

Interim Report:
**Blue-Ribbon Panel on the
Prevention of Foodborne
Cyclospora Outbreaks**

June 5, 2019

Table of Contents

| | |
|---|----|
| Introduction | 3 |
| Blue-Ribbon Panel Roster..... | 5 |
| Abstract | 9 |
| Working Groups: Interim Reports..... | 10 |
| I. Root Cause Assessment Working Group | 10 |
| II. Preventive Measures/Controls Working Group..... | 15 |
| III. Collaborative Approach Working Group..... | 18 |
| IV. Testing Validation Working Group | 21 |
| Summary Conclusions and Continuing Priorities | 22 |

Introduction

The 1996 cyclosporiasis outbreak in the United States and Canada associated with the late spring harvest of imported Guatemalan-produced raspberries was an early warning to public health officials and the produce industry that the international sourcing of produce means that infectious agents once thought of as only causing traveler's diarrhea could now infect at home. The public health investigation of the 1996 outbreak couldn't identify how, when, where, or why the berries became contaminated with *Cyclospora cayetanensis*. The investigation results were published in the *New England Journal of Medicine* in 1997.¹ I was asked to write an editorial to accompany the investigation report.² In my editorial, I noted the unknowns surrounding the *C. cayetanensis* contamination. The 1997 spring harvest of Guatemalan raspberries was allowed to be imported into both the United States and Canada—and again, a large outbreak of cyclosporiasis occurred. As in the 1996 outbreak, no source for the contamination of berries was found. Later in 1997, the Food and Drug Administration (FDA) prohibited the importation of future spring harvests of Guatemalan raspberries until a cause for the contamination could be demonstrated and corrective actions taken. While the FDA did not permit the 1998 importation of the raspberries into the United States, the berries continued to be available in Canada. Outbreaks linked to raspberries occurred in Ontario in May 1998.

When the U.S. Centers for Disease Control and Prevention (CDC)-led investigative team published its 1997 outbreak findings in the *Annals of Internal Medicine*,³ I was again asked to write an accompanying editorial.⁴ As I had done in my previous editorial, I highlighted how little we know about the factors associated with the transmission *Cyclospora* on produce and how to prevent it. Unfortunately, the state of the art for preventing foodborne, produce-associated cyclosporiasis had changed little since the 1996 outbreak despite the relatively frequent occurrence of such outbreaks.

Thirty-two years after that first Guatemalan raspberry-associated outbreak — and a year after produce-associated cyclosporiasis outbreaks that were linked to U.S.-grown produce — we have taken a major step forward in our understanding of these outbreaks and how to prevent them. After Fresh Express produce was implicated in one of the 2018 outbreaks, I was asked by the company leadership to bring together the best minds' around all aspects of produce-associated cyclosporiasis. The goal was to establish a Blue-Ribbon Panel to summarize state-of-the-art advancements regarding this public health challenge and to identify immediate steps that the produce industry and regulators can take to prevent future outbreaks. The panel was also formed to determine what immediate steps can be taken for any future outbreaks to expedite the scientific investigation to prevent further cases and inform public health officials.

The Blue-Ribbon Panel comprises 11 individuals with expertise in the biology of *Cyclospora*; the epidemiology of cyclosporiasis, including outbreak investigation; laboratory methods for identifying *C. cayetanensis* in human and food samples and the environment; and produce production. In addition, 16 expert consultants from academia, federal and state public health agencies (including expert observers from the FDA, CDC, U.S. Department of Agriculture, and California Department of Public Health), and industry, including producers and professional trade association science experts. The collaboration and comprehensiveness of this effort was remarkable. Many hundreds of hours of meetings and conference calls took place to determine our findings and establish our recommendations.

This document, "Interim Report: Blue-Ribbon Panel on the Prevention of *Cyclospora* Outbreaks in the Food Supply," summarizes the state-of-the art practices for the prevention of *C. cayetanensis* contamination of produce and priorities for research that will inform us as we strive to further reduce infection risk. Also, we make recommendations on how to more quickly identify and more effectively respond to produce-associated outbreaks when they occur. We greatly appreciate all the organizations represented on the panel and the expert consultants. The report does not, however, represent the official policy or recommendations of any other private, academic, trade association or federal or state government agency. Fresh Express has committed to continuing the Blue-Ribbon Panel process for as long as it can provide critical and actionable information to prevent and control *Cyclospora* outbreaks in the food supply.

