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Supplementary appendix 1

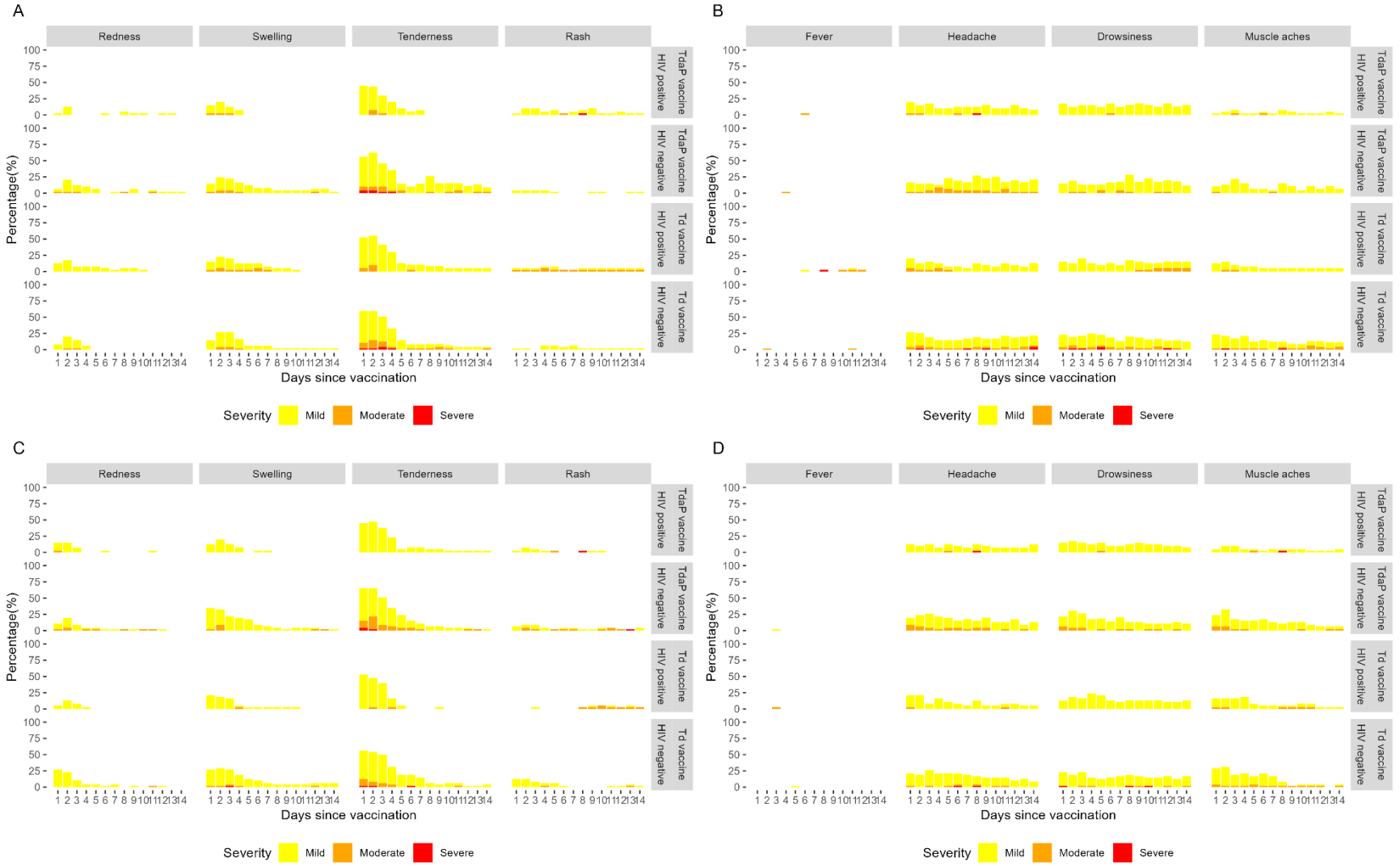
This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Nakabembe E, Greenland M, Amaral K, et al. Safety and immunogenicity of an acellular pertussis vaccine containing genetically detoxified pertussis toxin administered to pregnant women living with and without HIV and their newborns (WoMANPOWER): a randomised controlled trial in Uganda. *Lancet Glob Health* 2025; **13:** e81–97.

