REAL WORLD IMPLICATIONS OF A TB OUTBREAK – BONE ALLOGRAFT MATERIAL

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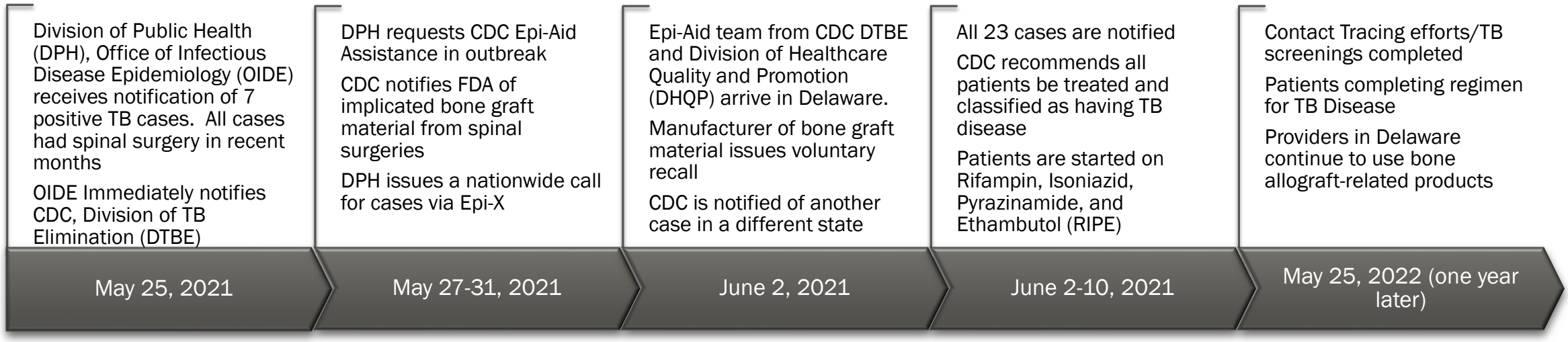
THE 30,000 FOOT OVERVIEW



DE IS A LOW INCIDENCE STATE FOR TB (<50 CASES PER YEAR)

TB Disease Data

	Incidence Rate*			Case Counts for Delaware		
Year	United States	Delaware	Total (Delaware)	New Castle County	Kent County	Sussex County
2021	TBD	TBD	41	26	15	0
2020	2.2	1.6	16	7	4	5
2019	2.7	1.8	18	2	8	8
2018	2.7	2.0	19	9	4	6
2017	2.8	1.6	15	7	5	3
2016	2.9	1.7	16	13	1	2
2015	3.0	2.2	21	17	2	2
2014	2.9	2.2	21	13	3	5
2013	3.0	1.9	18	9	5	4
2012	3.0	3.1	28	20	0	8

