Forum on Culture-Independent Diagnostics: Charting a Path for Public Health

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Enteric Diseases Laboratory Branch
NCEZID/DFWED

The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention
US disease agency in fiscal peril

Proposed budget changes threaten disease prevention and surveillance programmes.

BY MEREDITH WADMAN

When US President Barack Obama proposed a US$664-million cut in congressional funding for the US

Cuts to the CDC have already contributed to the loss of nearly 50,000 jobs in state and local health departments since 2008. This year, the administration argues that “efficiencies” will make possible the specific cuts it has proposed.
Forum on Culture-Independent Diagnostics: Charting a Path for Public Health

April 25-26, 2012; Atlanta, GA

Sponsored by CDC, APHL, and CSTE
Rapid ("Culture-Independent"; "Non-Culture") Tests
Rapid / Culture-Independent Tests versus Culture

<table>
<thead>
<tr>
<th></th>
<th>Culture</th>
<th>Rapid/culture-independent tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Speed</strong></td>
<td>Slow</td>
<td>Fast</td>
</tr>
<tr>
<td><strong>Infrastructure needed</strong></td>
<td>Significant</td>
<td>Minimal</td>
</tr>
<tr>
<td><strong>Expertise required</strong></td>
<td>Significant</td>
<td><strong>Minimal</strong></td>
</tr>
<tr>
<td><strong>Labor cost</strong></td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td><strong>Cost of materials</strong></td>
<td>Low</td>
<td>High</td>
</tr>
</tbody>
</table>
## Rapid / Culture-Independent Tests versus Culture

<table>
<thead>
<tr>
<th></th>
<th>Culture or standard tests (e.g. microscopy)</th>
<th>Rapid/culture independent tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td>Gold standard</td>
<td>Low to high</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>High</td>
<td>Low to high, almost always different</td>
</tr>
<tr>
<td><strong>Interpretation of positive findings</strong></td>
<td>Usually straightforward</td>
<td>Significant issues</td>
</tr>
<tr>
<td><strong>Range of pathogens detected</strong></td>
<td>All pathogens allowed by growth or test conditions</td>
<td>Limited to specific pathogen tested</td>
</tr>
<tr>
<td><strong>Allows for susceptibility testing &amp; genotyping?</strong></td>
<td>Yes</td>
<td>Generally no</td>
</tr>
</tbody>
</table>
Luminex launches xTAG™ Respiratory Viral Panel

Luminex Molecular Diagnostics, a division of Luminex Corporation, has launched xTAG Respiratory Viral Panel (RVP), an assay for the detection of multiple viral types and subtypes, including influenza, metapneumovirus and adenovirus. xTAG has been developed in association with a team of leading virologists and infectious disease specialists. The test can assess 12 viral targets at once and provide qualitative results in just few hours. The test has received 510(k) clearance from the US Food and Drug Administration (FDA) and CE mark for sale in Europe.

xTAG RVP was developed using LMD’s Universal Array which operates on the Luminex xMAP® system, a bioassay detection platform that can detect up to 100 different analytes simultaneously. The system uses lasers to read colour-coded microspheres that attach to specific nucleic acid sequences.

A doctor collects a sample containing viruses from a patient’s nasal cavity, throat, sinuses or bronchi. Nucleic acid is taken out from viruses found in the sample. Samples are then placed in a Luminex xMAP® instrument, where beads are read and analysed by lasers. The lasers identify the colour of the bead that is specific to a virus or subtype, and the presence or absence of the labeled primer. If a particular virus is present, the associated software identifies that as positive.

xTAG RVP facilitates physicians to determine whether a patient has cold, flu or another virus and to prescribe an effective treatment. The assay assists doctors in better decision-making in patient management, besides helping in limiting the spread of infection. This test will aid in reducing the overuse of antibiotics, which results into creating antibiotic resistant bacteria or superbugs.
Now you can test for 15 key bacteria, viruses, and parasites – all in under 5 hours

- xTAG® GPP is the first diagnostic to offer detection of 15 major gastrointestinal pathogens in a single test
- Results within 5 hours for timely and better patient care
- Fast turn-around time and multiplexing
Demise of GC Culture

- Rapid (hours)
- Urine specimen (vs urethral swab)
- Includes *Chlamydia trachomatis*
- High sensitivity/specificity
- No susceptibility data
- Specimen incompatible with culture
- Expensive
Impacts

- Patient Management
- Public Health Programs
  - Requiring accurate case counts
  - Isolate-requiring
Estimates of Foodborne Illness

Foodborne Illness Acquired in the United States—Major Pathogens
Blaine Snell, Robert M. Hechtman, Frederic J. Angulo, Robert V. Yolken, Marc Alain Wiblin, Shawn E. Roy, Jeffrey L. Jones, and Patricia M. Griffin

Foodborne Illness Acquired in the United States—Unspecified Agents
Blaine Snell, Patricia M. Griffin, Frederic J. Angulo, Robert V. Yolken, and Robert M. Hechtman

How Safe Is Our Food?
J. Glenn Morris, Jr.