Supplementary appendix

Contents

Figure S1: Reactogenicity- severity of solicited adverse reactions in 14 days after vaccination by study arm and HIV-infected status as selfreported in participant diaries in the safety analysis population.



A: Local adverse reactions following first vaccination; B: Systemic adverse reactions following first vaccination; C: Local adverse reactions following second vaccination; D: Systemic adverse reactions following second vaccination.

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus.

All participants received Td for their first vaccination. N represents the denominator for each adverse reaction in each study group. Fever was defined using the FDA Guidance for Industry: Toxicity Grading Scale for Health Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials and was graded as: No symptoms: <38.0^{o}C, Mild symptoms: 38.0-<38.5^{o}C, Moderate symptoms: 38.5-<39.0^{o}C, Severe symptoms: 39.0-40.0^{o}C, Potentially life-threatening symptoms: >40.0^{o}C. Data that were either not recorded or poorly recorded were considered missing data. Missing data were excluded in the numerator and denominator and so denominators do not reflect all those participants who were vaccinated but only those with completed reactogenicity data in participant diary cards.

Table S1. Uganda's National Expanded Program on Immunisation Schedule

VACCINE	**AGE OF ADMINISTRATION**
BCG	Birth
OPV	Birth, 6 weeks,10 weeks and 14 weeks
Pentavalent	6 weeks,10 weeks and 14 weeks
PCV	6 weeks,10 weeks and 14 weeks
IPV	10 weeks and 14 weeks
MR	9 months and 18 months
Rota	6 weeks and 10 weeks
Measles	9 months and 15 months
Yellow Fever	9 months
Td	Females of 15-49 years (5 doses given with an interval of +1 month, +6 months, + 1 year and +1 year with preceding dose)

BCG-Bacille-Calmette-Guerin Vaccine, OPV-Oral Polio Vaccine, Pentavalent=Diphtheria, Tetanus, Pertussis, Hepatitis B and Haemophilus influenza type b(Hib)

PCV-Pneumococcal Conjugate Vaccine, IPV -Inactivated Polio Vaccine, MR-Measles and Rubella Vaccine Td-Tetanus

Diphtheria Vaccine

Source: https://zdlh.gavi.org/sites/default/files/2023-11/UGANDA_ZDLH_landscape_2023.pdf
Date accessed: 31/05/2024

Table S2. Adverse event grading

Grade	Severity	Description
0	None	No symptoms
1	Mild	Asymptomatic or mild symptoms; no or minimal interference with usual social & functional activities, intervention not indicated
2	Moderate	Moderate symptoms causing greater than minimal interference with usual social & functional activities, intervention indicated
3	Severe	Severe symptoms causing inability to perform usual social & functional activities with intervention or hospitalization indicated
4	Potentially Lifethreatening	Symptoms causing inability to perform basic self-care functions with intervention indicated to prevent permanent impairment, persistent disability or death
5	Death	Death

Participants self-reported local and systemic adverse reactions following vaccination as none, mild, moderate, or severe for headache, drowsiness, muscle aches, redness, swelling, tenderness, and rash. Temperature was collected and fever was defined using the FDA Guidance for Industry: Toxicity Grading Scale for Health Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials and was graded as: No symptoms: <38.0°C, Mild symptoms: 38.0-<38.5°C, Moderate symptoms: 38.5<39.0°C, Severe symptoms: 39.0-40.0°C, Potentially life-threatening symptoms: >40.0°C.

Table S3. Summary of blood samples taken by visit for anti-pertussis toxin IgG and anti-filamentous hemagglutinin IgG concentrations antibodies

	HIV positive TdaP (N=40)	**HIV negative TdaP (N=50)**	**HIV positive Td (N=41)**	**HIV negative Td (N=50)**	**Overall (N=181)**
Maternal baseline					
Sample collected and included in modified intention-to-treat analysis	39	48	37	48	172
Sample collected but lost	1	2	4	2	9
Maternal second vaccination + 4 weeks					
Sample collected and included in modified intention-to-treat analysis	40	46	38	46	170
Sample not collected	0	4	1	0	5
Sample not collected but blood result received – excluded from analysis for potentially incorrect labelling	0	0	0	2	2

