Expanded Newborn Screening

Future Diagnostics Seminar in Turku, May 21 2015

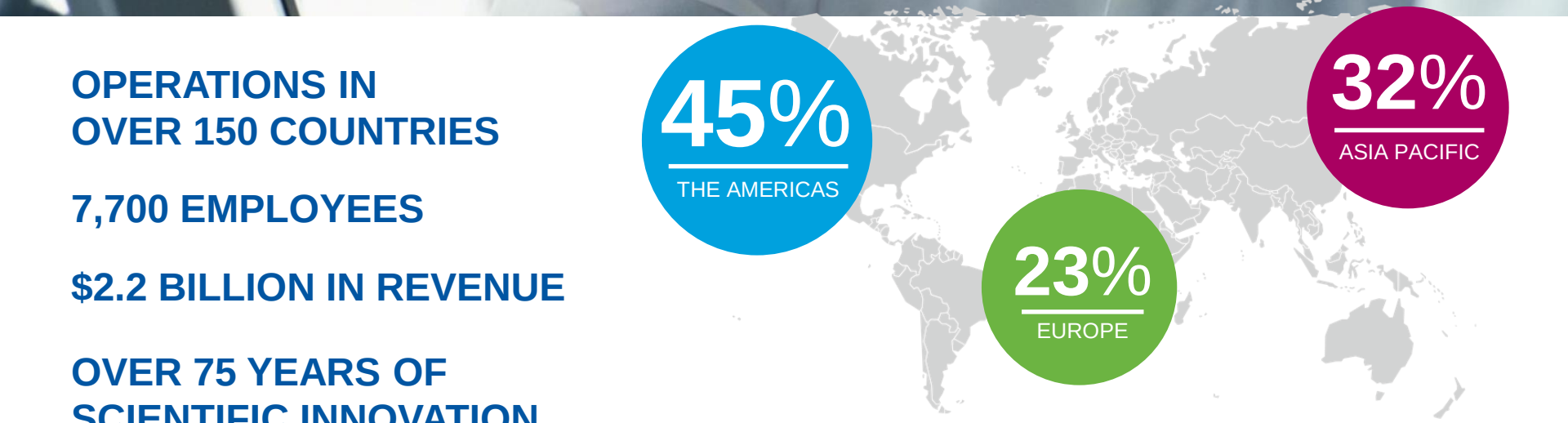
Marika Kase, Business Director, PerkinElmer Diagnostics

OPERATIONS IN OVER 150 COUNTRIES

7,700 EMPLOYEES

$2.2 BILLION IN REVENUE

OVER 75 YEARS OF SCIENTIFIC INNOVATION



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PERKINELMER – THE SCREENING COMPANY

A global supplier committed to maternal, fetal and newborn health

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TURKU SITE
ONE OF THE LARGEST MANUFACTURING AND R&D FACILITIES IN PERKINELMER

Centre of Excellence for
Diagnostics Devices

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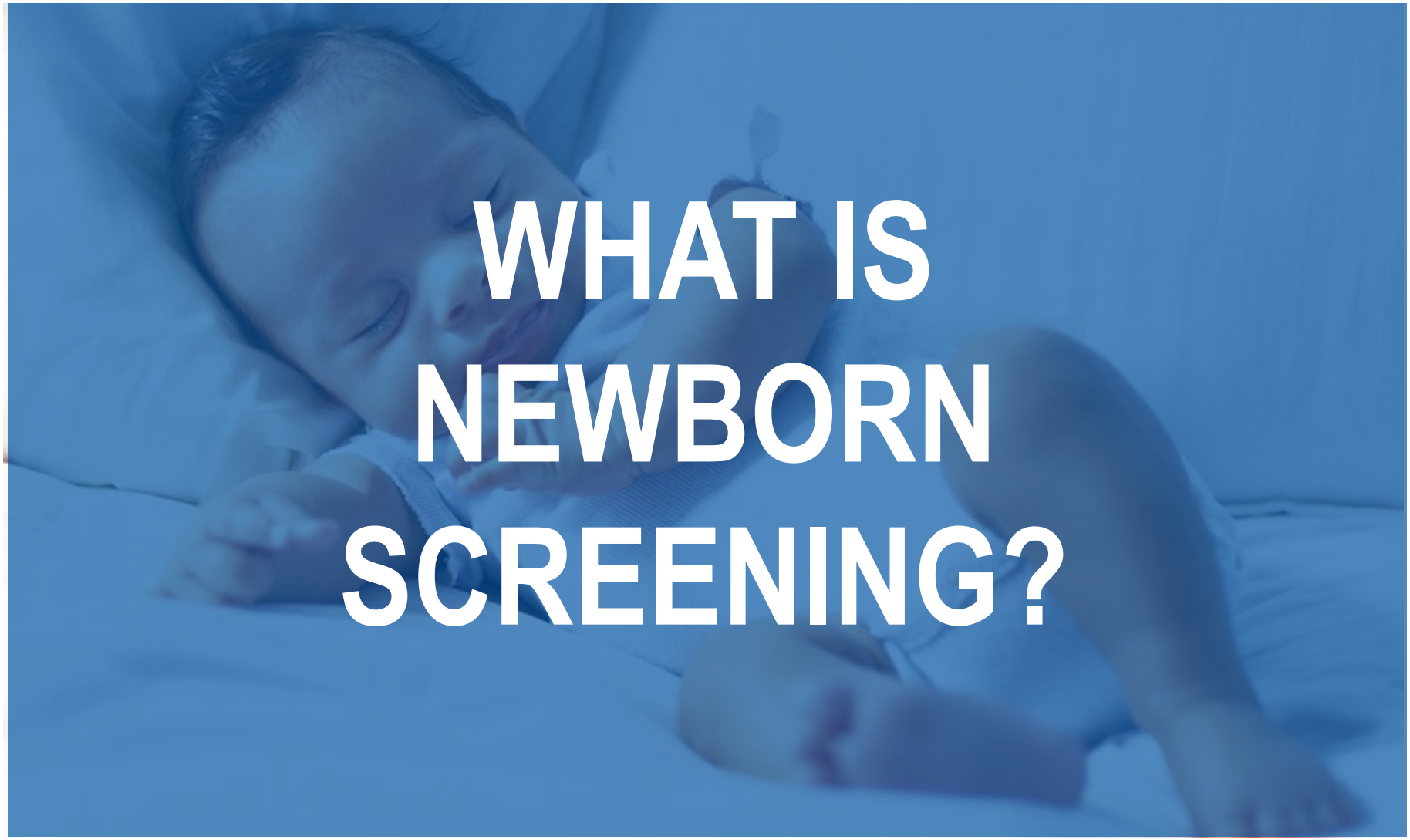