Thank you to all the individuals who contributed to this important effort. This unique partnership of individuals, organizations, and firms represents the best in collaborative and consequential public health action.

Sincerely,

Michael T. Osterholm, PhD, MPH
Regents Professor
McKnight Endowed Presidential Chair in Public Health
Director, Center for Infectious Disease Research and Policy
Distinguished University Teaching Professor,
Environmental Health Sciences, School of Public Health
Professor, Technological Leadership Institute College of Science and Engineering
Adjunct Professor, Medical School
University of Minnesota
AND
Chair, Blue-Ribbon Panel on the Prevention of Foodborne Cyclospora Outbreaks

References

1. **Herwaldt BL, Ackers ML, Cyclospora Working Group.** An outbreak in 1996 of cyclosporiasis associated with imported raspberries. *N Engl J Med* 1997 May 29;336(22):1548-56
2. **Osterholm MT.** Cyclosporiasis and raspberries—lessons for the future. (Editorial) *N Engl J Med* 1997 May 29;336(22):1597-9
3. **Herwaldt BL, Beach MJ, Cyclospora Working Group.** The return of Cyclospora 1997: another outbreak of cyclosporiasis in North America associated with imported raspberries. *Ann Int Med* 1999 Feb 2;130(3):210-20
4. **Osterholm MT.** Lessons learned again: cyclosporiasis and raspberries. (Editorial) *Ann Int Med* 1999 Feb 2;130(3):233-4

Roster: Blue-Ribbon Panel on the Prevention of Foodborne *Cyclospora* Outbreaks

Panel Members

Dr. Michael Osterholm - Chair

Regents Professor
McKnight Endowed Presidential Chair in Public Health
Director, Center for Infectious Disease Research and Policy
University of Minnesota

John Gurrisi - Facilitator

Director Food Safety & Product Quality
Fresh Express

Dr. Craig W. Hedberg

Professor, Division of Environmental Health Sciences
School of Public Health
University of Minnesota

Dr. Gerardo (Jerry) Lopez

Asst. Professor/Extension Specialist
School of Animal and Comparative Biomedical Sciences
University of Arizona

Dr. Ynes Rosa Ortega

Associate Professor
College of Agriculture and Environmental Sciences
Center for Food Safety
University of Georgia

Industry Members

James (Jim) Brennan

President and Senior Technology Executive
SmartWash Solutions, Taylor Farms

Hank Giclas

Senior Vice President, Strategic Planning, Science & Technology
Western Growers Association

Dr. Jennifer McEntire

Vice President, Food Safety and Technology
United Fresh Produce Association

Dr. Mansour Samadpour

Principal & CEO
IEH Laboratories & Consulting Group

Dr. Bob Whitaker

Chief Science and Technology Officer
Produce Marketing Association

Dr. Trevor V. Suslow

Vice President of Produce Safety
Produce Marketing Association

Federal and State Government (Observers) Providing Technical Assistance

***NOTE:** CDC, FDA, USDA and CDPH subject-matter experts participated in the Blue-Ribbon Panel as “observers,” as it was explained at the November 2018 in-person meeting. These agency experts provided technical assistance to the working groups. The technical assistance provided does not confer an *imprimatur* of approval or endorsement of the opinions, conclusions or recommendations contained within the report by any of these agencies.

Federal and State Government

U.S. Food & Drug Administration (FDA)

Dr. James Gorny

Senior Science Advisor, Division of Produce Safety
Office of Food Safety
Center for Food Safety and Applied Nutrition (CFSAN)

Kari Irvin

Deputy Director
CFSAN

William Correll

Director, Office of Compliance
CFSAN

Maria Knirk

Deputy Director, Division of Enforcement
Office of Compliance
CFSAN

U.S. Centers for Disease Control and Prevention (CDC)

Dr. Barbara L. Herwaldt

Medical Epidemiologist, Parasitic Diseases Branch
Division of Parasitic Diseases and Malaria
Center for Global Health

Dr. Anne Straily

Veterinary Epidemiologist, Parasitic Diseases Branch
Division of Parasitic Diseases and Malaria
Center for Global Health

California Department of Public Health

Emily Kelly

Epidemiologist, California Epidemiologic Investigation Service
Food and Drug Branch
Center for Environmental Health

Working Groups (* See Listing under Blue-Ribbon Panel)