Sample not collected – participant lost to follow-up or withdrew before visit	0	0	2	2	4
Maternal delivery					
Sample collected and included in modified intention-to-treat analysis	37	42	36	38	153
Sample collected but lost	0	0	0	2	2
Sample not collected	3	8	3	7	21
Sample not collected – participant lost to follow-up or withdrew before visit	0	0	2	3	5

	HIV positive TdaP (N=40)	**HIV negative TdaP (N=50)**	**HIV positive Td (N=41)**	**HIV negative Td (N=50)**	**Overall (N=181)**
Infant delivery					
Sample collected and included in modified intention-to-treat analysis	36	34	33	40	143
Sample collected but lost	0	0	1	0	1
Sample not collected	3	12	5	7	27

Sample not collected – participant lost to follow-up or withdrew before visit, or stillborn or died	1	4	2	3	10
Infant 18-week visit					
Sample collected and included in modified intention-to-treat analysis	35	43	35	44	157
Sample not collected	1	0	2	1	7
Sample not collected but blood result received – excluded from analysis for potentially incorrect labelling	0	0	1	0	1
Sample not collected – participant lost to follow-up, withdrew, stillborn, or died before visit	4	7	3	5	16

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus.

Table S4. Maternal clinical diagnoses relating to the preterm births

ID	**HIV status**	**Gestational age in weeks at delivery**	**Treatment arm**	**Clinical Diagnosis at delivery/plausible factors related to preterm births**
1	Negative	24	1	Chorioamnionitis
2	Negative	34	1	Severe pre-eclampsia
3	Positive	34	1	Severe pre-eclampsia
4	Positive*	35	1	Chronic HIV infection of more than 15 years, diagnosed in childhood

5	Negative	36	2	Pre-eclampsia with preterm premature rupture of membranes

Treatment arms: 1=Tdap 2=Td.

* Mother was diagnosed with HIV infection in childhood and had history of tuberculosis infection and treatment, she had fully recovered from TB at the time of enrolment into the study.

Table S5. Summary of unsolicited adverse events in women by study arm

	HIV positive TdaP (N=40)	**HIV negative TdaP (N=50)**	**HIV positive Td (N=41)**	**HIV negative Td (N=50)**	**Overall (N=181)**
Number of unsolicited adverse events in mothers	53	109	37	96	295
Number of unique participants with at least one adverse event*	22 (55%)	33 (66%)	19 (46%)	31 (62%)	105 (58%)
Severity					
Mild	31 (58%)	54 (50%)	18 (49%)	49 (51%)	152 (52%)
Moderate	18 (34%)	43 (39%)	19 (51%)	44 (46%)	124 (42%)
Severe	4 (7.5%)	8 (7.3%)	0 (0%)	3 (3.1%)	15 (5.1%)
Life threatening	0 (0%)	1 (0.9%)	0 (0%)	0 (0%)	1 (0.3%)
Death	0 (0%)	3 (2.8%)	0 (0%)	0 (0%)	3 (1.0%)
Causality					
Related	0 (0%)	1 (0.9%)	0 (0%)	0 (0%)	1 (0.3%)
Unrelated	53 (100%)	108 (99%)	37 (100%)	96 (100%)	294 (100%)
Causality degree					
Not related	53 (100%)	108 (99%)	37 (100%)	96 (100%)	294 (100%)

Possibly	0 (0%)	1 (0.9%)	0 (0%)	0 (0%)	1 (0.3%)
Definitely	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

	HIV positive TdaP (N=40)	**HIV negative TdaP (N=50)**	**HIV positive Td (N=41)**	**HIV negative Td (N=50)**	**Overall (N=181)**
Serious adverse event					
No	49 (92%)	97 (89%)	37 (100%)	93 (97%)	276 (94%)
Yes	4 (7.5%)	12 (11%)	0 (0%)	3 (3.1%)	19 (6.4%)
Serious adverse event severity					
Life threatening adverse event	0 (0%)	3 (25%)	0 (NA%)	2 (67%)	5 (26%)
Inpatient hospitalization or prolongation of existing hospitalization	3 (75%)	5 (42%)	0 (NA%)	0 (0%)	8 (42%)
Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions	0 (0%)	0 (0%)	0 (NA%)	1 (33%)	1 (5.3%)
Important medical events based upon appropriate medical judgement	1 (25%)	0 (0%)	0 (NA%)	0 (0%)	1 (5.3%)
Death	0 (0%)	4 (33%)	0 (NA%)	0 (0%)	4 (21%)