WHAT IS NEWBORN SCREENING?

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Newborn Screening

Newborn Screening

Prevent

The University of the Philippines-National Institutes of Health and PhilHealth, the Philippine Health Insurance Corporation.

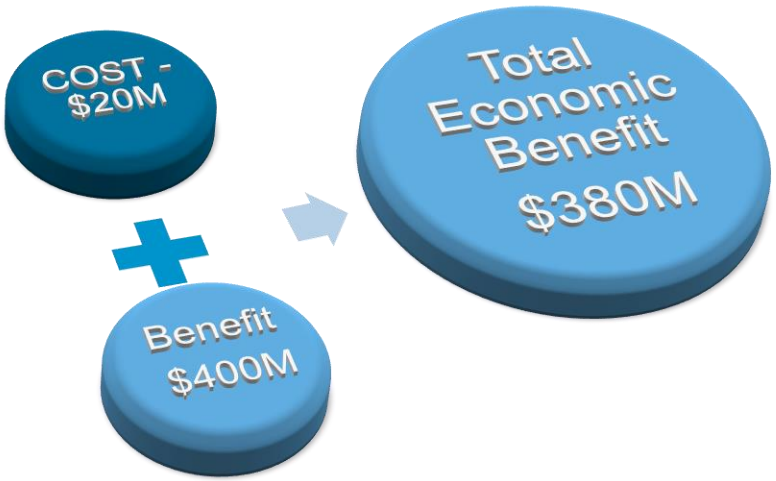
Newborn Screening
www.newbornscreening.ph