Foodborne diseases are a real threat to the United States. It seems that each year, more than 1 in 10 people in the United States get sick, and nearly 1 in 100 are hospitalized. Although the causes of these problems are often difficult to identify, many are caused by eating contaminated food. This may seem like a simple solution, but finding and eliminating the sources of contamination is often complex and time-consuming. The best way to prevent foodborne illnesses is to eat foods that are prepared and handled safely. This involves choosing the right foods, cooking them properly, and storing them correctly. By following these guidelines, we can help ensure that our food is safe to eat.
Variability in diagnostic test performance

Incidence of STEC infections in FoodNet, 2008–2011

2011: 60 (36%) of 184 broths sent public health laboratories could be confirmed as Shiga toxin-positive
Culture-Independent Diagnostics: Burden, Attribution, Trends

- Understand extent of issue
- Study test performance
- Redefine case definitions
Impacts

- Patient Management
- Public Health Programs
  - Requiring accurate case counts
  - Isolate-requiring
    - Subtype-based tracking programs
    - Susceptibility monitoring
    - Subtype-based attribution studies
## Selected Microbial Disease Agents Under Surveillance

<table>
<thead>
<tr>
<th>Agent</th>
<th>Public health surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Salmonella spp.</em></td>
<td>Subtype, AST</td>
</tr>
<tr>
<td>Shigatoxin-producing <em>E. coli</em></td>
<td>Subtype, AST</td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em></td>
<td>Subtype, AST</td>
</tr>
<tr>
<td><em>Mycobacterium tuberculosis</em></td>
<td>Genotype, AST</td>
</tr>
<tr>
<td><em>Bordetella pertussis</em></td>
<td>AST</td>
</tr>
<tr>
<td><em>Neisseria meningitidis</em></td>
<td>Subtype, AST</td>
</tr>
<tr>
<td><em>Legionella pneumophila</em></td>
<td>Subtype (outbreaks)</td>
</tr>
<tr>
<td>Influenza virus</td>
<td>Serotype, AST</td>
</tr>
<tr>
<td><em>Neisseria gonorrhoea</em></td>
<td>AST</td>
</tr>
<tr>
<td>Methicillin-resistant <em>Staphylococcus aureus</em></td>
<td>Subtype (outbreaks)</td>
</tr>
<tr>
<td><em>Cryptococcus neoformans</em></td>
<td>AST</td>
</tr>
</tbody>
</table>
Global Meat Trade

Source: Center for Global Food Issues
Global Mortality (low and middle income countries)*

1. Heart disease
2. Stroke
3. Lower respiratory infections
4. HIV/AIDS
5. Fetus/newborn (perinatal) conditions
6. Chronic obstructive pulmonary disease (COPD)
7. Diarrhea
8. Tuberculosis
9. Malaria
10. Road traffic accidents

U.S.
- Significant burden
- Societal cost ~$77B
- Largely preventable

Nationwide reporting began in 1912

Reported *Salmonella* infections in the United States, 1920-2006

INCIDENCE PER 100,000 POPULATION

- **Typhoid Fever**
- **Non-typhoid Salmonellosis**

**National salmonella serotype surveillance**

CDC, National surveillance data
Ice-Cream Associated Outbreak; U.S.A., 1994

>250,000 cases
48 States
Nationwide reporting began in 1912

Reported *Salmonella* infections in the United States, 1920-2006

- Typhoid Fever
- Non-typhoid Salmonellosis

CDC, National surveillance data

**National salmonella serotype surveillance**
87 labs in the PulseNet USA network

- CDC PulseNet headquarters
- Regional labs
- Local and secondary state labs
- Federal labs

December 2011
Electronic Data Transmission

Public health laboratories

PFGE patterns

National database at CDC
The decade's 10 biggest food-borne illness outbreaks

By Jacque Wilson, CNN
updated 11:04 AM EST, Fri September 30
## Outbreak Response Team Weekly Unit Meeting

### Active Clusters

All data are considered preliminary and subject to change. Document not for distribution.