Root Cause Assessment

Dr. Trevor V. Suslow – Leader*

Preventive Measures/Controls

Dr. Craig W. Hedberg – Leader*

Jim Brennan*

Dr. Bob Whitaker*

Dr. Trevor Suslow*

Dr. Barbara Herwaldt*

Collaborative Approach

Dr. Jennifer McEntire – Leader*

John Gurrisi*

Testing Validation

Dr. Gerardo (Jerry) Lopez – Leader*

Dr. Ynes Ortega*

Jim Brennan*

Dr. Mansour Samadpour*

Dr. Alexandre (Alex) daSilva
Senior Biomedical Research Microbiologist
CFSAN, FDA

Dr. Mauricio Durigan
Office of Applied Research and Safety Assessment
CFSAN, FDA

Helen Murphy
Research Microbiologist, Office of Applied Research and Safety Assessment
CFSAN, FDA

Dr. Robert Mandrell
Scientist
Retired Produce Safety and Microbiology Research Unit Leader
Agriculture Research Service
U.S. Department of Agriculture

Dr. Yvonne Qvarnstrom
Division of Parasitic Diseases and Malaria
Parasitic Diseases Branch
Center for Global Health, CDC

Dr. Michael J. Arrowood
Division Foodborne, Waterborne & Environmental Diseases
Waterborne Disease Prevention Branch, CDC

Amy M. Kahler
Division Foodborne, Waterborne & Environmental Diseases
Waterborne Disease Prevention Branch, CDC

Daniela de Jesus Cabrera
Research Associate
University of Arizona

Monique Torres
Research Associate
University of Arizona

Abstract

In the spring and summer of 2018, Fresh Express and other fresh produce suppliers were linked to a *Cyclospora cayetanensis* outbreak — with U.S.-grown fresh produce samples testing positive for the parasite. To address this issue, Fresh Express formed the Blue-Ribbon Panel on the Prevention of Foodborne *Cyclospora* Outbreaks, comprising scientists with deep expertise in the biology of the organism, food safety, outbreak response, and public health. The panel was charged with studying the parasite and identifying controls to limit further *C. cayetanensis*-associated outbreaks. After a November 2018 in-person meeting, the Blue-Ribbon Panel formed four working groups that continued to work on *C. cayetanensis* specific issues related to root-cause assessment, preventive measures/controls, collaborative approach, and testing validation over the next several months. This report contains the working groups' preliminary findings, recommendations, and continuing priorities to more effectively prevent and control *C. cayetanensis* outbreaks going forward.

Working Groups: Interim Reports

I. Root Cause Assessment Working Group

Charge to the Working Group

A review of available data and information, industry monitoring, and root-cause analysis may help identify potential contributing factors associated with produce contamination and develop possible additional preventive measures to reduce the risk of cyclosporiasis.

The purpose of this report is to provide the BRP with additional background that may be informative in framing an assessment using the Root Cause Analysis Tool (RCAT) for the 2018 cyclosporiasis outbreaks.

Although several outbreaks attributed to *C. cayetanensis* occurred during 2018 that were linked to fresh produce — particularly multi-commodity vegetable trays, cilantro, and others — this working group focused initial attention on the outbreak associated with a romaine lettuce mix. Others will be assessed as the group continues its collaborations.

Background

In connection with the outbreak linked to a romaine lettuce mix, trace-back to multiple product and raw material suppliers (at multiple implicated farm locations) was established.

This initial report differentiates RCAT from the better known root cause analysis (RCA), which reflects the greater absence of accessible, documented, factual, and verifiable information and data than would be required for launching a systematic process for substantially resolving the event-specific underlying origins or source of primary, secondary, or any subsequent or persistent contamination source(s). Though more limited and, most often, forward-looking, RCAT is generally relied on to assemble credible predicated factors — based on scientific principles and informed opinion or knowledge of problem-associated practices — to identify priority areas. These areas are then the focus of deeper investigation in the face of limited, sequestered, embargoed, or potentially conflicting information among involved parties.

This interim report is not intended to provide an instructional or operational guide to conducting an RCAT or RCA. The materials that follow are a best effort, using limited documentation and access to the most knowledgeable people, to construct a framework for the *C. cayetanensis* environmental assessment that future data can flesh out as official reports are made public. There is also a body of privately held information regarding the particular *C. cayetanensis* outbreak that may prove informative for the good of public health protection; however, it has not been made public by private companies.