Newborn Screening is covered by PhilHealth

PhilHealth

Health Economics

BENEFITS of CH screening = 20x the costs



*Grosse, SD and Van VlietG. Arch DisChild. 2011; 96(4):374–379

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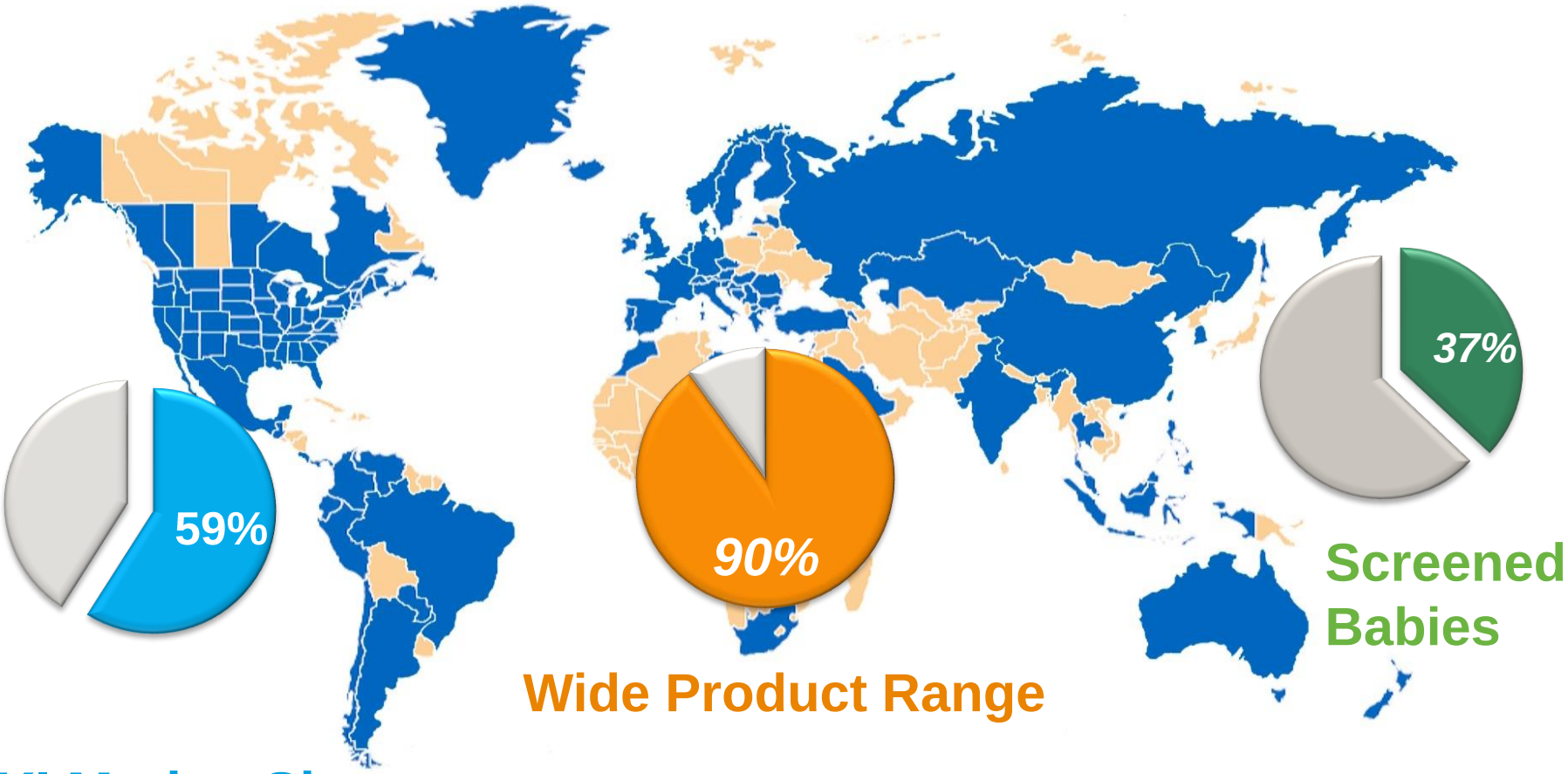
PerkinElmer is Global Leader



