Are you ready for Data Sharing?

Lessons Learned from the Fernald Community Cohort

A Large Database and Biobank with a 20 Year Heritage

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U.S. Department of Energy
Uranium Processing Plant at Fernald, Ohio

- Known as the Feed Materials Production Center (FMPC, 1952-1989)
- Processed uranium ore and recycled materials to make highly refined uranium metal products used in DOE nuclear weapons production complex
- Chemical separation: uranyl nitrate, U03, UF4, UF6

Fernald Medical Monitoring Program (FMMP)

Medical Monitoring Program established as a result of a litigation settlement

During the period from 1990 to 2008, the FMMP provided periodic medical examinations for persons who lived within a five mile radius of FMPC for at least a two year interval between 1952 and 1984. FMPC workers have a separate monitoring program.

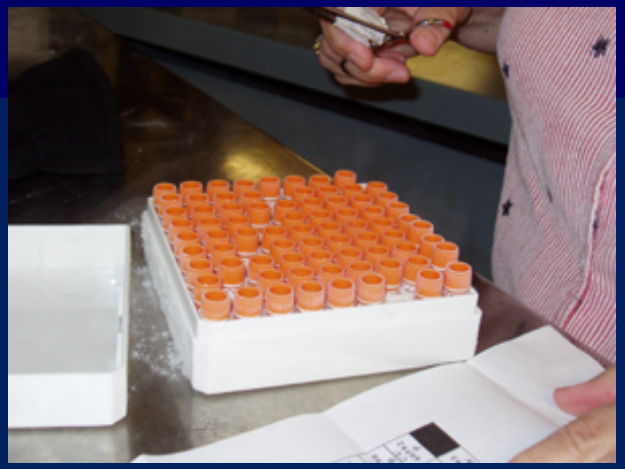
	Male	Female	
Adult	3967	4821	8788
Child	521	473	994
	4488	5294	**9782**

FMMP Adult Examinations

Yearly Questionnaire:
Health history; Smoking and alcohol use; Medications; Family history; Residence (address) history; Occupational, hobby, and exposure history; Detailed reproductive history; Contact persons; SF-36 health perception.

Physician Examination every 2 to 3 years:
Health history; Review of Systems; Medications; Social history; Comprehensive physical examination; laboratory tests; mammograms

Blood and urine obtained at time of first exam and frozen for later use. (Serum, Plasma, Whole blood, Urine [buffered and non-buffered])



Access to Data and Biospecimens

"Applying the precautionary principle"

