

Supplemental Digital Content 3: First day of fever, day of peak fever and antipyretic use by post-vaccination day (0-3) for all study groups combined in Pavia-Ruz (2013)¹⁰ based on reanalysis of the individual level dataset. Fever defined as $\geq 38^{\circ}\text{C}$ and causally related to vaccine.

| Day | Dose 1 | | | Dose 2 | | |
|-------|------------------------------------|-----------------------------------|--|------------------------------------|-----------------------------------|--|
| | First day of Fever (n=3251)* | Day of Peak Fever (n=3251)* | Number of children receiving antipyretic (n=3243)† | First day of Fever (n=2241)* | Day of Peak Fever (n=2241)* | Number of children receiving antipyretic (n=2295)† |
| 0 | 27 (0.8%) | 22 (0.7%) | 299 (9.2%) | 35 (1.6%) | 27 (1.2%) | 137 (6.0%) |
| 1 | 34 (1.0%) | 30 (0.9%) | 173 (5.3%) | 20 (0.9%) | 21 (0.9%) | 98 (4.3%) |
| 2 | 14 (0.4%) | 16 (0.5%) | 133 (4.1%) | 20 (0.9%) | 19 (0.8%) | 80 (3.5%) |
| 3 | 27 (0.8%) | 34 (1.0%) | 122 (3.8%) | 7 (0.3%) | 15 (0.7%) | 72 (3.1%) |
| Total | 102 (3.1%) | 102 (3.1%) | 440 (13.6%) ‡ | 82 (3.7%) | 82 (3.7%) | 196 (8.5%)‡ |

* Fever data denominator is all subjects with valid diary card record of systemic symptoms after receipt of vaccine. Fever observations report numbers of study participants with first day of fever or highest temperature during their fever episode occurring on that day, with percentages in parentheses.

† Antipyretic data denominator all patients within safety cohort of study. Antipyretic observations report number of study participants administered antipyretic medication on that day, with percentages in parentheses.

‡ Total indicates number of children with antipyretic on any day. Total does not equal sum of individual days as patients may have had antipyretics on multiple days post-vaccination.