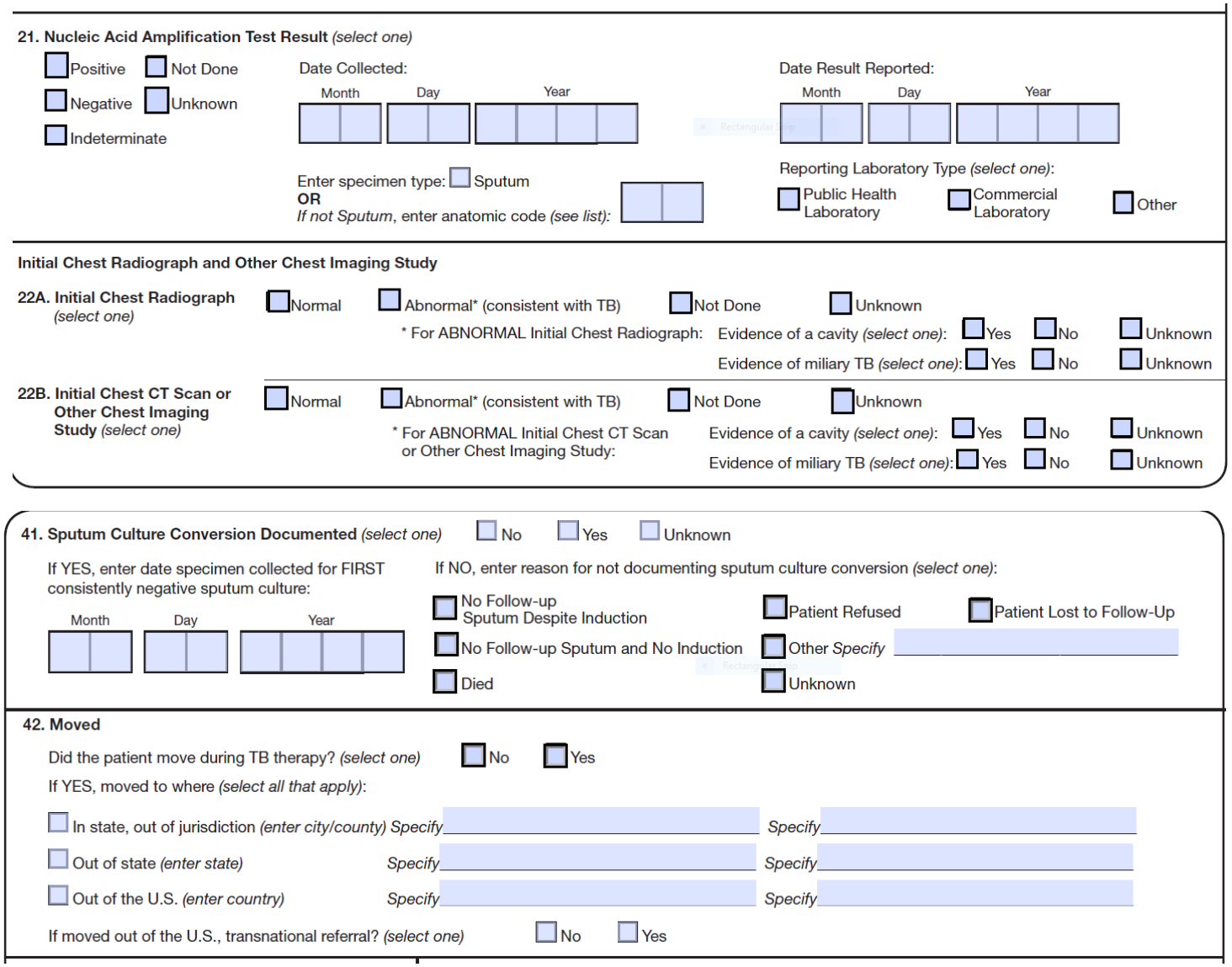
*Incidence rates are the number of confirmed cases of TB disease divided by the population in Delaware

HISTORY OF DELAWARE'S TB PROGRAM

- The Division of Public Health is the clinical provider for nearly all cases of Tb Disease
- The TB Nurse Consultant/program lead resigned in August 2020
- The TB program was moved under the Office of Infectious Disease Epidemiology in August 2020
- Most epi-related duties were still COVID-based and TB surveillance was done passively
- An Epidemiologist was designated to perform full-time TB work in November 2020

REPORT OF VERIFIED CASE OF TUBERCULOSIS

- Required for all TB Disease cases
- Updated 2020 version to capture more variables
- DE's surveillance system not equipped for updated RVCT
- Completed by clinic nurses and faxed to Epis for data entry and analysis



21. Nucleic Acid Amplification Test Result *(select one)*

☐ Positive ☐ Not Done
☐ Negative ☐ Unknown
☐ Indeterminate

Date Collected: Month Day Year

Date Result Reported: Month Day Year

Enter specimen type: ☐ Sputum
OR
If not Sputum, enter anatomic code *(see list)*:

Reporting Laboratory Type *(select one)*:
☐ Public Health Laboratory ☐ Commercial Laboratory ☐ Other

Initial Chest Radiograph and Other Chest Imaging Study

22A. Initial Chest Radiograph *(select one)*
☐ Normal ☐ Abnormal* (consistent with TB) ☐ Not Done ☐ Unknown
* For ABNORMAL Initial Chest Radiograph: Evidence of a cavity *(select one)*: ☐ Yes ☐ No ☐ Unknown
Evidence of miliary TB *(select one)*: ☐ Yes ☐ No ☐ Unknown