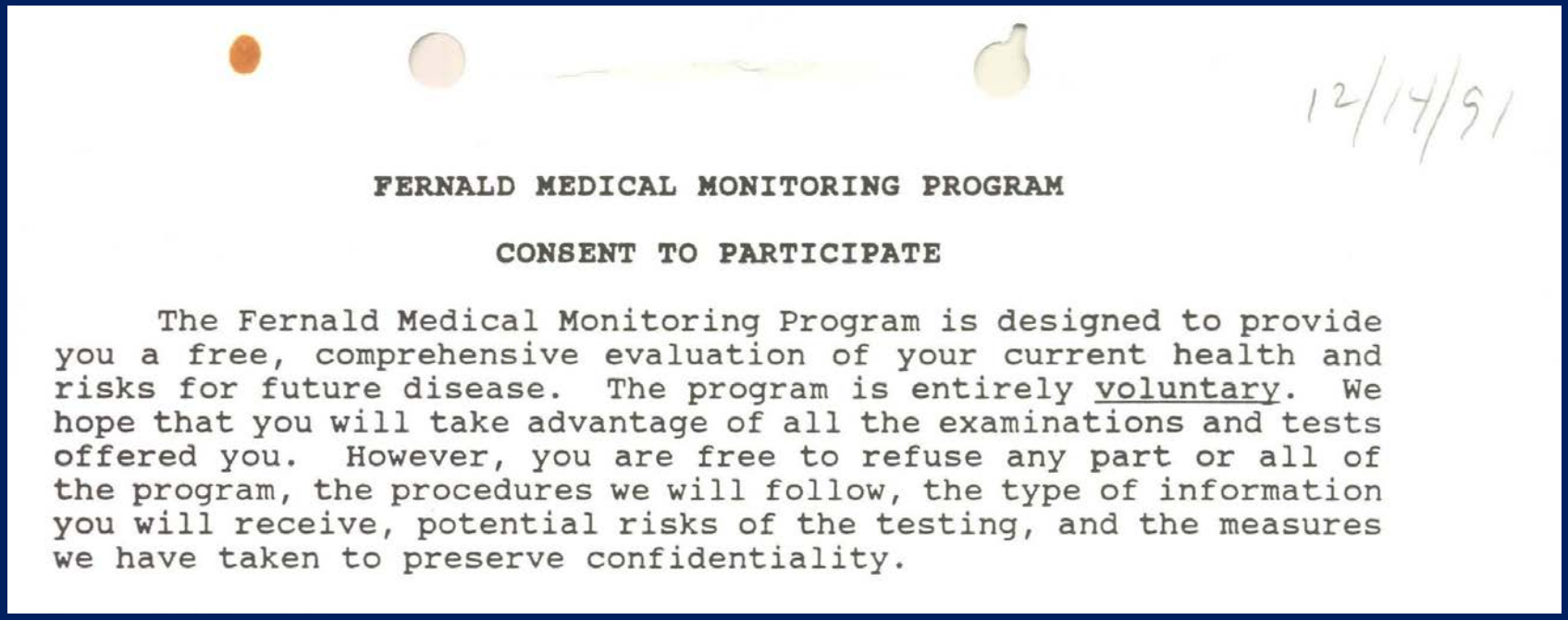
- **Any qualified researcher may apply to use the data and biospecimens for research. Application is online at FCC website. Research question, specific aims, study design, types of data**
- **Applications for access to the data and biospecimens are reviewed and approved by an Advisory Committee.**
- **Data files of de-identified data (no DOB or DOD), prepared for needs specific to investigators. Most data only analyses do not require separate IRB approval.**
- **Biospecimens provided to researchers after they obtain IRB approval for their studies.**
- **No follow-back – collection of additional data or biospecimens from FMMP cohort.**

Fernald Community Cohort Advisory Committee

Serve as delegates for study participants

Learning:
Consent requirements change over time

- In 1990 consent requirements were minimal.
- Be proactive about keeping your IRB informed.
- Reconsent is very difficult if you have not kept in contact.



12/14/91

FERNALD MEDICAL MONITORING PROGRAM

CONSENT TO PARTICIPATE

The Fernald Medical Monitoring Program is designed to provide you a free, comprehensive evaluation of your current health and risks for future disease. The program is entirely voluntary. We hope that you will take advantage of all the examinations and tests offered you. However, you are free to refuse any part or all of the program, the procedures we will follow, the type of information you will receive, potential risks of the testing, and the measures we have taken to preserve confidentiality.

1991 FMMP Consent Form

4) **Laboratory Tests** - Blood and urine samples will be obtained for a series of screening tests which will include blood counts, blood salts, liver and kidney function tests, a blood sugar, and an urinalysis. Two samples of blood will be obtained and frozen for future additional testing if necessary. Your blood will not be tested for HIV antibodies (AIDS test).

separately. No one is to have access to any of this information except as authorized by the Fernald Settlement Fund Trustees. If authorized by the Settlement Fund Trustees, scientific data or medical information may be analyzed and presented in court, at scientific meetings, or in professional

journals so that the overall results of this Program may be useful to others. However, no presentation or report shall include your name or any other identifying information which might compromise your right to privacy; and every reasonable effort shall be made to ensure your anonymity.