<table>
<thead>
<tr>
<th>Outbreak Log</th>
<th>Last wk on RL/HHS</th>
<th>#Wks FU</th>
<th>Isolate dates</th>
<th>Etiologic agent</th>
<th>Total ill</th>
<th>Total new</th>
<th>Last PN LL request</th>
<th>PN cluster #</th>
<th>PN pattern</th>
<th>PFGE in tops</th>
<th>Epi contact</th>
<th>Surv Epi</th>
<th>Priority</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>PATHOGEN: E. coli (n 2 )</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2011-0062 03/30 3 01/13/11 E. coli 14 0 03/28 1103PAEXH-1 □ Culpepper/ Culpepper Williams EXHX01.0126</td>
<td>□ -nothing new -monitoring</td>
<td>Vehicle Identified 3/28/11: 14 cases in 5 state CACO implicated Lebanon b is weighing futher options. We have been conducting robocalls in further testing among those</td>
<td>EXHA26.0570</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>2011-0013 03/23 8 12/27/10 E. coli 8 1 03/28 1102WIEXH-1 □ Pringle/Neil Pringle</td>
<td>□ -nothing new -monitoring</td>
<td>Vehicle Identified 3/28/11: This cluster comes from WI (4). Hazelum and Mixed vegetables. A voluntary recall was issued (CA). Hazelums have tested negative. New upload from WI case has</td>
<td>EXHX01.1159</td>
<td>EXHA26.3665</td>
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<tr>
<td>PATHOGEN: Salmonella (n 9 )</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>2010-0370 03/30 22 08/23/10 Salmonella Typhimurium 70 6 04/01 1010MLJPX-1 □ Capewell/B Nguyen arton EXHX01.0014</td>
<td>□ -Waiting CDC for EpiAid -assembling list of all these sold in US</td>
<td>Vehicle Identified 27/43 (63%) report any type of Salmonella 14028 strain; 29 unknown. A</td>
<td>JPPX01.0146</td>
<td></td>
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<tr>
<td>2011-0061 03/30 89 04/01/10 Salmonella Typhimurium 215 1 03/21 0909MAJX-1 □ Mettee/Bart Pringle JPXX01.0177</td>
<td>□ -multi-state conf call Tues at 4 -want to stop fling shipment</td>
<td>Hypoth Testing 3/28/11: We've received 34 cases. We've merged both clusters. Onset since 4/1/09. 64% rep</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2011-0066 03/30 3 02/07/11 Salmonella Panama 13 0 04/04 1102ORJKG-1 □ Schwensohn/ Schwensohn Williams JKGX01.0108</td>
<td>□ OR say they have a match? Vehicle Identified 4/4: Total of 13 isolates from epi investigation reports 12/18 Costco locations and a W Del Monte farm in Guatemala church event where Costco</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>2010-0384 01/26 17 12/21/09 Salmonella Enteritidis 372 18 04/04 1012WIJE garbage 1 □ Khan/Wrg Khan</td>
<td>Vehicle Identified</td>
<td>Khan/Wrg Khan</td>
<td>JEGX01.0034</td>
<td></td>
<td></td>
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</tbody>
</table>
2012 PulseNet-Triggered Outbreak Investigations (so far)

Clover sprouts sicken Jimmy Johns diners

Yellowfin tuna linked to salmonella outbreak in states
WASHINGTON (AP) - A yellowfin tuna sushi sashimi sold at restaurants and grocery stores in Columbia, federal health authorities said Tuesday, is linked to a salmonella outbreak that has sickened more than 150 people in nine states.

Taco Bell linked to recent Salmonella outbreak: report
(Red) - Yum Brands Inc. has been identified as the source behind a recent Salmonella outbreak in nine states.

Salmonella Outbreak Linked To Unpasteurized Tempeh Sickens 60

Recalled dog food tied to salmonella outbreak
By JoNeAleckia
At least 14 people in nine states have been sickened in an outbreak linked to a contaminated dog food.

Cargill Warns Of Salmonella-Tainted Ground Beef In Latest Recall
by APRIL FULTON

The Columbus D Hatchery in salmonella probe
MOUNT HEALTHY, Ohio (AP) - A mailman who says he's working closely with health officials is accused of being responsible for a salmonella outbreak traced to its chicks.