Hypothesis Generation — *C. cayetanensis* Outbreak Linked to Romaine Lettuce Mix

As evident from the other working group interim reports, identifying the problem is not a limitation to developing an RCAT hypothesis. Outbreak investigative evidence, epidemiology, trace-back, and secondary on-farm investigative follow-up strongly indicated raw material contamination to a domestic production source in California. *C. cayetanensis* was identified as the responsible agent and romaine lettuce as the probable food vehicle. Clearly, from the known biology of this signature human parasite, the scope of sensible presumptive direct and indirect sources of contamination is narrower than with recognized zoonotic and environmental pathogens. Therefore, the typical on-farm process of developing a five-step RCA plan or fishbone diagram of inputs, practices, environment, and human elements is either reduced or unnecessary to organize a hypothesis generation approach.

In this case, the priority questions for an RCAT factor determination may reasonably include:

1. Is contaminated environmental run-off, crop management source water, or harvest activity water a likely root cause?
2. Is direct human-sourced transfer of *C. cayetanensis* to raw materials during harvest a likely root cause?
3. Is the identified convergence of contract harvest labor and moveable harvest equipment a singular commonality as a contamination source and contract farm and harvest labor crew country/locale of origin sourcing the root cause of this specific *C. cayetanensis* contamination event?
4. Is indirect cross-contamination from *C. cayetanensis*-harboring fomites to raw materials a likely root cause?
5. Is direct or indirect mechanical or non-host fecal transfer of *C. cayetanensis* from an environmental point source (e.g., coprophagous [feces-consuming] vectors) or non-point source (e.g., vector movement between a contaminated environmental surface water and production field, equipment, etc.) to raw materials a likely root cause?
6. Are uncharacterized, regionally widespread environmental sources (e.g., wastewater watershed discharge; wastewater spray-fields) of *C. cayetanensis* the fundamental and foundational root cause of recently recognized domestic sources of raw product contamination?

Retrospective RCAT

The following RCAT matrix summarizes information obtained by a series of in-person interviews and farm location visits related to this outbreak. At the time of the preparation of this brief, the environmental assessment report from the California Department of Public Health (CDPH) had not been completed. However, enough corroboration of independently acquired information from other than the CDPH during this RCAT process was verbally acknowledged as substantially accurate to have confidence in the substance of this assessment.

| RCAT Factor | | Severity of Widespread Contamination in Raw Product | Probability | Plausibility (Specific to Potentially Implicated Farms) | Temporal Opportunity for Maturation |
|-------------|---|---|----------------|---|-------------------------------------|
| 1A | Environmental runoff | High | Moderate | Low | Yes |
| 1B | Agriculture water contamination | High | Low | Very low | Yes |
| 1C | Harvest use water | High | Very low | Very low | N/A |
| 2 | Farm laborer direct contact | Moderate | By policy, low | In practice, unresolved | No |
| 3A | Contract harvest crew | Moderate | High | Unresolved but plausible | Possible link to 3D |
| 3B | Farm and harvest worker origin | Moderate | High | High but unresolved | Possible link to 1A,3D,4A,4B,5A,5B |
| 3C | Condition of labor housing | Moderate | Low | Low | High |
| 3D | Harvest equipment | High | High | Implicated but unresolved | High |
| 4A | Cross-contamination from fomite — farm laborer clothing | Moderate | Low | Low but unresolved | Possible but unresolved |
| 4B | Cross-contamination from fomite — harvest knives | Low | Low | Low | Possible but unresolved |
| 4C | Cross-contamination from fomite — harvest platform | High | Low | Low | Possible but unresolved |
| 5A | Animal vector mechanical transfer | Low — generally moderate as focal point | Unknown | Unknown | Pre-acquisition — high |
| 5B | Coprophagous vector shedding | Low — generally moderate as focal point | Unknown | Unknown | Pre-ingestion — high |
| 6 | Regional persistent environmental source(s) | High | Low | Low but unresolved | High but unresolved |

Notes on a few key factors:

- The water sources used for crop production and management on both farm locations were unlikely to be sources of intrusion of human fecal contamination. Review of the sources didn't identify a plausible point or non-point route of contamination.
- At-harvest water treatment was reported not to have been used on the romaine lettuce designated for further processing.
- No water, farm, or environmental sample or swab was positive for *C. cayetanensis*. Details, including the number of samples taken, are not available at this time, but they will be made public when the investigative report is released.
- Contract farm laborers, including irrigators and harvest crews — as well as harvest equipment — were common to identified farms and a third non-implicated farm.
- The water sources used for crop production and management at this non-implicated farm location were unlikely sources of intrusion of human fecal contamination.
- Investigative follow-up by CDPH of a romaine harvest at a non-implicated farm, but an implicated and tracked contract harvest operation, resulted in molecular positives on romaine transported directly to a local cooler, using the protocol detailed in the Food and Drug Administration (FDA) Method BAM 19b: Molecular Detection of *Cyclospora cayetanensis* in Fresh Produce Using Real-Time PCR.
 - Romaine lettuce samples from this lot were collected directly upon arrival at the commercial cooler and taken from the original pallet bins.
 - Samples of unharvested romaine collected by the FDA from the same non-implicated farm did not yield *C. cayetanensis*.