Consent in 2007 and thereafter

7. **Blood and urine samples for research** - You are asked to take part in a component of the Fernald Medical Monitoring Program that includes collection of blood and urine samples for use in future research studies. Researchers will use blood and urine samples in conjunction with personal information in FMMP records to study how different components of blood and urine maybe related to disease and how genes, lifestyle, and our environment may lead to disease. We will ask you to donate 3 tubes of blood (about 4-6 teaspoons) that will be drawn from a vein in your arm at the same time as we are taking blood for the usual tests that are part of the FMMP examination. We also ask that you allow us to freeze a portion of your urine sample.

VI. RESEARCH

Research Using Data

If authorized by the Fernald Settlement Fund Trustees, scientific data or medical information may be analyzed and presented in court, at scientific meetings, or in professional journals so that the overall results of this Program may be useful to others. However, no presentation of results will include your name or any other identifying information, which might compromise your right to privacy; every reasonable effort shall be made to ensure your anonymity.

Under federal law, researchers who use information about the health of their research participants are required, except in specific circumstances, to get written permission to use their participants' health information for the research study. We are asking for your authorization to allow researchers approved by the Fernald Settlement Fund Trustees to use or disclose certain information about your health. Your information may be used for research studies currently being conducted (attached) or future research studies approved by the Fernald Settlement Fund Trustees.

Research Using Blood Samples

Your samples will only be released for research purposes to researchers who have been approved by the Fernald Settlement Fund Trustees.

The exact tests that will be performed in future research studies are not known at this time but are likely to include the following: 1) the study of blood proteins; 2) the study of genes and changes in genes that may be involved in hereditary and non-hereditary disease development; and 3) the study of how race/ethnicity, age, lifestyle, the environment, and other factors may play a role in disease development. At no time will your name and address, or any other identifying information, be given for research purposes without your permission. Instead, requests for use of the information in the study will be handled in the following way.

Researchers who are interested in using blood samples have to complete a research plan with specific information about their study, including a description of how they will use the information. Plans will be reviewed by a group of experienced scientists and the Fernald Trustee, who will judge each plan for its scientific merit, its potential contribution to the prevention or cure of disease, and for the qualifications of the research team. Because we realize that the information and samples you provide are an invaluable contribution to science, their use in any research study will be carefully weighed. If a plan is approved, your information and samples will only be shared by us with an approved researcher after your name and address, and any other identifying information, have been removed and a code number has been given.

If an approved researcher would like to collect more information and/or blood samples, not routinely collected by the research staff, we will contact you to explain the study, and you will have the choice of whether to participate before you would be contacted directly by the researcher.

By signing this consent form you agree to give to the FMMP all rights to the access and control of any obtained blood, urine or tissue. The FMMP may retain, preserve, or dispose of these samples and may use them in future research studies for an unlimited period of time. The results of future studies conducted may be published or presented to scientific groups, but you will not be identified by name in these publications.

Get Ready: Data Collection

- Document, document, document
- Exam protocols (revisit and revise every year, keep yearly protocols)
- Questionnaire QxQs – yearly (yes, it takes much effort)
- Data entry protocols for each form
- Laboratory data – document methods and laboratory reference intervals for each year
- Code, code, code – everything you can! $

Plan Ahead: Derived Variables

- Standardized derived variables will maintain consistency in analyses (and protect the credibility of your cohort)
- Standardized application of missing data rules
- Provide SAS code
- Also willing to provide source variables

- Smoking pack years (yearly and cumulative); same for alcohol
- Diet nutrient analysis
- Exposure metric for uranium – air, water, organ doses; prevents need to distribute geocodes

Plan Ahead: Family Relationships

- Document family relationships within the cohort within the database (data have been collected)
- Start early so that you can verify with second data collection
- Select software carefully; $

