California Norovirus Laboratory Network (NLN)
2017-2018 Norovirus Season
Triannual Report (October 2017 to January 2018)

Published by: California Department of Public Health, Viral and Rickettsial Disease Laboratory (VRDL), Respiratory and Gastroenteric Diseases Section
Chao-Yang Pan, Alice Chen, Thalia Huynh, Tasha Padilla, and Debra A. Wadford

CONTENTS

INTRODUCTION

This is the first triannual report issued by the VRDL to inform Norovirus Laboratory Network (NLN) member laboratories and California local health departments about current norovirus relevant topics, particularly about circulating and emerging strains detected from California outbreaks of acute viral gastroenteritis tested by NLN labs. In addition to norovirus, this report contains information about norovirus-negative gastroenteritis outbreaks characterized by the VRDL, including rotavirus, sapovirus, astrovirus, and gastroenteric adenoviruses 40 and 41. Outbreaks in this report are defined as being two or more cases of clinical acute gastroenteritis linked by time, person and place. Lab-confirmed outbreaks are those in which norovirus has been detected by a laboratory method (e.g., PCR) from 2 or more outbreak patient specimens.

NOROVIRUS NOMENCLATURE

Naming of noroviruses is based on typing of region B of the polymerase gene and region C of the capsid gene. For example, the current most commonly detected strain, **GII.P16-GII.4 Sydney**, is so named because the genetic sequence of polymerase region B corresponds to the genogroup II 16 strain (GII.P16) while the sequence of capsid region C matches genogroup II.4 Sydney (GII.4 Sydney). Thus, the **GII.P16-GII.4 Sydney** virus is a recombinant between a norovirus with the GII.P16 polymerase and the GII.4 Sydney capsid genes.

INCREASED REPORTS OF NOROVIRUS ACTIVITY RELATIVE TO OCT 2016- JAN 2017

From October 2017 through January 2018, the NLN reported 74 suspected norovirus outbreaks to VRDL. Of the 74 suspect outbreaks, 52 (70%) were confirmed by real-time PCR testing (Table 1). Los Angeles County recorded the most confirmed reported outbreaks with 17, followed by San Diego County with 8 (Table 2, Figure 1). As shown in Table 1, outbreaks were overwhelmingly caused by Genogroup II (GII) viruses (47/52, 90%) compared to Genogroup I (GI) viruses (5/52, 10%). Of the 47 GII outbreaks reported by the NLN, 35 (74%) were genotyped by VRDL; **GII.P16-GII.4 Sydney** was the predominant genotype, identified in 43% (15/35) of the GII outbreaks (Table 3)**.**

Table 1: **Norovirus Testing Reported by the NLN, October 2017—January 2018**

Month Reported	Total Outbreaks	Lab-Confirmed Outbreaks	Total Specimens	Positive Specimens	Genogroup I Outbreaks	Genogroup II Outbreaks
October	4	4	33	14	1	3
November	15	10	106	50	0	10
December	33	23	210	99	3	20
January	22	15	117	60	1	14
Total	**74**	**52 (70%)**	**466**	**223 (48%)**	**5 (10%)**	**47 (90%)**

Table 2: Reporting from NLN Labs: Number of Outbreaks (OBs) Tested, October 2017—January 2018

Public Health NLN Lab	Total Suspect Norovirus OBs Reported by NLN	Total Laboratory-Confirmed Norovirus OBs	Number of Non-norovirus OBs characterized
Alameda	3	3	0
Contra Costa	0	0	0
Fresno	0	0	0
Humboldt	1	1	0
Long Beach	1	1	0
Los Angeles	30	17	0
Monterey	0	0	0
Napa-Solano-Yolo-Marin	0	0	0
Orange	2	1	0
Placer	0	0	0
Riverside	4	4	0
Sacramento	3	1	0
San Bernardino	0	0	0
San Diego	10	8	1 (sapovirus)
San Joaquin	1	0	0
San Luis Obispo	1	1	0
San Mateo	3	2	0
Santa Barbara	1	0	0
Santa Clara	4	4	0
Shasta	0	0	0
Sonoma	0	0	0
Stanislaus	0	0	0
Tulare (for Fresno)	5	4	0
Ventura	3	3	0
VRDL (for Butte, Santa Cruz)	2	2	0
Total	**74**	**52**	**1**