Recommendations (Preventive/Knowledge Development)

- Survey environmental water sources for *C. cayetanensis* using validated methods for FDA BAM 19b.
 - Environmental watershed sources are not used for crop management in the implicated growing region, but published research has documented that other indicators of human waste contamination are present.
 - FDA BAM 19b is currently undertaking collaborative studies to define validated protocols for environmental testing.
- Conduct further assessment of need and implementation of screening and possible deferral of employment until consecutive tests are negative of H-2A labor pool sources (temporary foreign farm workers) before transportation to the United States. It has been suggested that prophylactic antimicrobial treatment be considered for these workers before arrival to the United States. However, additional study of the efficacy and the safety of the potential widespread use of antimicrobial treatment should be completed before serious consideration be given to this approach.
- To further investigate the root causes of the 2018 romaine outbreak, conclusive evidence for the absence of cold-storage inventory romaine lettuce from a different production region, used at the implicated regional processor, should be resolved.
 - This romaine lettuce, similarly contaminated with *C. cayetanensis*, may be the leading indicator of epi-curve cases attributable to this farm labor pool.
- As validated, apply tools for *C. cayetanensis* subtyping to resolve the possibility of multiple sources of contamination, which may include endemic community sources at the regional processing facility.

Recommendations (Incident Response and Active RCA Actions)

- Evaluate agriculture water sources and adjacent and regional environmental water bodies for evidence of human wastewater and septic sources. Published survey data indicate that environmental watershed and surface water bodies had widespread prevalence of human norovirus, suggestive of a human fecal waste source connection (Tian P, Yang D, Shan L, et al. Concurrent detection of human norovirus and bacterial pathogens in water samples from an agricultural region in central California coast. *Front Microbiol* 2017 Aug 21;8:1560).
- Assess the area for evidence of noncompliance with sanitary facility use and non-farm employee human encampments.
- Increase efforts to attribute animal vector cross-contamination potential, especially birds, from contaminated environmental water bodies receiving non-point source runoff.

II. Preventive Measures/Controls Working Group

Charge to the Working Group

The purpose of the Preventive Measures/Controls Working Group was to review available information in order to guide the development of preventive measures to reduce the risk for transmission of *C. cayetanensis* from farm to fork. The initial focus was centered on developing practical preventive measures and controls for the fresh produce industry by drawing on existing information, outbreak investigations and data, and research studies or other sources that can be immediately applied to reduce the risk of cyclosporiasis from farm to fork. With annual outbreaks occurring, a reasoned level of immediate prevention and best practices will benefit the industry and public health.

Observations

U.S. foodborne outbreaks of *C. cayetanensis* infection have occurred seasonally, which, for outbreaks involving an identified produce item and its source, has reflected the seasonality of infection and endemic human transmission where the produce was grown. The seasonality differs among cyclosporiasis-endemic regions, but the environmental and other factors that account for the seasonality have not been identified.

The routes of contamination of the implicated produce have not been definitively established. However, for example, for outbreaks linked to Guatemalan raspberries, on the basis of various types of evidence — including from environmental assessments — the leading hypothesis is that agricultural water sprayed on the berries was contaminated.

- Notably, outbreaks associated with Guatemalan raspberries were characterized by high attack rates among exposed individuals and illness following consumption of only a few berries. This suggests both a low infectious dose and fairly uniform contamination of the implicated berries.

Although industry-wide efforts to prevent contamination of romaine lettuce by pathogenic bacteria focus on the use of agricultural water, several key features of *C. cayetanensis* differ from STEC and need to be addressed in preventing *Cyclospora* transmission.