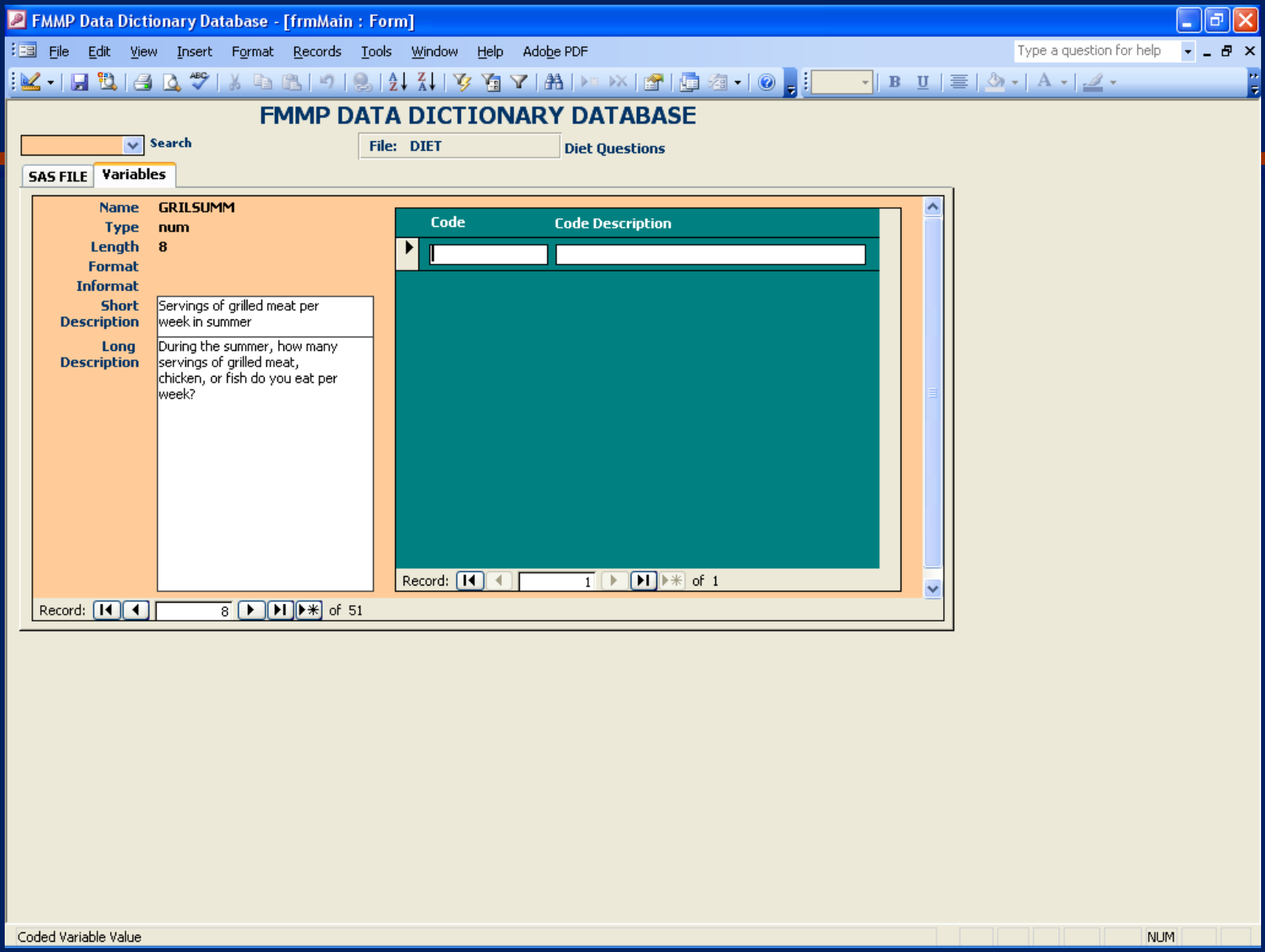
- Studies: heritability, family dynamics, risk factors
- Selected study biospecimens are independent of each other (by blood relation) can be selected – software plus personnel effort