PerkinElmer Complete Solution

SAMPLE COLLECTION

226 Sample Collection Device

SAMPLE PREPARATION

PANTHERA-PUNCHER™ 9

ANALYTES

TSH	IRT
T4	GALT
PKU	TGAL
G6PD	BTD
17OHP	AAAC
	TREC

SAMPLE PROCESSING & MEASURING

GSP®

MSMS system

EnLite

DATA PROCESSING & REPORTING

SPECIMEN GATE® LABORATORY

SCREENING CENTER™

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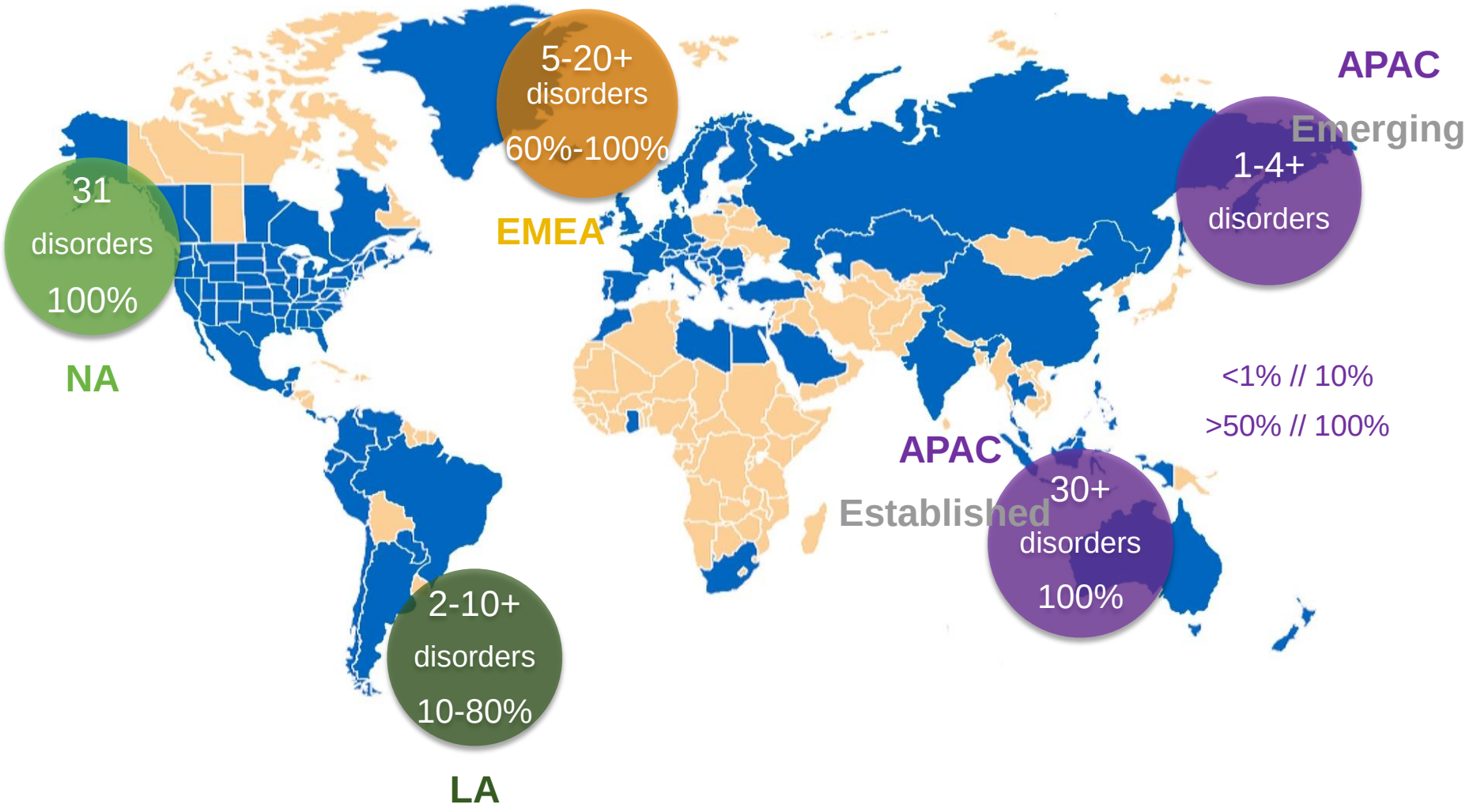
Newborn Screening Programs World Wide



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HRSA's Recommended Uniform Screening Panel, RUSP

HRSA *Health Resources and Services Administration*

Recommended Uniform Screening Panel[1]
Core[2] Conditions[3]
(as of April 2013)

ACMG Code	Core Condition	Metabolic Disorder			Endocrine Disorder	Hemoglobin Disorder	Other Disorder
		Organic acid condition	Fatty acid oxidation disorders	Amino acid disorders			
PROP	Propionic acidemia	X					
MUT	Methylmalonic acidemia (methylmalonyl-CoA mutase)	X					
Cbl A,B	Methylmalonic acidemia (cobalamin disorders)	X					
IVA	Isovaleric acidemia	X					
3-MCC	3-Methylcrotonyl-CoA carboxylase deficiency	X					
HMG	3-Hydroxy-3-methyglutaric aciduria	X					
MCD	Holocarboxylase synthase deficiency	X					
ßKT	ß-Ketothiolase deficiency	X					
GA1	Glutaric acidemia type I	X					
CUD	Carnitine uptake defect/carnitine transport defect		X				
MCAD	Medium-chain acyl-CoA dehydrogenase deficiency		X				
VLCAD	Very long-chain acyl-CoA dehydrogenase deficiency		X				
LCHAD	Long-chain L-3 hydroxyacyl-CoA dehydrogenase deficiency		X				
TFP	Trifunctional protein deficiency		X				
ASA	Argininosuccinic aciduria			X			
CIT	Citrullinemia, type I			X			
MSUD	Maple syrup urine disease			X			
HCY	Homocystinuria			X			
PKU	Classic phenylketonuria			X			
TYR I	Tyrosinemia, type I			X			
CH	Primary congenital hypothyroidism				X		
CAH	Congenital adrenal hyperplasia				X		
Hb SS	S,S disease (Sickle cell anemia)					X	
Hb S/ßTh	S, ßeta-thalassemia					X	
Hb S/C	S,C disease					X	
BIOT	Biotinidase deficiency						X
CCHD	Critical congenital heart disease						X
CF	Cystic fibrosis						X
GALT	Classic galactosemia						X
HEAR	Hearing loss						X
SCID	Severe combined immunodeficiences						X

1. Selection of conditions based upon "Newborn Screening: Towards a Uniform Screening Panel and System." *Genetic Med.* 2006; 8(5) Suppl: S12-S252" as authored by the American College of Medical Genetics (ACMG) and commissioned by the Health Resources and Services Administration (HRSA).
2. Disorders that should be included in every Newborn Screening Program.
3. Nomenclature for Conditions based upon "Naming and Counting Disorders (Conditions) Included in Newborn Screening Panels." *Pediatrics.* 2006; 117 (5) Suppl: S308-S314.