They Don't Eat Hedgehogs - But They Do Like Hedgehogs
ON SEPTEMBER 6, 2012

Up to 1 million mangoes recalled in Salmonella outbreak
Up to 1 million mangoes are being recalled voluntarily because they may be contaminated with Salmonella, as a preventive measure in the wake of 103 infections nationwide, a food distributor announced Thursday.

Largest Turtle-Linked Salmonella Outbreak Sickens 107 People, Mostly Kids

Indiana farm linked to salmonella-tainted cantaloupe

CDC: 103 salmonella infections linked to cantaloupe
<table>
<thead>
<tr>
<th>Year</th>
<th>Pathogen</th>
<th>Food</th>
<th>Amount recalled</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td><em>Listeria monocytogenes</em></td>
<td>Cantaloupe</td>
<td>Unknown</td>
</tr>
<tr>
<td>2011</td>
<td><em>Salmonella</em> Heidelberg</td>
<td>Ground turkey products</td>
<td>&gt;36,000,000 lbs</td>
</tr>
<tr>
<td>2010</td>
<td><em>Salmonella</em> Enteritidis</td>
<td>Shell eggs</td>
<td>&gt;500,000,000 eggs</td>
</tr>
<tr>
<td>2010</td>
<td><em>Salmonella</em> Montevideo</td>
<td>Ready-to-eat Italian sausage products/pepper</td>
<td>&gt;1,263,754 lbs</td>
</tr>
<tr>
<td>2009</td>
<td><em>E. coli</em> O157:H7</td>
<td>Cookie dough</td>
<td>300,000 cases of product</td>
</tr>
<tr>
<td>2009</td>
<td><em>Salmonella Typhimurium</em></td>
<td>Peanut butter/peanut products</td>
<td>&gt;3000 types of products</td>
</tr>
<tr>
<td>2008</td>
<td><em>E. coli</em> O157:H7</td>
<td>Ground beef</td>
<td>5,300,000 lbs</td>
</tr>
<tr>
<td>2007</td>
<td><em>Salmonella</em> I 4,5,12:i:-</td>
<td>Frozen pot pies</td>
<td>Millions of pot pies</td>
</tr>
<tr>
<td>2007</td>
<td><em>E. coli</em> O157:H7</td>
<td>Frozen pizza</td>
<td>5,000,000 pizzas</td>
</tr>
<tr>
<td>2007</td>
<td><em>E. coli</em> O157:H7</td>
<td>Ground beef (3 outbreaks)</td>
<td>35,400,000 lbs</td>
</tr>
<tr>
<td>2006</td>
<td><em>Salmonella</em> Tennessee</td>
<td>Peanut butter</td>
<td>326,000,000 lbs</td>
</tr>
<tr>
<td>2004</td>
<td><em>Salmonella</em> Enteritidis</td>
<td>Raw almonds</td>
<td>13,000,000 lbs</td>
</tr>
<tr>
<td>2003/’09</td>
<td><em>E. coli</em> O157:H7</td>
<td>Blade Tenderized Frozen Steak</td>
<td>865,046 lbs</td>
</tr>
<tr>
<td>2002</td>
<td><em>Listeria monocytogenes</em></td>
<td>Ready-to-eat poultry products</td>
<td>27,400,000 lbs</td>
</tr>
<tr>
<td>2002</td>
<td><em>E. coli</em> O157:H7</td>
<td>Ground beef</td>
<td>18,600,000 lbs</td>
</tr>
<tr>
<td>2000</td>
<td><em>Listeria monocytogenes</em></td>
<td>Ready-to-eat poultry products</td>
<td>16,900,000 lbs</td>
</tr>
<tr>
<td>2000</td>
<td><em>E. coli</em> O157:H7</td>
<td>Ground beef</td>
<td>1,100,000 lbs</td>
</tr>
<tr>
<td>1998</td>
<td><em>Listeria monocytogenes</em></td>
<td>Hot dogs, deli meats</td>
<td>35,000,000 lbs</td>
</tr>
<tr>
<td>1998/’08</td>
<td><em>Salmonella Agona</em></td>
<td>Toasted oats cereal</td>
<td>&gt;3,000,000 lbs</td>
</tr>
<tr>
<td>1997</td>
<td><em>E. coli</em> O157:H7</td>
<td>Frozen ground beef</td>
<td>25,000,000 lbs</td>
</tr>
</tbody>
</table>
Industries Stimulated to Change by PulseNet-Triggered Investigations