22B. Initial Chest CT Scan or Other Chest Imaging Study *(select one)*
☐ Normal ☐ Abnormal* (consistent with TB) ☐ Not Done ☐ Unknown
* For ABNORMAL Initial Chest CT Scan or Other Chest Imaging Study: Evidence of a cavity *(select one)*: ☐ Yes ☐ No ☐ Unknown
Evidence of miliary TB *(select one)*: ☐ Yes ☐ No ☐ Unknown

41. Sputum Culture Conversion Documented *(select one)* ☐ No ☐ Yes ☐ Unknown

If YES, enter date specimen collected for FIRST consistently negative sputum culture: Month Day Year

If NO, enter reason for not documenting sputum culture conversion *(select one)*:
☐ No Follow-up Sputum Despite Induction ☐ Patient Refused ☐ Patient Lost to Follow-Up
☐ No Follow-up Sputum and No Induction ☐ Other *Specify*
☐ Died ☐ Unknown

42. Moved

Did the patient move during TB therapy? *(select one)* ☐ No ☐ Yes

If YES, moved to where *(select all that apply)*:

☐ In state, out of jurisdiction *(enter city/county)* *Specify* *Specify*
☐ Out of state *(enter state)* *Specify* *Specify*
☐ Out of the U.S. *(enter country)* *Specify* *Specify*

If moved out of the U.S., transnational referral? *(select one)* ☐ No ☐ Yes

MAY 2021 – THE CASES

- Twenty-three new cases exceeded the 2020 TB incidence rates entirely (one case resided in a nearby state).
- New case definition – imaging included in classifying cases
- Imaging revealed abscesses, osteomyelitis, discitis, and/or pulmonary TB
- Some patients had >5 scans and numerous smears/PCR/cultures performed on various sources. In some cases, the infection broke through the surface of the skin causing open, draining, wounds

CASE INFORMATION – CONTINUED

- Repeat surgical procedures and/or removal of hardware from spinal surgeries was discouraged, (due to increased risk of TB aerosolization), but the TB caused some hardware to loosen or detach
- Most cases reported severe pain and had repeat hospital occurrences for pain control
- CDC recommended sputum collection on all cases, even if it appeared there was no pulmonary involvement, but in some cases, it was hard to induce sputum
- Given the sensitivity of the issue, all were aware of the potential legal implications

GUIDELINES FOR TB TRANSMISSION-BASED PRECAUTIONS

CDC's Division of Health Care Quality and Control performed on-site infection control assessments to develop guidelines for transmission-based precautions. The following guidelines were established:

PATIENT CHARACTERISTIC	PRECAUTIONS	DISCONTINUATION CRITERIA
UNDER EVALUATION FOR PULMONARY OR LARYNGEAL TB	Airborne + Standard	Likelihood of infectious TB deemed negligible and either There is another diagnosis that explains the clinical syndrome 3 sputum smears are negative (8-24 hours apart, 1 early morning)
PULMONARY OR LARYNGEAL TB (CONFIRMED)	Airborne + Standard	Patient on effective therapy, improving clinically, with 3 negative sputum smears on separate days
DISSEMINATED OR MILIARY TB	Airborne + Standard	Patient on effective therapy, improving clinically, with 3 negative sputum smears on separate days
EXTRA-PULMONARY TB, DRAINING LESION (EX: WOUND)	Airborne + Standard + Contact	Patient is improving clinically **and has 3 consecutive negative cultures from drainage**

Source: CDC DTBE, DHQP September 9, 2021

THE ROLE OF THE HOSPITAL AND THE ROLE OF OIDE IN CONTACT INVESTIGATIONS – WHO SHOULD BE SCREENED?

Hospital A

- All health care providers (HCP) in surgical suites, all perioperative personnel
- Environmental services
- Decontamination personnel
- Any HCP who entered room of case that needed airborne precautions
- Patients in common spaces with case that needed airborne precautions, including roommates

Division of Public Health

- Everyone else!
- The bulk of contacts were HCPs, so OIDE's focus included mostly outpatient providers (not associated with hospital), family, and social contacts
- Given how ill many cases were, several had few contacts outside of the home
- OIDE established greater than 100 contacts

INVESTIGATING CONTACTS

Contact determination was based on criteria set forth by CDC. Preferred screening methodology is Interferon Gamma Release Assay (IGRA), such as QuantiFERON testing.

