Reporting Biomonitoring
Results to Individuals and
Medical and Public Audiences:
Challenges and Opportunities

Asa Bradman, PhD
September 25, 2007
UC Berkeley Center for Children’s Environmental Health Research
Outline

• What is CHAMACOS?
• Why do it
• What have we found?
• Case studies
A Community-University Partnership

Children’s Hospital Oakland Research Institute

Berkeley University of California

California Environmental Protection Agency

Battelle Laboratories

Children’s Hospital Oakland Research Institute

Center for Health Assessment of Mothers and Children of Salinas

California Department of Health Services

CRLA

South County Outreach Effort

Clinica de Salud del Valle de Salinas

California Rural Legal Assistance
CHAMACOS Study Area

Salinas Valley, CA
Agriculturally Applied Organophosphates
Average Annual Pounds
From 1999 through 2001

Agricultural pesticide use in California is reported to the Department of Pesticide Regulation per the Public Land Survey (FLG) System.

Pounds applied per FLG section (1 sq mi)
- 0
- 1 to 100 lbs.
- 101 to 1000 lbs.
- 1001 to 5000 lbs.
- Participant Residency
- County boundary
- Highway

Prepared by Rusty Scalzi, Bob McLaughlin & Martha Hardy
Environmental Health Investigations Branch
California Department of Health Services

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Results of Community Assessment

The Community has an interest in Environmental Health Research.

“There is a need to know how the environment is affecting us.”

Children’s Health is a priority concern in the Community.

“I think you will get a very positive response from the women. They are very interested in their children’s health and how to improve it. You need to give them access to their results.”

The Center must share results with the Community.

“I think the reaction of the community is going to be positive but you guys need to keep them informed about the study and talk the way you’ve talked to me about the community’s long term benefits from the study, and plans to stay in the community for further studies.”

Research must be culturally sensitive.

“Hire people who can work effectively with our community, people who understand the culture.”
Objectives

• Assess exposures to pregnant women and children.

• Determine relationship with:
  • neurodevelopment
  • growth
  • respiratory disease

• Reduce exposures to children and pregnant women with interventions and community outreach.

• Inform policies to reduce the incidence of environmentally-related disease
Biological Specimen Collection
Up to 75,000 samples stored

<table>
<thead>
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<th>Delivery</th>
<th>6 M</th>
<th>1 Y</th>
<th>2 Y</th>
<th>3½ Y</th>
<th>5 Y</th>
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</table>
Prenatal and Child Total Dialkyl Phosphate (DAP) Metabolites

Geometric Mean (95% CI) for Total DAPs

Maternal

Child

Total DAPs (nmol/L)

1st pregnancy 2nd pregnancy Mean pregnancy Post-Partum Child 6 month Child 12 month Child 24 month
Maternal Exposure to OCs

Comparison of serum organochlorine (OC) levels in the CHAMACOS Cohort and NHANES 1999-2000 populations

(All values are nanogram/gram lipid)

OPs and Neonatal Neurodevelopment

Percentage of Neonates with >3 Abnormal Reflexes
(Brazil'lon Neonatal Behavior Assessment Scale)

Quintile of prenatal DAP metabolites

Χ²_trend = 6.7

Young et al 2005
## Neurodevelopment at 2 years

<table>
<thead>
<tr>
<th>OPs</th>
<th>Bayley MDI</th>
<th>CBCL PDD</th>
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<tbody>
<tr>
<td>Prenatal OPs</td>
<td>$\beta$ (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td></td>
<td>-3.5 (-6.6, -0.5)</td>
<td>2.3 (1.0, 5.2)</td>
</tr>
</tbody>
</table>

Eskenazi et al., EHP, 2007
DDT Linked to Developmental Delays in Babies

Children exposed to the pesticide DDT while in the womb experience development problems, researchers say.

The pesticide was banned in the US and UK in the 1970s, but it is still used in some countries to kill malaria-barring mosquitoes.

It was already known DDT was used to protect against malaria, but it is now thought to be one of the causes of microcephaly in children, where the brain is underdeveloped.

DDT Study Finds New Hazard to Young Children

Babies born in the US to mothers emigrating from Mexico show mental and physical impairment, a UC Berkeley survey finds.

UC Berkeley scientists measured levels of various pesticides in 390 pregnant women, nearly all of whom were born in Mexico, and tested the mental and motor skills of their infants and toddlers, who were born in the Salinas Valley.

NDT is used to protect against malaria, but it is now thought to be one of the causes of microcephaly in children, where the brain is underdeveloped.

“DDT has effects that no one even thought to test for back when it was in use,” said Dr. Walter Rogan, an epidemiologist with the National Institute of Environmental Health Sciences. He was not involved in the study, published in the journal Pediatrics.