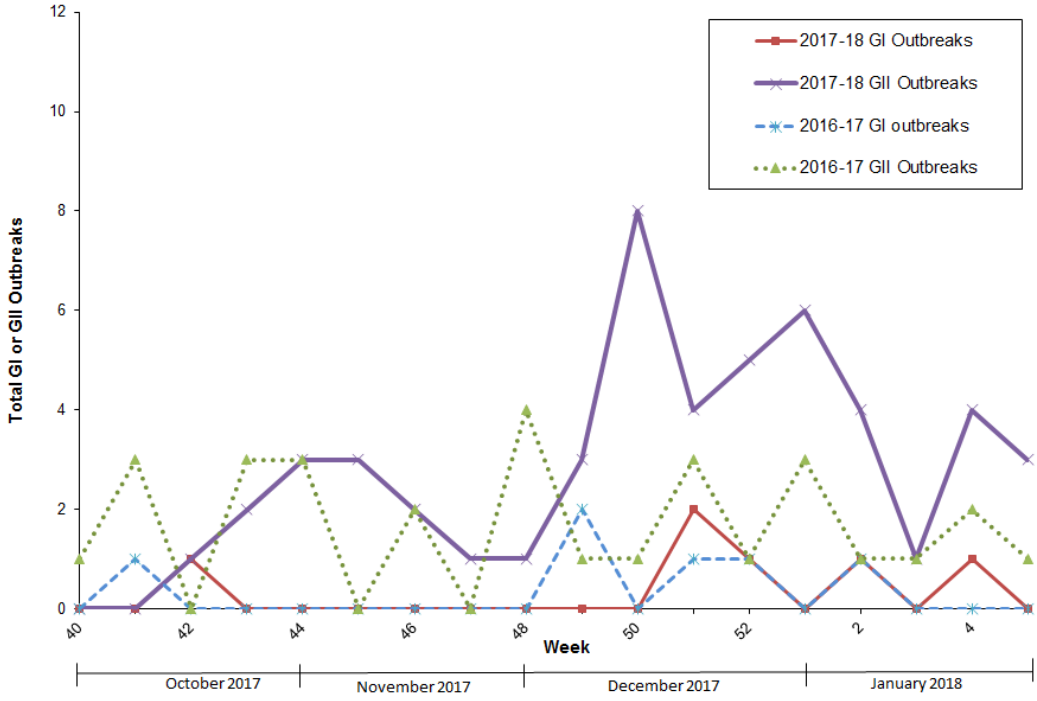
Last season, between October 2016 and January 2017, the NLN reported 58 suspected outbreaks, of which 34 outbreaks (59%) were confirmed by real-time PCR testing. Specimens from 25 of the 34 outbreaks were further characterized by VRDL. GI and GII were associated with 3 and 22 outbreaks, respectively. Similar to the current season, **GII.P16-GII.4 Sydney** was the most commonly detected genotype from October 2016 through January 2017 (Figure 2), identified in 14 of 25 outbreaks (56%) received by VRDL.