Wounds considered infectious until 3 negative consecutive CULTURES (not smears) are obtained.

Office of Infectious Disease Epidemiology Contacts

contacts identified	126
contacts evaluated	45 (35.7%)
TB disease	0
TB infection	0

Contacts were called twice and notified of their exposure by certified letter. Nearly 2/3 of contacts chose not to respond or be fully screened.

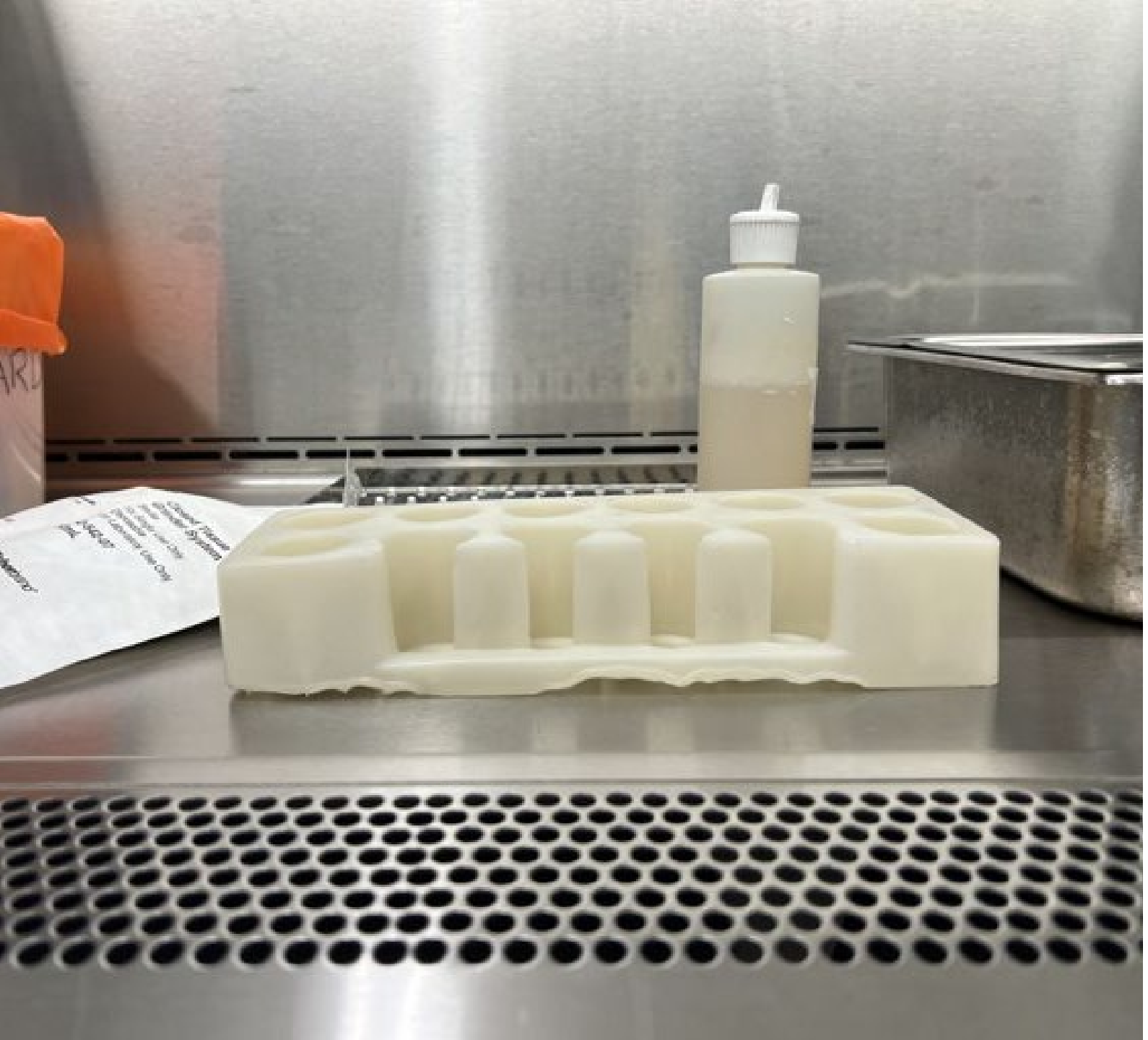
LAB BURDEN – REAL-TIME PCR ON NON-VALIDATED SOURCES (BONE AND WOUNDS)