- *Cyclospora* is more resistant to routine chemical disinfection processes than STEC. Thus, water testing and treatment targeted to control STEC may not be adequate to control *C. cayetanensis*
- Water source protection is focused on animal reservoirs, primarily cattle, whereas *C. cayetanensis* is not known to have an animal reservoir hosts. Though animals may ingest *C. cayetanensis* oocysts and mechanically spread them through their feces, they are not known to become infected or to amplify the number of oocysts. Thus, prevention of human fecal contamination appears to be the primary need for water source protection.
- *C. cayetanensis* appears to require at least 1 to 2 weeks under favorable environmental conditions to become infectious. This lengthy extrinsic maturation period must be taken into account when considering the possibility and plausibility of fresh produce becoming contaminated through various means and for the oocysts (if not already infective when the produce becomes contaminated) to have sufficient time, under favorable conditions, to become infective by the time that the contaminated produce is consumed.

Additionally, the working group took the following into consideration:

- Environmental studies of water contamination are being conducted in Arizona and are planned in California to assess the presence of *C. cayetanensis* in agricultural water.
- Although previously unexposed persons with untreated infection can have remitting-relapsing symptoms for weeks to months, more information is needed about the duration of asymptomatic vs. symptomatic shedding of the parasite in untreated persons in cyclosporiasis-endemic regions, including the potential for a long-term carrier state.
- The potential role of contaminated agricultural equipment used in propagation or harvesting of fresh produce is unknown.
- Worthy of attention: Septic system control issues and potential watershed/ground water infiltration from sewage systems.
- Substantial discussion surrounded the *C. cayetanensis* lifecycle reliance on a human host and the human waste factor involvement as a factor in *C. cayetanensis* illness outbreaks linked to fresh produce.
- With respect to human waste, it is essential to use a risk-based analysis and preventive controls model.
- Human carriers may or may not be symptomatic and, if aware of illness, may not seek treatment, thus potentially spreading infection.
- Many temporary workers on H-2A class visas work the fields to grow and harvest produce.
- Fresh produce growers, harvesters, processors, and handlers must be aware of the means by which human waste could enter the water system, especially open water sources, water used for overhead or furrow irrigation, ditches in which water accumulates, and sewage system infiltration of reservoirs.
- A key question to consider is the significant presence of recreational vehicles (RVs) and portable toilets along fields and open water sources in growing regions, as well as investigation into the processes used to manage the human waste they generate.
- The types of compounds used for portable toilet sanitation are likely not consistent or effective in killing *C. cayetanensis*.
- Similarly, sanitizers used on harvesters and other field equipment or on processing equipment may not effectively kill *C. cayetanensis*; chlorine produce wash water is ineffective in killing the oocysts.
- RV waste management, field sanitary facilities, and in-ground sanitary practices are not known or managed.
- Field food safety and hygiene practices such as handwashing are monitored, but other possible points of contamination from feces, such as boots or clothing, are not addressed.
- Barriers exist to clinical testing of workers in the United States.

Recommendations

- Source protection for agricultural water should emphasize protection against human fecal contamination.
- Because humans appear to be the primary reservoir for *C. cayetanensis*, surveillance of diarrheal illness among workers involved in propagation and harvesting of fresh produce should be conducted, and workers with diarrheal illnesses be tested for *C. cayetanensis* and other enteric infections.
- Equipment used in propagation and harvesting of fresh produce should be maintained and cleaned to prevent *C. cayetanensis* transmission.
- Prevention measures need to account for the extrinsic maturation period of *C. cayetanensis*. This should include awareness of events and activities in the field at least 1 to 2 weeks before harvest, or at the time of harvest with regard to water, equipment, or environmental materials that were contaminated 1 to 2 weeks earlier.

III. Collaborative Approach Working Group

Charge to the Working Group

Optimize industry monitoring and RCA to research outbreak investigation findings to identify and communicate innovative methods and actions to reduce the incidence of produce-associated cyclosporiasis. This will be done by drawing from new and creative collaborative approaches between federal, state, and local public health agencies, regulatory agencies, and private-sector growers and processors or those in the wholesale and retail distribution chain.

Approach

It was determined that this effort should be informed by industry professionals as well as the government officials who actively investigate cyclosporiasis outbreaks.