Table 3: Norovirus Genotypes from Reported Norovirus Outbreaks, October 2017—January 2018

Genogroup I Genotypes	**Number of OBs**
GI.P4-GI.4	1
GI.P7-GI.7A	2
Total	3
Genogroup II Genotypes	**Number of OBs**
GII.Pe-GII.4 Sydney *(originally 2012 GII.4 Sydney)*	3
GII.P4 New Orleans-GII.4 Sydney *(a recombinant strain of the 2012 GII.4 Sydney with GII.4 New Orleans now circulating as a minor variant [see Figures 3 and 4])*	4
GII.P7-GII.6	1
GII.P7-GII.14	1
GII.P12-GII.3	4
GII.P16-GII.1	1
GII.P16-GII.4 Sydney *(aka "GII.4 Sydney 2015", currently the predominant circulating norovirus variant [Figures 3 and 4])*	15
GII.P16-GII.2 *(emerged in 2016, associated with several school OBs)*	5
GII.P17-GII.17B	1
Total	35

Figure 1: **Number of Laboratory-Confirmed Norovirus Outbreaks Identified by Local Health Jurisdiction, October 2017—January 2018**

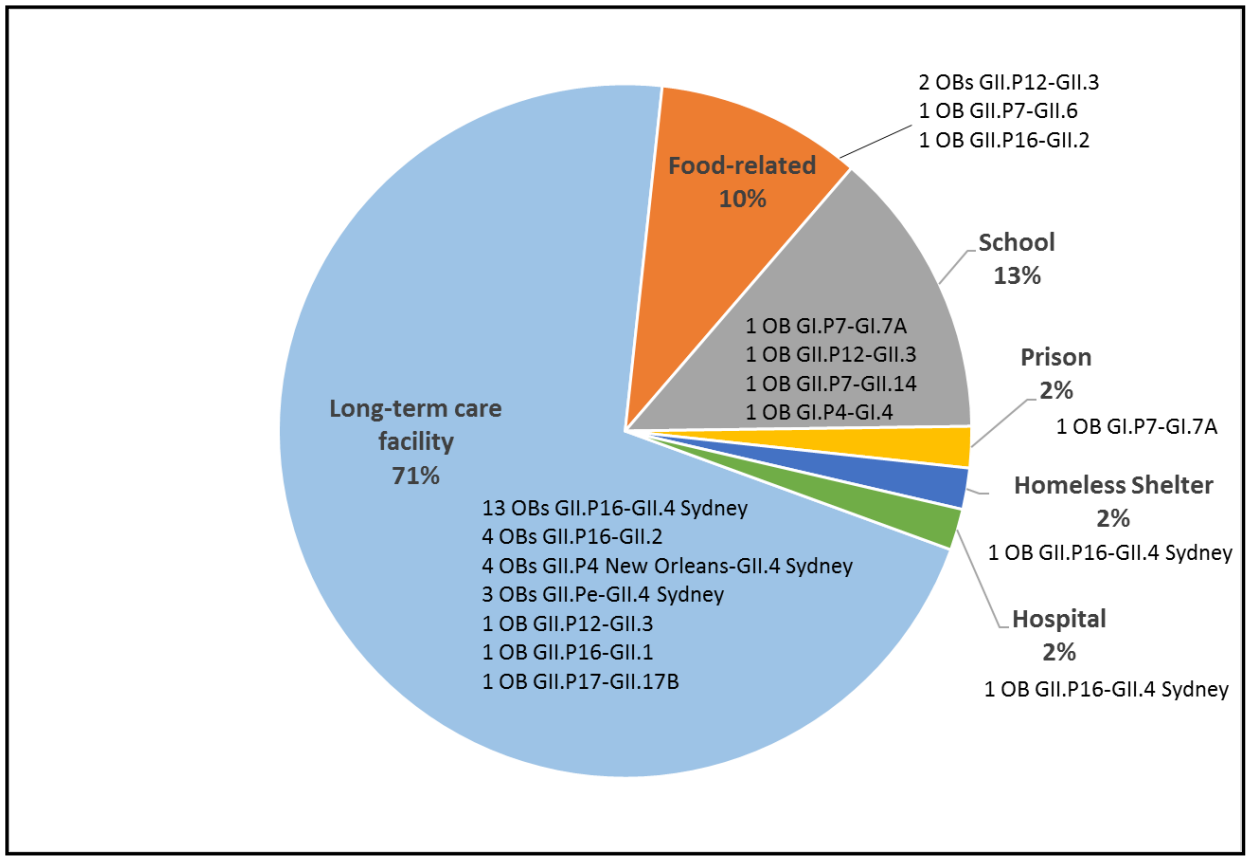
Figure 2: Laboratory-Confirmed Norovirus Outbreaks Reported by the NLN, October 2017—January 2018