Recommended Uniform Screening Panel[1]
SECONDARY[2] CONDITIONS[3]
(as of April 2013)

ACMG Code	Secondary Condition	Metabolic Disorder			Hemoglobin Disorder	Other Disorder
		Organic acid condition	Fatty acid oxidation disorders	Amino acid disorders		
Cbl C,D	Methylmalonic acidemia with homocystinuria	X				
MAL	Malonic acidemia	X				
IBG	Isobutyrylglycinuria	X				
2MBG	2-Methylbutyrylglycinuria	X				
3MGA	3-Methylglutaconic aciduria	X				
2M3HBA	2-Methyl-3-hydroxybutyric aciduria	X				
SCAD	Short-chain acyl-CoA dehydrogenase deficiency		X			
M/SCHAD	Medium/short-chain L-3-hydroxyacl-CoA dehydrogenase deficiency		X			
GA2	Glutaric acidemia type II		X			
MCAT	Medium-chain ketoacyl-CoA thiolase deficiency		X			
DE RED	2,4 Dienoyl-CoA reductase deficiency		X			
CPT IA	Carnitine palmitoyltransferase type I deficiency		X			
CPT II	Carnitine palmitoyltransferase type II deficiency		X			
CACT	Carnitine acylcarnitine translocase deficiency		X			
ARG	Argininemia			X		
CIT II	Citrullinemia, type II			X		
MET	Hypermethioninemia			X		
H-PHE	Benign hyperphenylalaninemia			X		
BIOPT (BS)	Biopterin defect in cofactor biosynthesis			X		
BIOPT (REG)	Biopterin defect in cofactor regeneration			X		
TYR II	Tyrosinemia, type II			X		
TYR III	Tyrosinemia, type III			X		
Var Hb	Various other hemoglobinopathies				X	
GALE	Galactoepimerase deficiency					X
GALK	Galactokinase deficiency					X
	T-cell related lymphocyte deficiencies					X

1. Selection of conditions based upon "Newborn Screening: Towards a Uniform Screening Panel and System." *Genetic Med.* 2006; 8(5) Suppl: S12-S252" as authored by the American College of Medical Genetics (ACMG) and commissioned by the Health Resources and Services Administration (HRSA).
2. Disorders that can be detected in the differential diagnosis of a core disorder.
3. Nomenclature for Conditions based upon "Naming and Counting Disorders (Conditions) Included in Newborn Screening Panels." *Pediatrics.* 2006; 117 (5) Suppl: S308-S314.

RUSP – 31 primary and 25 secondary disorders

MSMS EXPANDED NEWBORN SCREENING

Expanded Newborn Screening

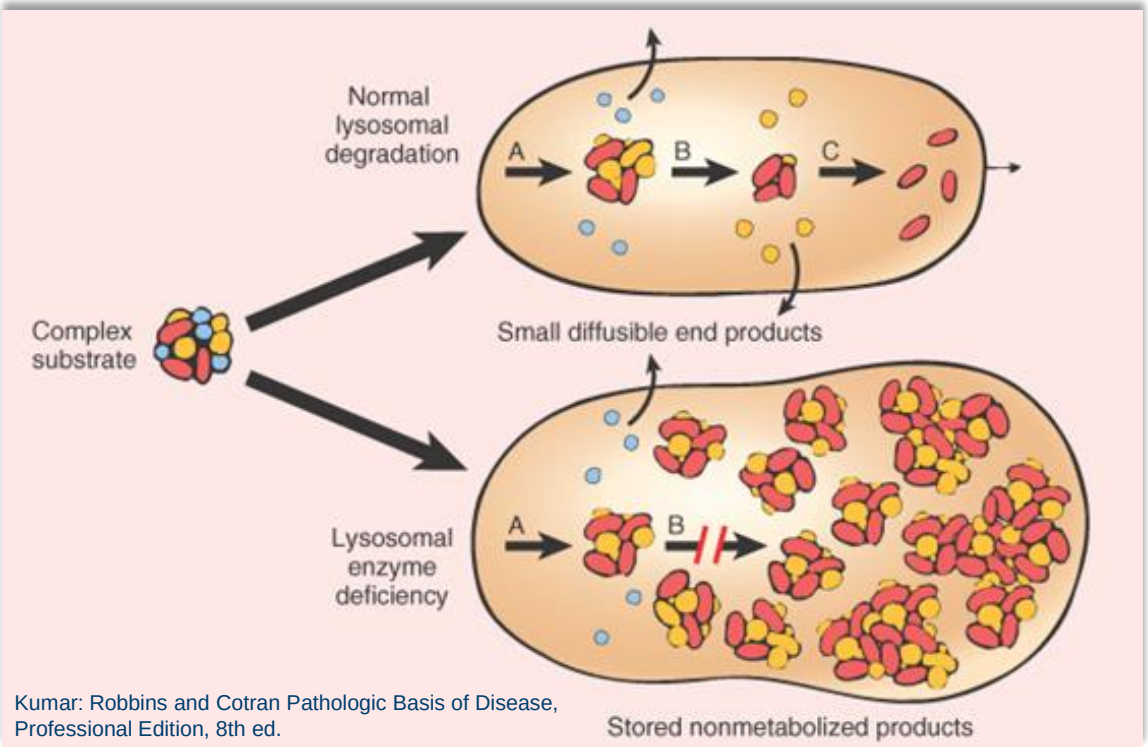
- Simultaneous detection of amino acids and acylcarnitines and organic acids – 40+ disorders can be recognized from a single DBS sample by MSMS

