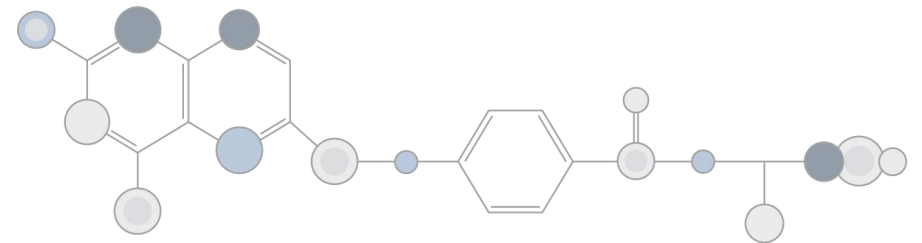




# Further discussion

Please feel free to submit a question via the chat box for any of our speakers

**FOLATE TASK** TEAM

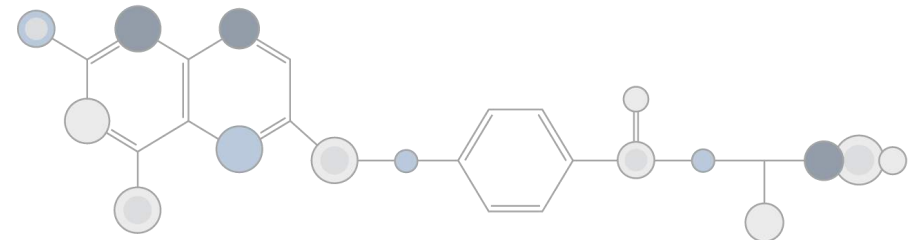


# Closing remarks from Dr. Martinez

For more information please contact Dr. Martinez at  
[folatetaskteam@nutritionintl.org](mailto:folatetaskteam@nutritionintl.org)

A recording of this webinar and a PDF of the slides will  
be made available via the Folate Task Team webpage  
at <https://www.nutritionintl.org/what-we-do/nteam/folate-task-team/>

**FOLATE TASK TEAM**



# Thank you!

**FOLATE TASK** TEAM