Because DDT was banned more than 30 years ago in the United States and most developed countries, the findings have particular relevance for the ongoing, controversial use in Africa to combat malaria.
Distribution of Average Cumulative Pesticide Dose Estimates for CHAMACOS Women

14.7% of estimated cumulative dose equivalents exceeded a reference value derived by applying a 100-fold uncertainty factor to the chlorpyrifos POD ($\text{BMD}_{10}/100 = 14.8 \, \mu\text{g/kg/day}$)

Castorina et al, 2004
PON1 Activity Varies by Age and Genotype

- PON1 newborns lower than adults; therefore, greater susceptibility to OP’s
- Children with QQ genotype have low level of enzyme; therefore, may be at highest risk

Furlong et al, Holland et al, 2006
Median DM Metabolite Levels by Fruit and Vegetable consumption

- 6M - p<0.01: >1/day = 19, 0-1/day = 12
- 12M: >1/day = 33, 0-1/day = 22
- 24M: >1/day = 56, 0-1/day = 44
CHAMACOS Biomonitoring Uses

- Characterize exposure
- Evaluate exposure trends
- Evaluate health effects
- Estimate risks
Case Studies in Communication

- IRB education
- Community involvement
- Challenges by the medical community.
- Final approach.
- Technical challenges
- General community
Forbidden to return individual results (1999)
Community Engagement

- CPHS agreed to reevaluate decision.
- Convened meetings with wide range of community and research partners.
Community Engagement

• Doctors strongly objected to returning individual results – burden of interpreting non-clinical tests.

• Advocates strongly supported returning individual results – right to know.

• Industry supported returning individual results – individual right.
Final approach accepted by IRB

• Participants can request results (opt in).

• Participants informed:
  ✓ In person;
  ✓ Results placed in context of population and reference data (NHANES);
  ✓ Emphasize research context;
  ✓ Offer follow-up testing;
  ✓ Don’t stigmatize;
  ✓ If known risk (e.g., lead), follow guidelines.
  ✓ Only ~20 have asked for results;

• Secondary protocol to re-test “high” results.
History Repeats Itself: CPHS II

CPHS II: 12/8/06

“test results for individual subjects … not … meaningful and … likely to cause unnecessary alarm … members felt strongly that… subjects … only be provided with a copy of the manuscript.”
Technical Challenges

Biomarkers may not reflect exposure.

For example, DAPs in the environment and food suggest urinary OP biomarkers require additional interpretation.
Technical Challenges

For many non-persistent compounds, good intra-individual correlation over a day. Poor over several days.
Correlation of DAP metabolites in spot urine samples collected 1-6 days apart

<table>
<thead>
<tr>
<th>Days between collection (n)</th>
<th>Total DAPS</th>
<th>Dimethyls</th>
<th>Diethyls</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (288)</td>
<td>0.34**</td>
<td>0.38**</td>
<td>0.18**</td>
</tr>
<tr>
<td>2 (241)</td>
<td>0.21**</td>
<td>0.27**</td>
<td>0.03</td>
</tr>
<tr>
<td>3 (210)</td>
<td>0.12</td>
<td>0.17*</td>
<td>0.00</td>
</tr>
<tr>
<td>4 (144)</td>
<td>0.03</td>
<td>0.07</td>
<td>0.02</td>
</tr>
<tr>
<td>5 (72)</td>
<td>0.13</td>
<td>0.16</td>
<td>0.05</td>
</tr>
<tr>
<td>6 (25)</td>
<td>-0.05</td>
<td>-0.09</td>
<td>-0.22</td>
</tr>
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</table>

**p<0.01
*p<0.05
Correlation of 24 hr samples collected three days apart ($n=25$)

<table>
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<tr>
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<th>Value</th>
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<tr>
<td>Total DAPS</td>
<td>0.11</td>
</tr>
<tr>
<td>Dimethyls</td>
<td>0.11</td>
</tr>
<tr>
<td>Diethyls</td>
<td>0.06</td>
</tr>
<tr>
<td>$p&gt;0.6$</td>
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</tr>
</tbody>
</table>
24 hr urine samples:
Within and between individual variability

Estimated within and between variability (SD)
Between 0.36
Within 1.01
Technical Challenges

- Individual sampling results for some non-persistent chemicals may be meaningless.
- Whereas population exposure range is well characterized.
Reporting results to the General Community
Research partners and advisory boards:

- All findings presented during in-person meetings;
- Submitted journal articles provided for comment;
- Press releases distributed for comment;
- Review is advisory only;
General community:

- Frequent participant fora.
- Presentations to broad cross-section of community:
  - Migrant education;
  - Community groups
  - Churches;
  - Local governments;
  - Grower organizations
Community Outreach
Outreach and translation

In the home.

In the community.

In the fields.
Investigators

**Exposure Studies**
- Asa Bradman
- Tom McKone
- Dana Barr CDC
- Rosemary Castorina
- Martha Harnly, DHS
- Jim Leckie, Stanford
- Marcia Nishioka, Batelle
- Lesliam Quiros

**Health Studies**
- Brenda Eskenazi
- Ira Tager
- Kim Harley
- Laura Fenster, DHS
- Caroline Johnson
- Michael Lipsett, DHS
- Janet Macher, DHS

**Mechanism Studies**
- Nina Holland
- John Casida

**Biostatistical Core**
- Nick Jewell
- Alan Hubbard
- Amy Marks

**Intervention and Community Outreach**
- Abbey Alkon, UCSF
- Lisa Goldman
- Alicia Salvatore
- Celina Trujillo

**Clinica de Salud**
- John Silva
- Max Cuevas

**Natividad Medical Center**
- Marc Tunzi
• California Wellness Foundation
• Switzer Foundation
• UC Mexus