- Combined prevalence of all detectable disorders ~1 : 3,000

Potential LSD Candidates for Newborn Screening

Disorder	Prevalence	Therapy	Requires Early Detection
Pompe	1 : 40,000	ERT/SRT	+
MPS-I	1 : 100,000	ERT/SRT	+
Fabry	1 : 40,000*	ERT/SRT	+/-
Gaucher	1 : 57,000	ERT/SRT	+/-
Krabbe	1 : 100,000	BMT	+
Niemann-Pick A/B	1 : 250,000	?	?
MPS-II	1 : 136,000	ERT	+
MPS-IVA	1 : 250,000	ERT	+
MPS-VI	1 : 300,000	ERT	+

LSD affects Normal Functioning of Cells



Kumar: Robbins and Cotran Pathologic Basis of Disease, Professional Edition, 8th ed.

Accumulation of glycoproteins, lipids, mucopolysaccharides

Cell enlargement, dysfunction, death

Global LSD Newborn Screening Status

	Pompe	MPS-I	Fabry	Gaucher	Krabbe	Niemann-Pick A/B
Illinois, US	●	●	●	●	●	●
Missouri, US	●	●	●	●	●	
New York, US	●	●			●	
Washington, US	●	●	●			
Taiwan	●	●	●	●		
China			●			
Austria	●	●	●	●		●
Hungary	●	●	●	●		●
Italy	●	●	●	●		
Japan	●		●	●		

● Newborn Screening ● NBS Pilot Study

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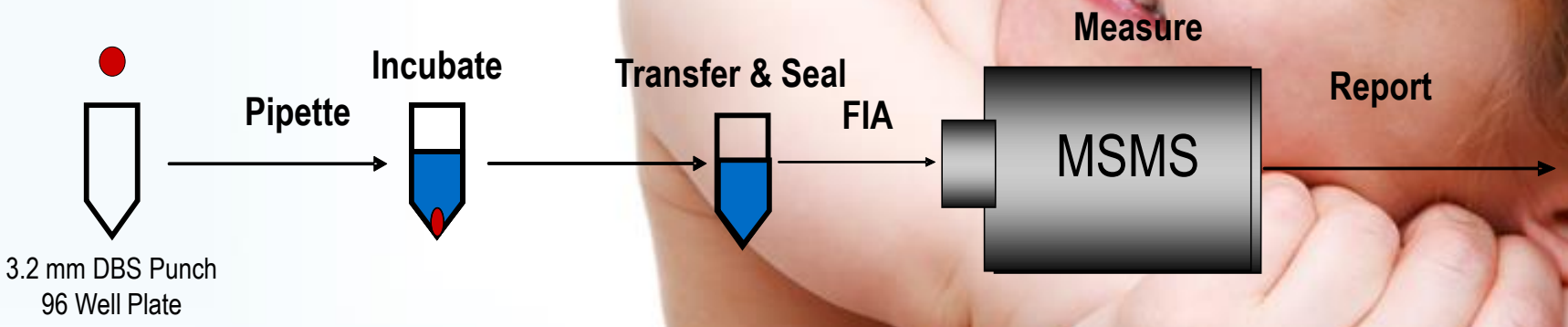
PKI MSMS Kits for NBS

- NeoBase AAAC
- LSD (in development)