MOST REPORTED NOROVIRUS OUTBREAKS OCCUR AT LONG-TERM CARE FACILITIES

Long-term care facilities (LTCFs) are settings conducive for recognizing cases and outbreaks of acute gastroenteritis, and therefore are more likely to produce more specimens for laboratory confirmation of suspect norovirus outbreaks than other settings (such as schools or restaurants). Therefore, as is typical for other time frames, it is not unexpected that the majority (37/52 outbreaks, or 71%) of norovirus outbreaks identified by NLN labs from October 2017 through January 2018 occurred at LTCFs. Likewise, due to the availability of specimens, more outbreaks at LTCFs were genotyped than for any other setting.

Figure 3: Norovirus Genotypes by Setting for Outbreaks (OBs) Tested by the NLN, October 2017—January 2018 (N=38)



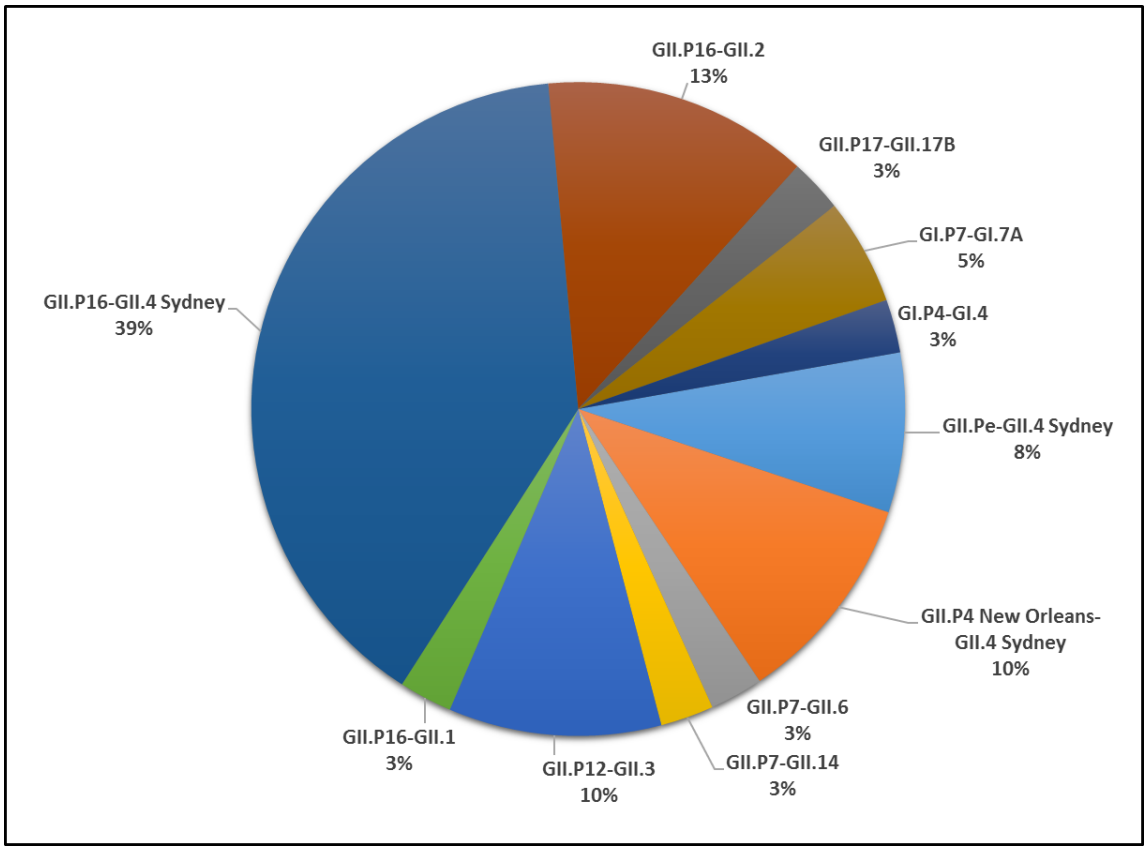
NOROVIRUS GENOTYPING AND CALICINET

Laboratory-confirmed (i.e., PCR-positive) norovirus outbreaks are genotyped by sequencing segments of the polymerase gene (region B) and the capsid gene (region C). Table 3 indicates genotypes identified by the VRDL for norovirus outbreaks reported by the NLN. As stated above, **GII.P16-GII.4 Sydney** was the predominant genotype (15/38 outbreaks, or 39%) identified in California norovirus outbreaks reported by the NLN (Figure 4).

The VRDL is a CaliciNet-certified laboratory and submits all norovirus outbreak sequences to the CaliciNet database at the U.S. Centers for Disease Control and Prevention (CDC). Between October 2017 and January 2018, the VRDL submitted specimens from 27 different norovirus outbreaks to CaliciNet/CDC. In addition to the VRDL, two other NLN members, Los Angeles County Public Health Laboratory and Orange County Public Health Laboratory, are also CaliciNet-certified laboratories, and each independently submits norovirus sequences to CaliciNet/CDC.

The CaliciNet/CDC database allows norovirus sequences to be compared and queried in real-time for situational awareness of strains associated with outbreaks and facilitates a rapid response for investigation, prevention, and control of norovirus outbreaks. See Figures 5 and 6 for examples of phylogenetic trees (dendrograms) generated from regions B and C sequence analyses that show relatedness of noroviruses from different OBs and help to identify linked outbreaks.