Observations and Recommendations

Near-term measures to improve *Cyclospora* surveillance and investigations

- Because cyclosporiasis has historically been associated with fresh produce, a national hypothesis-generating questionnaire (HGQ) specific to *C. cayetanensis* focuses only on fresh produce.
 - **Recommendation:** Review the current HGQ with industry to account for changes in consumer preferences and to ensure that product descriptions are clear and readily delineated.
- Investigation processes are similar to other foodborne outbreaks except that, with a 2-week incubation period, case-patients are interviewed about 6 weeks later.
 - **Recommendation:** Improve the process for collecting food history data. Loyalty/shopper card data should be made readily available upon request.
- Clinical diagnosis has increased owing to better detection methods (including culture-independent methods) for rapid and specific diagnostic identification of *C. cayetanensis* in clinical samples. The CDC posts annual case counts that show the dramatic rise in cases. All cases are grouped together because of the lack of the ability to distinguish relatedness through genotyping.
 - **Recommendation:** Share updated case counts regularly, highlighting thresholds at which investigations are initiated and distinguishing outbreak cases from unrelated cases.
 - **Recommendation:** Improve governmental and subsequent industry communication to convey the uncertainty around reasons for observed rises in case counts.
- Defining an outbreak of cyclosporiasis relies on the epidemiologic assessment of person, place, and time clustering of cases rather than on subtype characteristics of the organism. During an outbreak, reporting at a pre-determined frequency may not be sufficient.
 - **Recommendation:** Establish state and CDC alignment around criteria for including an illness in the outbreak case count.
 - **Recommendation:** Informally share updated case counts related to the outbreak with company contacts so firms can make decisions to protect public health.

- **Recommendation:** Ensure that potentially involved firms have access to summaries of all cluster investigations — not just related to their product — because epidemiologic analysis of case exposure data may be the sole source of evidence linking a food source to the outbreak.
- **Recommendation:** Communicate that to the public multiple, different food products may be causing illness, and that overall case counts are not reflective of one large outbreak.

Long-term measures to improve *Cyclospora* surveillance and investigations

- The inability to genotype prevents sorting cases by relatedness.
 - **Recommendation:** Aggressively work to develop genotyping or other typing methods that can be used to identify linked cases.
- Because of the uniqueness of the organism, very few laboratories, particularly at the state level, are equipped to analyze food samples for *C. cayetanensis*. When food samples are available for analysis, implicated firms may perceive the lack of lab capacity as a lack of urgency by investigators.
 - **Recommendation:** Expand the matrices validated for FDA method 19B (or any updated method). Improve the capacity of public and private laboratories to analyze food samples for *Cyclospora*, and prioritize samples related to outbreaks over samples taken as part of surveillance sampling.
 - **Sub-recommendation:** Improve the capacity of states to analyze samples for *Cyclospora*. This can be prioritized by states that typically have the most cases or where fresh produce historically associated with *C. cayetanensis* is grown.
- When epidemiology is strong and the source is known or presumed, the FDA leads industry calls. The CDC relies on the FDA to serve as a liaison with industry.
 - **Recommendation:** Develop relationships between the produce industry and the CDC's parasitology group so that, as appropriate, the CDC can request industry information (e.g., supply chains, seasonality).
- Because the ecology of *C. cayetanensis* differs from other foodborne pathogens, the on-site investigation into root causes of contamination differs. There is a general investigation (GAPs) framework that is followed, and also a tailored component, informed by agency specialists who focus on that pathogen.
 - **Recommendation:** Improve training and education within the food industry (e.g., distribution of the fact sheet and accompanying webinars and discussions coordinated by trade associations, with input from academics and government agencies) regarding *C. cayetanensis*, its host, life cycle, effective (and ineffective) treatments and controls, and recommended preventive measures.
- Because the ecology of *Cyclospora* differs from vegetative pathogens and is not as well understood, investigators should consider outbreaks as an opportunity to aggressively investigate (e.g., aggressive sampling and testing of product, environment, workers); currently limited lab capacity may prevent aggressive sampling. Impediments to assessing worker carriage of the parasite should be addressed.

- **Recommendation:** Focus on activities occurring weeks before products were harvested, keeping in mind the long *C. cayetanensis* life cycle.
- **Recommendation:** Conduct microscopic analysis, not just polymerase chain reaction (PCR), to determine the presence of sporulated oocysts; sporulation is a biologic indicator of the organism's viability. A PCR-positive fecal or environmental sample may not correlate directly to public health risk.

IV. Testing Validation Working Group

Charge to the Working Group

Improved detection, particularly from potential environmental sources, is a necessary tool to help confirm what is hypothesized to potentially be contributing to contamination events. Of those currently doing research on *Cyclospora*, including regulatory agencies such as the FDA, there is a need to align validated common methodologies.