- Ready-to-eat & “ready-to cook” foods
- Peanut products
- Leafy greens
- Sprouts
- Dog food
- Spices
- Beef
- Eggs
- Tree nuts
- Other vegetables
- Poultry
- Mellon
- Eggs
- Chicken & broccoli & cheese
The foodborne disease surveillance system is to the food industry what radar is to automobile drivers – it is the “threat” of being caught that helps drive compliance with best safety practices.

from Mike Doyle, Ph.D;
CDC Public Health Grand Rounds November 2009
Under-appreciated Sources of Infection

- Salmonella in reptiles and amphibians
- Salmonella in baby chicks and ducks
- Vibrio vulnificus after fish handling
- Salmonella in “feeder” mice
- Salmonella in owl pellets
- Salmonella from microbiology lab exposure
- Salmonella and “pocket pets”

Multiple pathogens from live bird markets

STEC in petting zoos
PulseNet Cost Effectiveness Study (CIFOR; APHL; CDC)

An Economic Evaluation of the PulseNet Surveillance System

Robert L. Scharff, PhD, J.D.
Department of Consumer Sciences
College of Education and Human Ecology
The Ohio State University
Columbus, OH

Craig Hedberg, PhD
Division of Environmental Health Sciences
University of Minnesota School of Public Health
Minneapolis, MN
83 member countries from 7 national and regional PulseNet networks
Diffuse outbreak of EHEC caused by molding meat manufactured by one factory

From Dr. Kiyosu Taniguchi
International Outbreaks of Shigellosis in Denmark and Australia in 2007 associated with imported baby corn from Thailand

By author name and date
Two outbreaks of Shigella sonnei infections simultaneously detected in Denmark and Australia were found to be linked to the same baby corn packing house in Thailand. PulseNet played a key role in confirming this link when

International outbreak of Shigella sonnei associated with air travel to Hawaii in 2004

By multiple authors, Japan Journal of Infectious Diseases, July 13, 2006
In September 2004, investigation of outbreaks of Shigella sonnei in Japan and Hawaii revealed the following:
The collaboration through PulseNet USA linked both outbreaks to the same flight to Hawaii. In the United States, the Department of Health contacted a potential outbreak of S. sonnei and PulseNet USA participants in Hawaii listened by posting a different

Escherichia coli O157:H7 Infections Associated with Ground Beef from a U.S. Military Installation --- Okinawa, Japan, February 2004

In February 2004, the Okinawa Prefectural Chubu Health Center (OCHC) and the Okinawa Prefectural Institute of Health and Environment (OIHE), Japan, investigated three cases of Escherichia coli O157:H7 infection in a Japanese family associated with eating ground beef. Public health officials from multiple agencies in Japan and the United States collaborated on this investigation, which resulted in a voluntary recall of approximately 90,600 pounds of frozen ground beef in the United States and at U.S. military bases in the Far East. This was the first reported instance in which Japanese public health officials identified contaminated, commercially distributed ground beef that was produced in the United States. This report summarizes epidemiologic and laboratory investigations conducted by OCHC and OIHE. The results underscore the importance of using standardized molecular subtyping methods.
“A Big Victory for Public Health”

FDA decision to withdraw the use of Baytril in poultry

In a landmark decision, U.S. Food and Drug Administration (FDA) recently ordered the withdrawal of Baytril, an enrofloxacin, from use in poultry. This decision was made after years of opposition from the pharmaceutical industry and public health interests. Public health experts and contributions from the National Antimicrobial Resistance Monitoring System (NARMS) showed convincing evidence of the widespread resistance to fluoroquinolones in poultry. The ruling of FDA is considered a “big victory for public health.”

Please refer to the letter on the reverse side of this page for more details.
Current PulseNet methods (PFGE) and Next-Generation Methods (e.g. whole-genome sequencing) are Isolate-Dependent
Nationwide reporting began in 1912.

Reported *Salmonella* infections in the United States, 1920-2006

CDC, National surveillance data
## E. Coli O104:H4 Outbreak; 2011

### Number of cases reported to the WHO as for 21 July 2011

<table>
<thead>
<tr>
<th>Country</th>
<th>Deaths</th>
<th>HUS cases</th>
<th>Non-HUS cases</th>
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<tbody>
<tr>
<td>Austria</td>
<td>0</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Canada</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Denmark</td>
<td>0</td>
<td>10</td>
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<tr>
<td>France</td>
<td>0</td>
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<tr>
<td>Germany</td>
<td>48</td>
<td>857</td>
<td>3078</td>
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<td>Greece</td>
<td>0</td>
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**World health officials scramble to stem deadly E. coli outbreak**

By the CNN Wire Staff  
June 3, 2011 4:13 am, EDT

Tomatoes and cucumbers are displayed on May 30, 2011 in a stall in a supermarket in Paris.