Figure 4: Norovirus Genotypes for Outbreaks (OBs) Tested by the NLN October 2017—January 2018 (N=38)



NOTES

1. Thank you to all who attended and participated in the California Norovirus Laboratory Network Surveillance Meeting on November 3, 2017 in Richmond, CA. We hope this meeting was useful and provided new ideas to improve norovirus surveillance and outbreak response throughout California.

2. Currently, all norovirus outbreak specimens from California's state prisons are sent to Quest Diagnostics for testing. VRDL is working with Quest Diagnostics to obtain specimens from state prison norovirus outbreaks for genotyping.

3. Many thanks to our CDPH Infectious Disease Branch/Disease Investigations Section epidemiology colleagues (Jeff Higa, Vi Peralta, Selam Tecle, Sarah Rutschmann, and Dr. Seema Jain) for their immense assistance with outbreak investigations and for reviewing this report.

REMINDERS

1. Please send a minimum of **TWO positive stool specimens and their nucleic acid extracts per outbreak** to VRDL for norovirus genotyping; **more than TWO is preferred**. Please submit one specimen and its corresponding nucleic acid extract per patient.
2. Please submit norovirus negative outbreak specimens (defined as at least 3 norovirus negative specimens) to VRDL for further testing.
3. Please provide CalREDIE identifiers whenever possible. VRDL will provide, upon request, real-time RT-PCR primers and probe and controls.
4. Please let Chao Pan know if you require technical support: Chao-Yang.Pan@cdph.ca.gov
5. Please send your jurisdiction's weekly NLN report to Alice Chen: Alice.Chen@cdph.ca.gov
6. VRDL requires the VRDL General Purpose Laboratory Submittal Form for all specimens. Please include a Gastroenteritis Outbreak Information Summary Form with the individual VRDL Submission forms. Please refer to the "NOROVIRUS TESTING QUICK SHEET" on the VRDL's website for further instructions. All necessary VRDL forms can be found here (https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/VRDL_Specimen_Submittal_Forms.aspx)
7. VRDL can perform norovirus PCR testing if your laboratory lacks the resources. Please work with your environmental health colleagues, epidemiologists and health officers to promote laboratory investigation of suspect acute viral gastroenteritis outbreaks.