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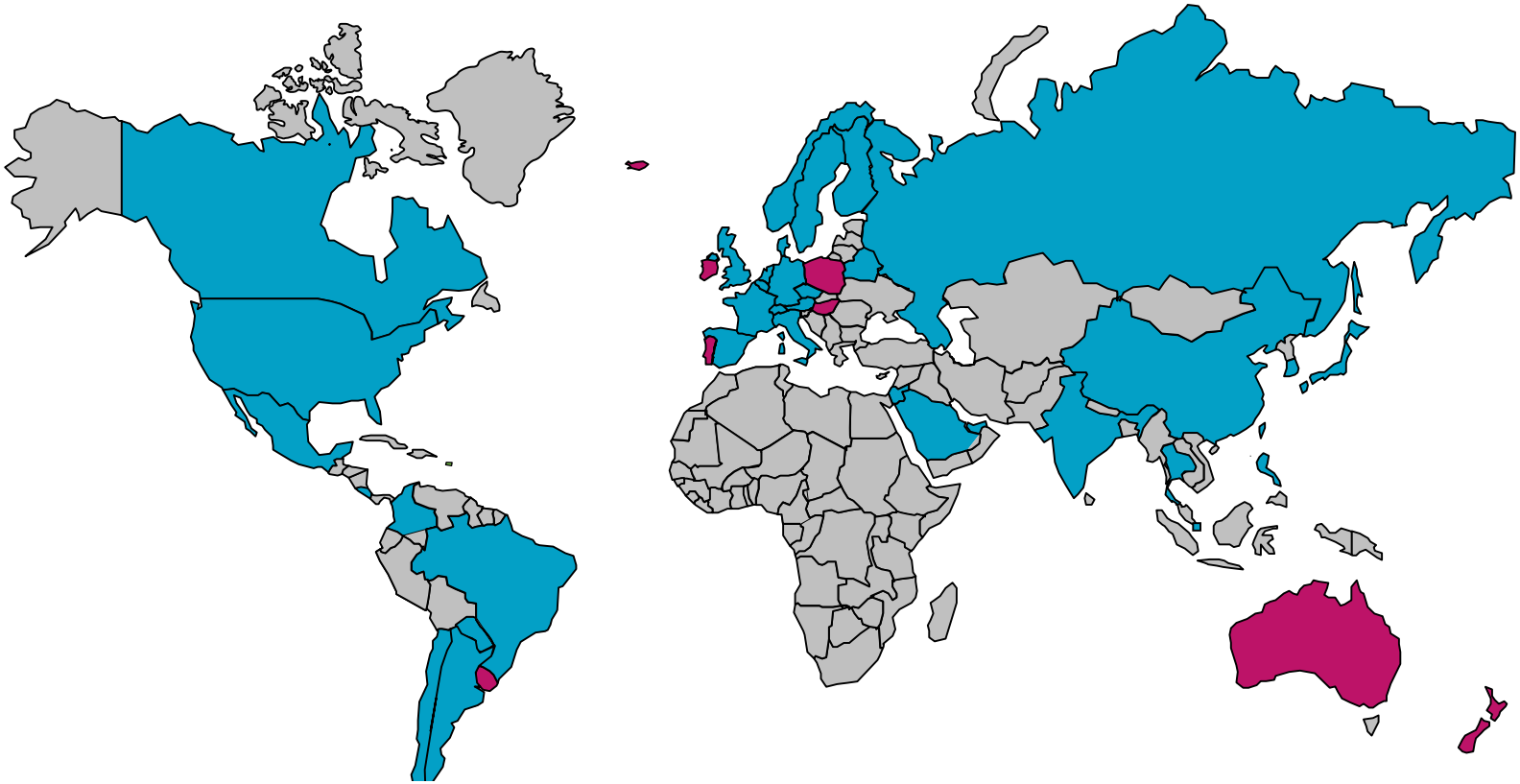
Global Expanded Screening Programs and Use of PerkinElmer NeoBase Kits



150 laboratories in 37 countries use PKI MSMS solution


SCID
SEVERE COMBINED
IMMUNODEFICIENCY

Newborn Screening for SCID

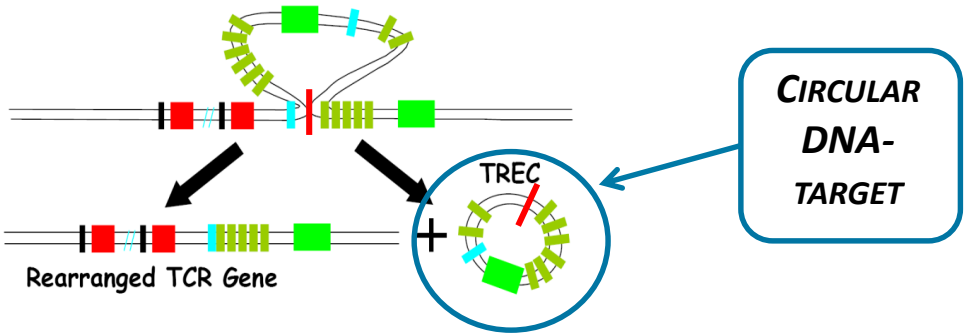
SCID

Late May 2010: HHS Secretary agreed to add SCID to the Uniform National NBS Panel in the US

TREC Test for SCID NBS

TREC

- SCID babies do not have TRECs
- TREC is circular DNA that can be quantified utilizing amplification (PCR)
- TREC assay for SCID screening – The 1st molecular biology assay in routine NBS



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EXPANDED NBS IN JAPAN

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Japan Newborn Screening History

1977	Nation-wide neonatal screening using Gathrie
1992	Expansion to 6 mandatory diseases
1997	Pilot screening using MSMS (Fukui Univ)
2004	National project of “Newborn mass screening using MSMS” (PI: Prof Yamaguchi, Shimane Univ)
2011	MHLW (Ministry of Health, Labor and Welfare) announcement to recommend MSMS in NBS
2014	Nation-wide screening using MSMS with an expansion to primary panels of 19 disorders

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Expansion to primary panels of 19 disorders

[Endocrine] – ELISA, EIA
1) Congenital hypothyroidism
2) Cangenital adrenal hyperplasia
3) Galactosemia