### STORY HIGHLIGHTS

- **NEW** Spain's produce "safe for all consumers," Spanish official says

(CNN) -- Infectious disease detectives worldwide rushed Thursday to find the cause of an outbreak of a rare strain of E. coli that has spread to 10 countries and is blamed for at least 16 deaths and hundreds of illnesses.
General Strategies to Address Issue

- **Short-term**: Preserve isolates
- **Longer-term**: Develop culture-independent pathogen characterization methods
- **Very long-term**: paradigm shifting technologies
Short-term: Preserve isolates

- Modify reimbursement?
- Work with medical industry to make new tests compatible with public health needs
- Change criteria for medical device licensure?
- Modify State reporting rules
- Develop isolate recovery capacity for PHLs*
- Sentinel susceptibility surveillance*

*Requires new $$$
Targeted sequencing/detection

- CDC STEC genomics project
- 100,000 Pathogen Genome Collaborative (UC Davis, FDA, CDC, BGI)
Culture-Independent Subtyping/Virulence Assays: Targets

Conserved primer sites

- Characterize
- Variable region

Variable primer sites

Strain/species

A

B

C

Scoring

Allele
- Different sequence
- Different size (MLVA)

Presence/Absence
- Amplicon produced
- No amplicon
# STEC Detection and Genotyping Assay

## Targets and timeline for assay development

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**SNP**

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## Timeline

- **Summer 2011**:
- **Fall 2011**:
- **Fall 2012**:

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*Image of the CDC logo*
The “100K Pathogen Genome Project” is a public database of food pathogen genomes that will provide a roadmap for public-private development of methods to aid in quick identification and tracking of pathogens back to their source.

**100K Genome Project**

- Consortium
  - Sequencing to be done at BGI@UCDavis
  - Initial ~500 genomes will be closed
  - Genomes will be placed in the public domain
  - Metadata submission

- Outcomes
  - Population based assessment for new assay design
  - Clinical vs food isolates
  - Outbreak and trace back
    - Examine biogeography of genome to focus
    - SNPs for local divergence
    - Virulence and AR
  - An entire collection of isolates that match genomes

- Additional partnerships
  - Unique isolates
  - World wide representation
  - Food industry
  - Government
  - Academia

**Organisms of Interest**

- Salmonella
- *E. coli*
- Listeria
- Campylobacter
- Vibrio
- Norovirus
- Hepatitis A
- Shigella
- Yersinia
- Clostridium
- Enterococcus
- Cronobacter

More information: BCWEIMER@UCDAVIS.EDU
The Surveillance Process

Laboratory Reporting Takes Time

1 – 3 days

Contact with health care system: 1 – 5 days

Patient Eats Contaminated Food

Patient Becomes Ill

Diagnosis: 1 – 3 days

Stool Sample Collected

Salmonella Identified

Shipping: 0 – 7 days

Public Health Laboratory Receives Sample

Serotyping & DNA fingerprinting: 2 – 10 days

Case Confirmed as Part of Outbreak

1 – 3 days
Very Long-term: Paradigm-shifting Technologies

- Single cell isolation and sequencing; MS screening, “Lab-on-a-chip” technology
- Metagenomics
Metagenomic Approach

- Sequence selected targets (e.g. 16S, 18S rRNA)
- “Deep sequencing” (all genetic material in sample)
  - Assemble and identify contigs
  - Extract and analyze sequences of interest
Etiology of Acute Gastroenteritis in the U.S.

Total Cases
- Viruses: 67%
- Bacteria: 30%
- Parasites: 3%
- Unknown: 82%

Known Etiology
- Viruses: 67%
- Bacteria: 30%
- Parasites: 3%
- Unknown: 18%
“Proof-of-concept”

Evaluate sample preparation technologies, "enrichment" strategies

Build analysis capability / capacity

Develop links (MicrobeNet, Human microbiome project, 100K Pathogen Genome Project)

Analyze real world samples from outbreaks of known and unknown etiology
High probability, high impact issue

Risks of inaction and benefits of change are significant
Selected Microbial Disease Agents Under Surveillance

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<td><em>Cryptococcus neoformans</em></td>
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In this situation, “it takes money to save money”