The next California NLN Triannual Report will be published in June 2018.

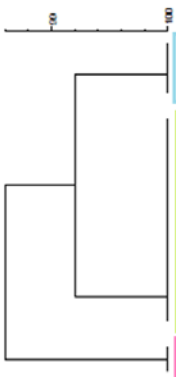
TECHNICAL APPENDIX

Norovirus Molecular Epidemiology

Comparison of Two Analyses (Figures 5 & 6)

Figure 5: Dendrogram of Norovirus GII.P16-GII.2 Outbreaks from Three Counties

Three 2017 County A outbreaks (OB 3298, 3300, and 3301) show identical polymerase B and capsid C sequences indicating they are linked, possibly by a common source (all three outbreaks are within the same branch enclosed by the light green box). **GII.P16-GII.2** outbreaks from Counties B (OSC-172) and C (OSC-177) have sequence differences in the polymerase B and capsid C regions resulting in separate branches (represented by the pink and blue boxes), indicating that they are not linked. **NOTE:** virus from outbreak specimens within a branch (or colored box) are identical in sequence, indicating a high likelihood that they are linked to a common source, while different branches (indicated by different colored boxes) represent viruses with slightly divergent sequences, indicating that outbreaks in different colored boxes are not closely related and likely not linked to a common source.



Key	LabOBNumber	VRDL OB number	VRDL ID number	OutbreakDate	OutbreakCity	OutbreakCounty	OutbreakSetting	Transmission	SEQ_RegB-C-GII_Genotype
2017-SP-0375	2017-OB-182	OSC-177	V17T05702	2017-11-02	City D	County C	School	Person-to-Person	GII.P16-GII.2
2017-SP-0377	2017-OB-182	OSC-177	V17T05704	2017-11-02	City D	County C	School	Person-to-Person	GII.P16-GII.2
2017-SP-0380	2017-OB-182	OSC-177	V17T05707	2017-11-02	City D	County C	School	Person-to-Person	GII.P16-GII.2
2017-SP-0343	2017-OB-175	OB 3298	V17T05591	2017-10-31	City A	County A	Long-term Care Facility	Person-to-Person	GII.P16-GII.2
2017-SP-0344	2017-OB-175	OB 3298	V17T05593	2017-10-31	City A	County A	Long-term Care Facility	Person-to-Person	GII.P16-GII.2
2017-SP-0384	2017-OB-184	OB 3300	V17T05757	2017-11-04	City B	County A	Long-term Care Facility	Person-to-Person	GII.P16-GII.2
2017-SP-0385	2017-OB-184	OB 3300	V17T05759	2017-11-04	City B	County A	Long-term Care Facility	Person-to-Person	GII.P16-GII.2
2017-SP-0386	2017-OB-184	OB 3300	V17T05770	2017-11-04	City B	County A	Long-term Care Facility	Person-to-Person	GII.P16-GII.2
2017-SP-0387	2017-OB-184	OB 3300	V17T05772	2017-11-04	City B	County A	Long-term Care Facility	Person-to-Person	GII.P16-GII.2
2017-SP-0388	2017-OB-185	OB 3301	V17T05761	2017-11-11	City A	County A	Long-term Care Facility	Person-to-Person	GII.P16-GII.2
2017-SP-0389	2017-OB-185	OB 3301	V17T05763	2017-11-11	City A	County A	Long-term Care Facility	Person-to-Person	GII.P16-GII.2
2017-SP-0390	2017-OB-185	OB 3301	V17T05768	2017-11-11	City A	County A	Long-term Care Facility	Person-to-Person	GII.P16-GII.2
2017-SP-0363	2017-OB-177	OSC-172	V17T05715	2017-10-22	City C	County B	Other-Catered Event	Foodborne	GII.P16-GII.2
2017-SP-0364	2017-OB-177	OSC-172	V17T05716	2017-10-22	City C	County B	Other-Catered Event	Foodborne	GII.P16-GII.2