Get Ready: Data Dictionary

- From the start, plan for a well-designed data dictionary
- Takes time and money! $$
- Think “outside”, not just “in-house”

- Specialized software – SAS descriptors are not sufficient but better than nothing
- Coded or searchable variables
- Variables linked across years

Data Dictionary Database



Getting Ready: Credibility

- Demonstrate that the (unexposed) cohort is large enough to provide significant statistical power for genomic and proteomic studies
- Demonstrate the “credibility” of the cohort by producing more peer reviewed publications.
- (Demonstrate that the racial and ethnic homogeneity of the population is an advantage)
- (Demonstrate that a significant portion of the population has not had exposure beyond background levels – uranium particulates; radon)

Learnings: Data Sharing Policy

- Disclosures
- Students or Trainees – ensure supervision by making the faculty member the PI
- IRB approval – or exempt? Need to know for data file preparation
- Meeting or conference call of Advisory Committee?
- Sample size calculation – are sufficient data available for sufficient statistical power?
- Yearly reports; time limitation on manuscript submission and publication
- Standard statement for description of the cohort; check description and grant acknowledgment
- Return or destroy data files – difficulty to ensure compliance. Better to have strong statements re use outside of approval

Learnings: Costs for Data Sharing

- Data files - $1200 for basic fee (includes up to 10 hours of consultation with the Research Director or Research Coordinator; 2 hours of effort for preparing data files
- Additional preparation - $100 per hour for consultation and $80 per hour for data manager
- Other cost considerations – additional outside medical records; identification of phenotypes using operational definitions
- Preliminary data for grants – charge?

- Needed to develop a Charge Center so that costs could be charged to grants; indirect costs additional for non-UC/CCHMC investigators

- What about revenue from patents for new predictive biomarkers or imaging procedures?

Getting Ready: Website

- Website will publicize the availability of data and biospecimens; also will reduce investigator time in consultations with investigators
- Description of cohort; questionnaires and other data collection instruments; laboratory methods (including exposure biomarkers)
- Protocols and timelines
- Code sets
- Data dictionary
- Outcome frequencies; exposed person frequencies
- Publications resulting from data sharing
- $$$$$$$ - our website is woefully out of date


SO-LOW
BIOLOGICAL HAZARD

Learnings: Biospecimen Inventory

- Inventory database and queries: investment in design pays off
- Redundancy is good (binders and database)
- Keep up with software updates
- Periodic back-ups of computer inventory database.
- QC queries for duplicate records or no records
- Periodic freezer inventories, especially after samples have been moved because of freezer maintenance issues

Learnings:

Periodic quality assessment of samples are an important component of quality assurance

- Determine long term stability of specimens for future analyses
- Determine DNA quantity and quality for future analyses; inventory database for DNA aliquots and dilutions
- Test the specimen locator system
- Determine future needs and resources for specimen preservation; $$$$$ for freezer oversight, maintenance contracts, backup systems

Learnings: Biospecimen Sharing Policy

- Sample size application – how many biospecimens are really needed?
- Prioritization of samples of exposed persons
- Should biospecimens be returned?
  - Serum, plasma and urine; paraffin-fixed tissue
  - Split aliquots – documentation in inventory
  - Whole genome amplified DNA?
- Meeting of Advisory Committee
- Sufficient funds? Prevents “squirreling” of biospecimens

Learnings: Costs for Biospecimen Sharing

- Costs
- Basic fee: Originally, $500 for up to 200 samples; $50 for each 50 additional samples
  - for preparation work (persons who meet eligibility requirements, locate biospecimens in inventory, select which ones to pull [use of biospecimen, freezer location])
  - Cost structure changed by Charge Council
- Additional charge of $6+ per sample (team of 4 persons)
- Charge center and additional indirect cost for “outside” investigators
- A few samples for preliminary data – charge?

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