

## Appendix IV: Subject Database Methods

In order to specifically identify the number of individuals involved in the research, and better understand what happened to them, the nearly 10,000 pages from the Cutler Documents were read and analyzed with a particular focus on information about individual research subjects. Commission staff created a comprehensive database of individual subject information from these records.

### *Creation of Subject Database*

A great deal of historical research was done to help interpret the Cutler Documents. The Commission relied heavily on *Modern Clinical Syphilology* (1944) by John H. Stokes, Herman Beerman, and Norman R. Ingraham, which was considered the definitive text on syphilis at the time. In addition, the Commission consulted regularly with Dr. Jonathan Zenilman, Chief of the Infectious Diseases Division of the Johns Hopkins Bayview Medical Center.

For data extraction and analysis purposes, the data sources were divided into two categories: research notebooks and additional archive documents.

### Research Notebooks

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The Cutler Documents include four research notebooks, two laboratory notebooks (Notebooks 1 and 2), and two clinical notebooks (Notebooks 3 and 4). The laboratory notebooks primarily contain laboratory test results. The clinical notebooks primarily contain research subject histories and clinical notes. All notebooks contain entries written in both English and Spanish.

The primary data of interest included patient profile information (e.g., name, age, subject number, study population), inoculation data, treatment data, and information that independently raised ethical concerns (e.g., evidence of deceit on the part of the researchers or resistance on the part of the subjects).

Based on a detailed reading of Notebook 1 and a review of Notebooks 2, 3, and 4, an initial coding scheme was developed to capture relevant information from the notebooks in an Excel database. Four coders then used the preliminary coding scheme to code a sample of about 10 pages from each of the four notebooks. Following each preliminary coding trial, the data were

discussed and the codes refined with input from Dr. Zenilman. Once the preliminary coding and revisions were complete, double coding began, with two coders working on the laboratory notebooks and two on the clinical notebooks (the coders working on the clinical notebooks had moderate to high Spanish fluency). Each pair of coders worked through a number of pages of their notebook independently, then met to reconcile their coding. One member of each team maintained the master database with reconciled data. The coding scheme was revised iteratively, as new information was encountered that was not being adequately captured. When the coding scheme was revised, previously coded data were recoded to reflect the revised scheme.

The rules employed during coding included:

- Use one line for each entry about each person per date. Simple direct Spanish translation permitted (e.g., “orinas” in the data source became “urines” in the database)
- Long or complex Spanish translations should be preceded in the database by ‘[Translation]’
- Where handwriting cannot be interpreted, denote as ‘[illegible]’
- Where handwriting is difficult to interpret, use brackets [] to denote coder’s interpretation of entry
- Coding test results
  - N (any variation) = negative
  - P (any variation) = positive
  - D (any variation) = doubtful
  - WP = weakly positive
  - QNS = quantity not sufficient
  - If there is a N, D, or WP and a P on the same line, code as “conflicting”
  - If there is a N and a D on the same line code as “negative”

A detailed data interpretation and coding key is available upon request.

### Additional Cutler Documents

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Additional Cutler Documents included Dr. Cutler’s final research reports, photographs, correspondence, individual experiment files, and about a dozen miscellaneous documents.<sup>706</sup> There were also approximately 7,000 research subject note cards. Overall, the content of these data sources was much less

rich than that of the Research Notebooks, with the possible exception of the subject note cards. There was a tremendous amount of variation in the contents of the note cards, with some cards containing nothing but a name or subject number and some cards containing detailed clinical notes about a named individual.

All of these documents were single-coded, meaning that only one person coded any given document. Each coder's work was regularly audited for faithful recording of data from the source documents, appropriate application of the coding scheme, and consistency.

### *Subject Database Quality Control*

Once all sources were coded, separate databases were combined into one master Subject Database, with over 30,000 lines of data on over 5,000 individual subjects. The database was checked for obvious coding errors (e.g., a name where a date should be, mode of inoculation where a test result should be) and corrected where necessary. The Subject Database was saved and archived.

In order to identify the total number of subjects involved in the studies, as well as information about inoculation and treatment, further quality control of the database began. The first step was to review the names, where possible, in an effort to ensure that any given individual was only counted once. A new column was created ("Full Name Clean") to hold the best assessment of an individual's name in cases where ambiguity existed. A paradigmatic case is one where one (or many) line includes information on A. Gomes and another line (or many) includes data on A. Gomez. In this instance, if it was found that a second piece of information (subject number, date, population, age, or experiment number) on each individual matched, those two lines of data were assumed to be on the same individual. All lines with information on that individual were then assigned either the majority name or the most logical name—in our example, all lines would be assigned the name of "A. Gomez" in the Full Name Clean column. The First Name and Last Name columns were always left untouched, changing the name only in the Full Name Clean column.

If a line of data could not be assigned to a unique individual, the data were not included in our subsequent calculations.