Figure 6: Dendrogram of Norovirus GII.P16-GII.4 Sydney Outbreaks from Four Counties

Two separate **GII.P16-GII.4 Sydney** outbreaks (within the purple box) in 2018 from County D (OB 3329) and County E (OB 3343) show identical sequences in the polymerase B and capsid C regions, indicating they are linked. Two **GII.P16-GII.4 Sydney** outbreaks from Counties F (OB 3319) and G (OB 3348) have sequence differences in polymerase B and capsid C regions that result in separate branches to the dendrogram (within the orange and red boxes, respectively), indicating that they are not linked.

Key	LabOBNumber	VRDL OB number	VRDL ID number	OutbreakDate	OutbreakCity	OutbreakCounty	OutbreakSetting	Transmission	SEQ_RegB-C-GII_Genotype
2018-SP-0014	2018-OB-004	OB 3329	V18T00729	2018-01-12	City E	County D	Hospital	Person-to-Person	GII.P16-GII.4 Sydney
2018-SP-0016	2018-OB-004	OB 3329	V18T00733	2018-01-12	City E	County D	Hospital	Person-to-Person	GII.P16-GII.4 Sydney
2018-SP-0029	2018-OB-010	OB 3343	V18T00922	2018-01-16	City F	County E	Long-term Care Facility	Unknown	GII.P16-GII.4 Sydney
2018-SP-0030	2018-OB-010	OB 3343	V18T00923	2018-01-16	City F	County E	Long-term Care Facility	Unknown	GII.P16-GII.4 Sydney
2018-SP-0031	2018-OB-010	OB 3343	V18T00924	2018-01-16	City F	County E	Long-term Care Facility	Unknown	GII.P16-GII.4 Sydney
2018-SP-0032	2018-OB-010	OB 3343	V18T00925	2018-01-16	City F	County E	Long-term Care Facility	Unknown	GII.P16-GII.4 Sydney
2017-SP-0460	2017-OB-205	OB 3319	V18T00298	2017-12-31	City G	County F	Long-term Care Facility	Unknown	GII.P16-GII.4 Sydney
2017-SP-0461	2017-OB-205	OB 3319	V18T00299	2017-12-31	City G	County F	Long-term Care Facility	Unknown	GII.P16-GII.4 Sydney
2017-SP-0462	2017-OB-205	OB 3319	V18T00300	2017-12-31	City G	County F	Long-term Care Facility	Unknown	GII.P16-GII.4 Sydney
2017-SP-0463	2017-OB-205	OB 3319	V18T00302	2017-12-31	City G	County F	Long-term Care Facility	Unknown	GII.P16-GII.4 Sydney
2017-SP-0464	2017-OB-205	OB 3319	V18T00428	2017-12-31	City G	County F	Long-term Care Facility	Unknown	GII.P16-GII.4 Sydney
2018-SP-0039	2018-OB-014	OB 3348	V18T01022	2018-01-21	City H	County G	Long-term Care Facility	Person-to-Person	GII.P16-GII.4 Sydney
2018-SP-0040	2018-OB-014	OB 3348	V18T01024	2018-01-21	City H	County G	Long-term Care Facility	Person-to-Person	GII.P16-GII.4 Sydney
2018-SP-0041	2018-OB-014	OB 3348	V18T01026	2018-01-21	City H	County G	Long-term Care Facility	Person-to-Person	GII.P16-GII.4 Sydney