[Amino Acidemias] – HPLC, Guthrie
4) PKU
5) MSUD
6) Homocystinuria

2014

Congenital hypothyroidism
Congenital adrenal hyperplasia
Galactosemia

MSMS Expansion

[Primary panels]
1) **PKU**
2) **MSUD**
3) **Homocystinuria**
4) **CIT-1**
5) **Arginosuccinic aciduria**
6) **Methylmalonic academia**
7) **Propionic academia**
8) **Isovaleric aciddmia**
9) **3-MCC deficiency**
10) **HMG-CoA lyase deficiency**
11) **Multiple carboxylase deficiency**
12) **Glutaric aciduria type 1**
13) **MCAD**
14) **VLCAD**
15) **TFP(LCHAD) deficiency**
16) **CPT1 deficiency**

[Secondary panels]
17) Citrine deficiency
18) β-ketothiolase deficiency
19) CPT2 deficiency
20) TRANS
21) Carnitine uptake defect
22) Glutaric aciduria type 2

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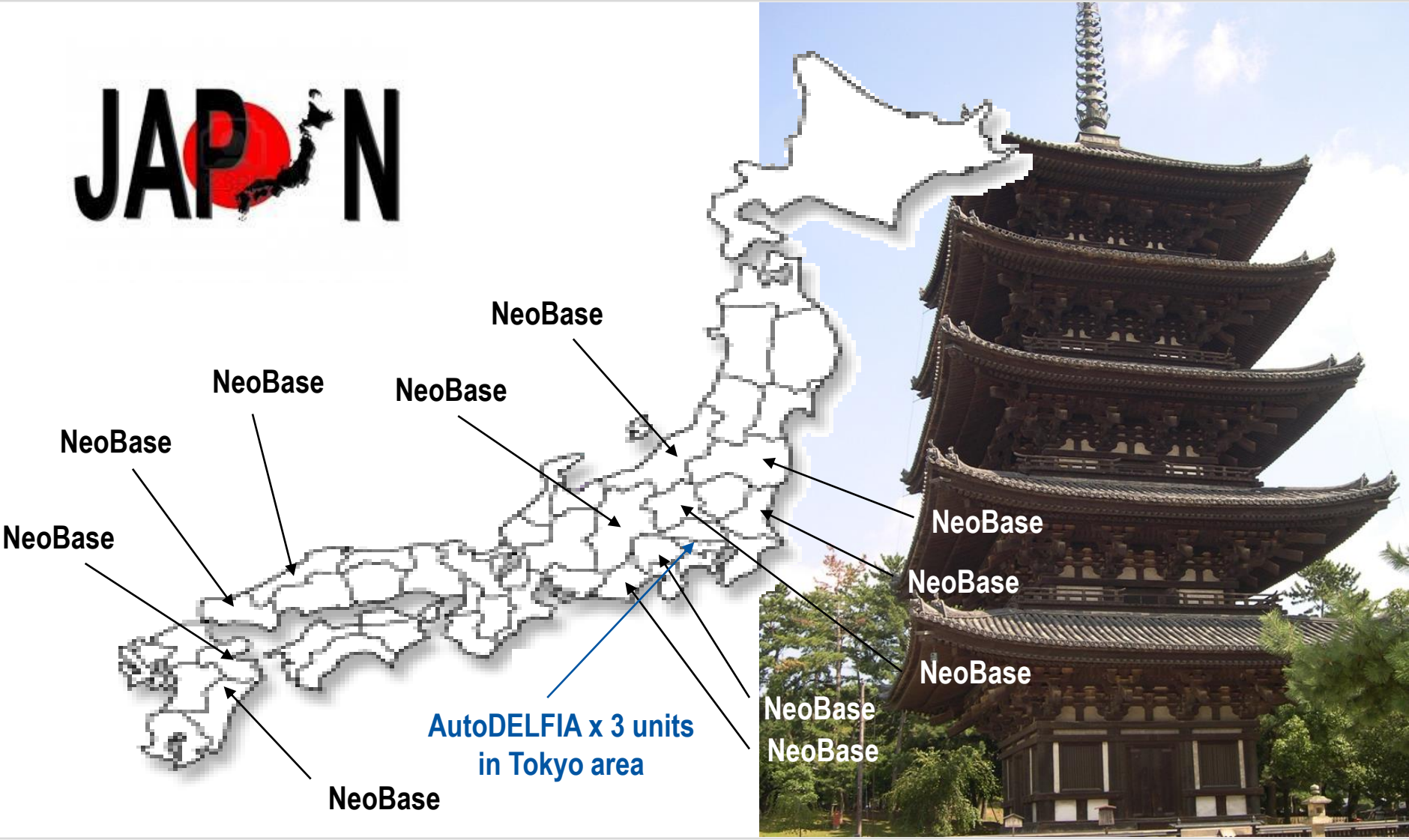
PerkinElmer presence in Japan



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ありがとうございます

Arigatou gozaimasu

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