- DPHL validated a real-time multiplex PCR protocol adapted from Wadsworth Center
- Utilizing since February 2016 for the detection of Mycobacterium tuberculosis complex (TBC) and Mycobacterium avium complex (MAC) DNA from clinical specimens and cultured isolates
- MTB complex: M. africanum, M. bovis, M. bovis BCG, M. canettii, M. microti and M. tuberculosis
- MA Complex: M. avium, M. avium subsp. avium, M. avium subsp. avium M. avium subsp. paratuberculosis, M. intracellulare, M. chimaera, M. arosiense, M. colombiense, M. marseillense, M. bouchedurhonense, and M. timonense
- Primers: TBCSAV, TbextRD9, MAC

TB-PCR: CURRENT STATUS

- Respiratory specimens, including expectorated sputum, induced sputum, bronchial aspirates, tracheal aspirates, broncheoalveolar lavage (BAL), fine needle aspirates, tissues, lymph node, and lung biopsies

- Culture broths/isolates

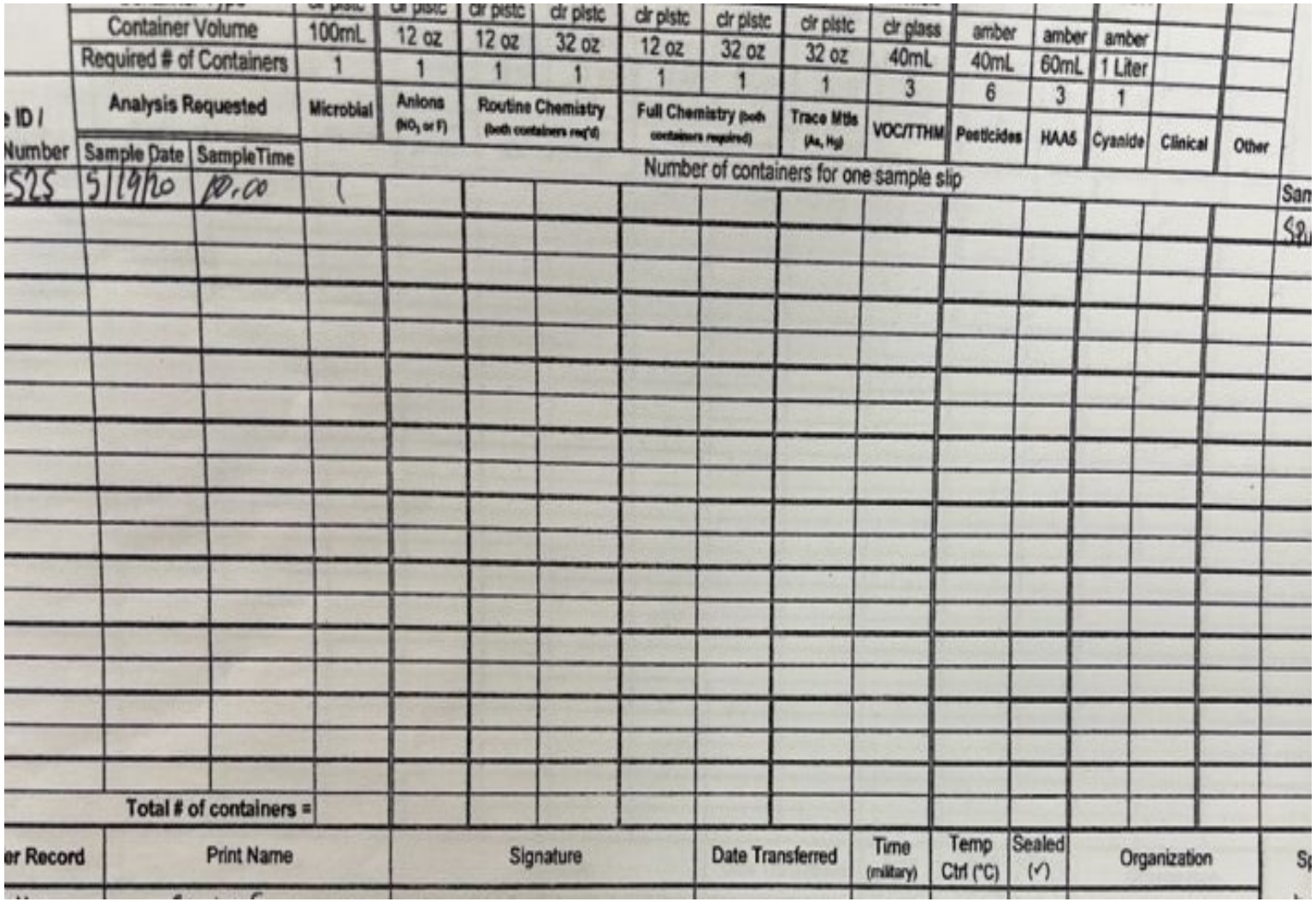


OFF LABEL USE OF TB-PCR

- Testing non-validated sources is considered off label
- [insert source] is not a validated source. Please interpret negative results with caution
- PCR results for first bone sample – used tissue grinder, heat-killed, positive results within 24 hours of receipt

LEGAL IMPLICATIONS – CHAIN OF CUSTODY

- First sample that came to lab contained no notice of any outbreak
- Upon sample testing positive, lab made aware of situation and started a retroactive chain of custody on sample/ any other samples sent before CoC was known to be started
- Began chain of custody at hospital labs for any further sample submitted
- Prepared to always prove proper handling of sample



	Container Volume	100mL	12 oz	12 oz	32 oz	12 oz	32 oz	32 oz	40mL	40mL	60mL	1 Liter			
	Required # of Containers	1	1	1	1	1	1	1	3	6	3	1			
	Analysis Requested	Microbial	Anions (NO_3, or F)	Routine Chemistry (both containers req'd)		Full Chemistry (both containers required)		Trace Mtls (As, Hg)	VOC/TTHM	Pesticides	HAA5	Cyanide	Clinical	Other	