In order to enable calculation of the number of subjects exposed to syphilis, gonorrhea, and chancroid, an additional column was added to the database: “STD Exposure.” Based on data available about each unique individual, the STD Exposure column was populated with the disease used in exposure, for those individuals who were exposed. Frequently the disease involved in the exposure was explicit, but in instances where it was not, the disease was determined based on knowledge about the exposure methods used for each disease and the populations in which various experiments were conducted, based on the retrospective reports that Dr. Cutler authored on the experiments.

In a second round of data review, an attempt was made to fill in missing but known data (e.g., if there are 12 lines about A. Gomez—per the Full Name Clean column—and one of them lists age, age was filled in for all corresponding lines about him). In cases where an individual’s population (Commercial Sex Worker, Prisoner, Psychiatric Patient, Soldier) was missing, an effort was made to determine the population by comparing the date and nature of the experiment in which the individual was involved with the timeline of all of the experiments (assembled from Dr. Cutler’s final reports.) In cases where there was an obvious conflict between the database and Dr. Cutler’s reports (e.g., chancroid inoculation in a population not reported by Dr. Cutler to have been involved in chancroid experiments), the original archive documents were checked and the data verified or corrected. There were a number of commercial sex workers who were mentioned in the documents and were referred to Dr. Cutler for potential involvement in the inoculation studies, but who never participated. These individuals were identified as a discrete population (“Referred by VDSPH”) and included in the database, but in all cases, the only data available for these individuals were gonorrhea test results. The database was also double checked for individuals who have the exact same name in the Full Name Clean column, but were clearly not the same person (e.g., A. Gomez who was in the prison and A. Gomez who was in the mental health hospital), to ensure that both individuals were counted.

Challenges in distinguishing between penicillin used as a prophylaxis for syphilis following exposure and penicillin used as a treatment for diagnosed syphilis infection arose. After consulting with Dr. Zenilman, the following standard was applied: as the incubation period of syphilis for lesion development is mean 21 days, all dosages of penicillin before 21 days were

considered prophylactic in nature, and all dosages after 21 days were considered treatment.

In all cases, where no data were available or reasonably interpretable, the cell was left with “nd,” denoting no data.

### *Limitations*

Limitations inevitably attach to trying to interpret and analyze incomplete and decades-old data sources. The documents contained a mix of English and Spanish written by multiple individuals with varying levels of fluency, proficiency with spelling, and penmanship. They reflect inconsistency in the spelling of individuals’ names and assigning the subject numbers, further complicating this investigation; for example, on one page, an individual’s name would be recorded as “Gomez,” but the next entry referencing the same person might be noted as “Gomes,” likewise for “J.O. Hernandez” and “Jorge Oscar Hernandez.”

In addition, though Dr. Cutler’s final reports provide some information on timing and some experimental details, they are not comprehensive, as, for example, there are experimental results in the Research Notebooks that were not mentioned in the final reports. Conversely, Dr. Cutler includes over 10 experiments in his Final Syphilis Report for which the Commission did not find corroborating evidence in the contemporaneous laboratory or clinical notes. For example, Dr. Cutler describes a superficial inoculation gonorrhea experiment in the Guatemalan Army on May 9, 1947, but there are no additional subject data available in the Cutler Documents to evidence this experiment.<sup>707</sup> The reason for this discrepancy is unclear; however, there is reason to believe that the Commission is not in possession of all of the clinical notes from the Guatemala experiments. For example, one of the clinical notebooks includes an instruction to please “[s]ee Miss [Alice] Walker’s record book.”<sup>708</sup> This referenced notebook is not among those included in the Cutler Documents.

Additionally, the experiments described in these documents were conducted in the 1940s, at a time when diagnosis and treatment methods for STDs were not as settled as they are today, and the syphilis organism was poorly understood. Sixty-five years later, it is difficult to know what the researchers thought and understood about the diseases they were working with and the

tests they were conducting. Given this, the Commission did not attempt to identify how many people were clinically infected or how many people received adequate treatment. In the case of syphilis, for example, the serological testing conducted was unreliable and highly dependent on the skill, precise method, and consistency of an individual laboratory and the quality of the clinical assessment. As a result, the database focuses on the number of individuals exposed to, rather than infected with, STD.

Lastly, due to time and resource constraints, research records deemed of greatest significance, specifically the majority of the clinical and laboratory notebooks, were double-coded (meaning by two or more people), but the majority of records were single-coded. Periodic audits were conducted of all work.

### *Figures 6, 7, and 8*

Figures 6, 7, and 8 were created using amalgamated data from the Subject Database derived from the Cutler Documents. As Dr. Cutler’s retrospective counts of his experiments are inconsistent, these figures are based on an independent count of days on which intentional exposure to STD occurred for an individual or population. This exposure day count excludes days on which commercial sex workers alone were exposed, as Dr. Cutler did not consider these instances “experiments” or the sex workers as “subjects.”