Key Learnings/Findings

- The group concurred on the need to validate a global testing standard for *C. cayetanensis* that encompasses clinical, food, and environmental samples and addresses DNA extraction method, typing profile for sequencing markers, mitochondrial DNA, equipment, different chemistries, etc.
- The working group can be useful in generating this standard.
- Testing for *C. cayetanensis* is very different than testing for bacterial pathogens with far greater challenges (oocysts, testing stage in infectivity cycle, DNA extraction, environmental concentration of oocysts, etc.).
- Is it possible to come to a consensus between various testing methodologies as to whether variations of the 19b method to optimize detection across clinical, food, and environmental platforms? That strategy can move us toward the global standard.
- There was strong group consensus that sharing experiences and data in the working group are beneficial.

Recommendations

- Produce an explanatory fact sheet and develop standardized, validated methodologies.

Next Steps

- There was general discussion surrounding the need for continuing collaboration by the working group to move toward a more definitive, scientifically supported, universally applicable testing methodology, as no reliable method across needed testing platforms exists.
- Members discussed various research under way that is making progress, and the role the working group can play in sharing findings and collaborating.
- Many challenges remain, but mitochondrial genome sequencing holds significant promise.
- Validated testing methodology is critical to protect public health, confirm infective oocysts, and provide concrete rule-in/rule-out direction for the industry and for regulators.

Summary Conclusions and Continuing Priorities

Prevention

- Survey environmental water sources for *C. cayetanensis* using validated methods that should be available in the near future.
- Conduct further assessment of need and implementation of screening for *C. cayetanensis* clinical infection and asymptomatic carriage of H-2A labor pool sources before transportation to the United States. Additional studies are needed to determine the efficacy and safety of considering prophylactic treatment of asymptomatic infected individuals.
- Review the potential for cold-stored romaine lettuce at the implicated regional processor to be a leading indicator of epi-curve cases attributable to this farm labor pool.
- Apply tools for *C. cayetanensis* subtyping to resolve the possibility of multiple sources of contamination.
- Produce an explanatory fact sheet regarding *C. cayetanensis* infection for public education.
- Develop standardized, validated laboratory test methodologies for human specimen and environment sample testing.
- Use commonsense practices per the following food safety management systems: HACCP, GAP, GHP, SSOPs, and GMP.
- Raise *C. cayetanensis* awareness and GHPs to reduce potential contamination.
- Increase vigilance among growers and farm personnel of human waste in agriculture waters.
- Provide and properly train farm crews on the care and use of restroom and handwashing facilities, as well as appropriate usage oversight.
- Develop health and hygiene awareness programs for farm personnel.
- Exclude ill personnel from handling all raw produce and food contact surfaces. They should be evaluated for enteric pathogen infection and — if documented through laboratory testing to be infected with a specific pathogen — treated as is medically indicated.

Incident Response

- Evaluate agriculture water sources and adjacent and regional environmental water bodies for evidence of human wastewater and septic sources.
- Assess the area for evidence of noncompliance with sanitary facility use and non-farm employee human encampments.
- Increase efforts to attribute animal vector cross-contamination potential, especially birds from contaminated water bodies.

Collaboration

- Review the current HGQ with industry to account for changes in consumer preferences and to ensure that product descriptions are clear and readily delineated.
- Improve collection of food history data via loyalty/shopper cards and credit cards.
- Share updated case counts regularly, highlighting thresholds at which investigations are initiated and distinguishing outbreak cases from individual cases.

- Improve governmental and industry communication to convey the uncertainty around case counts.
- Establish state and CDC alignment around criteria for including an illness in the outbreak case count.
- Informally share updated case counts with company contacts so companies can make decisions to protect public health.
- Ensure that potentially involved companies have access to summaries of all cluster investigations.
- Communicate that multiple, different food products may be causing illness, and that overall case counts are not reflective of one large outbreak.
- Aggressively work to develop genotyping or other typing methods that can be used to identify linked cases.
- Expand the matrices validated for FDA method 19B (or any updated method), improve the capacity of laboratories to analyze food samples for *C. cayetanensis*, and prioritize samples related to outbreaks.
- Improve the capacity of states to analyze samples for *C. cayetanensis*.
- Develop relationships between the produce industry and the CDC's parasitology group so that, as appropriate, the CDC can request industry information.
- Improve training and education within the food industry regarding *C. cayetanensis*, its host, life cycle, effective treatments and controls, and recommended preventive measures.
- Focus on activities occurring weeks before products were harvested, keeping in mind the long *C. cayetanensis* life cycle.
- Conduct microscopic analysis, not just PCR, to determine the likelihood that the organism is infectious.