ID / Number	Sample Date / SampleTime	Number of containers for one sample slip													
525	5/19/20 10:00	1													
	Total # of containers =														

er Record	Print Name	Signature	Date Transferred	Time (military)	Temp Ctrl (°C)	Sealed (✓)	Organization

REFLECTIONS – ONE YEAR LATER

Lessons learned.....

- Coordination of schedules and information sharing between providers is difficult: surgeons, infectious disease doctors, pulmonologists, and public health practitioners involved throughout the process
- Cases predominantly resided in one county, increasing burden on that public health clinic
- Some cases had draining wounds for months leading to prolonged isolation
- Some cases felt stigmatized by Directly Observed Therapy or Video Directly Observed Therapy, a requirement in Delaware

FURTHER REFLECTIONS – ONE YEAR LATER

- Epidemiologists took on RVCT reporting to assist clinic nurses, this role was not transferred back to nurses
- Cases and contacts seemed reluctant about contact investigation.
- Some cases chose to use private physicians, but were then responsible for medication costs and regular copays
- **Real-world implications of human-derived material not tested for TB, prior to surgical use**

REFLECTIONS – ONE YEAR LATER

What went well.....

- Strong collaboration between Hospital, DPH (Lab/Epi), CDC.
- CDC Epi-Aid (12+ hour days of chart abstraction), CDC Public Health Associate to assist with contact follow-up.
- DPH's Community Health Services treating the biggest TB surge in over a decade
- Use of "off-label" testing to rapidly detect TB in non-respiratory specimens.
- **Sequestration of units that were on the shelf = decreased morbidity and mortality**

QUESTIONS? COMMENTS?

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