Death					
Fresh Stillbirth	-	3 (75%)	-	-	3 (75%)
Macerated stillbirth	-	1 (25%)	-	-	1 (25%)

Medical review required					
No	2 (3.8%)	0 (0%)	1 (2.7%)	6 (6.3%)	9 (3.1%)
Yes	51 (96%)	109 (100%)	36 (97%)	90 (94%)	286 (97%)
Body system category					
	HIV positive TdaP (N=40)	**HIV negative TdaP (N=50)**	**HIV positive Td (N=41)**	**HIV negative Td (N=50)**	**Overall (N=181)**
Cardiovascular	5 (9.4%)	6 (5.5%)	0 (0%)	10 (10%)	21 (7.1%)
Central Nervous System	2 (3.8%)	11 (10%)	2 (5.4%)	8 (8.3%)	23 (7.8%)
Digestive	7 (13%)	19 (17%)	6 (16%)	7 (7.3%)	39 (13%)
Immune	2 (3.8%)	3 (2.8%)	0 (0%)	1 (1.0%)	6 (2.0%)
Musculo-Skeletal	6 (11%)	10 (9.2%)	3 (8.1%)	11 (11%)	30 (10%)
Reproductive	8 (15%)	17 (16%)	4 (11%)	16 (17%)	45 (15%)
Respiratory	9 (17%)	9 (8.3%)	8 (22%)	13 (14%)	39 (13%)

Urogenital	14 (26%)	28 (26%)	14 (38%)	24 (25%)	80 (27%)
Infection	0 (0%)	6 (5.5%)	0 (0%)	6 (6.3%)	12 (4.1%)
Timing					
Between first and second vaccination	8 (15%)	28 (26%)	4 (11%)	18 (19%)	58 (20%)
Between second vaccination and delivery	27 (51%)	52 (48%)	24 (65%)	47 (49%)	150 (51%)
After delivery	18 (34%)	29 (27%)	9 (24%)	31 (32%)	87 (29%)

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus.

Percentages are column percentages and the denominators are the number of adverse events. There were no non-fatal unsolicited adverse events in women leading to study withdrawal.

*Denominators are the number of participants in the study arm.

Table S6. Summary of unsolicited adverse events in infants by study arm

	HIV positive TdaP (N=40)	**HIV negative TdaP (N=50)**	**HIV positive Td (N=41)**	**HIV negative Td (N=50)**	**Overall (N=181)**
Number of unsolicited adverse events in infants	101	115	65	94	375
Number of unique participants with at least one adverse event*	28 (70%)	36 (72%)	22 (54%)	33 (66%)	119 (66%)
Severity					
Mild	32 (32%)	75 (65%)	22 (34%)	59 (63%)	188 (50%)
Moderate	63 (62%)	39 (34%)	39 (60%)	34 (36%)	175 (47%)
Severe	3 (3.0%)	1 (0.9%)	3 (4.6%)	1 (1.1%)	8 (2.1%)
Death	3 (3.0%)	0 (0%)	1 (1.5%)	0 (0%)	4 (1.1%)
Causality					
Unrelated	101 (100%)	115 (100%)	65 (100%)	94 (100%)	375 (100%)
Serious adverse event					
No	95 (94%)	113 (98%)	61 (94%)	93 (99%)	362 (97%)
Yes	6 (5.9%)	2 (1.7%)	4 (6.2%)	1 (1.1%)	13 (3.5%)

Serious adverse event severity					
Life threatening adverse event	0 (0%)	0 (0%)	1 (25%)	0 (0%)	1 (7.7%)
Inpatient hospitalization or prolongation of existing hospitalization	2 (33%)	1 (50%)	2 (50%)	1 (100%)	6 (46%)

	HIV positive TdaP (N=40)	**HIV negative TdaP (N=50)**	**HIV positive Td (N=41)**	**HIV negative Td (N=50)**	**Overall (N=181)**
Congenital anomaly/ birth defect	1 (17%)	1 (50%)	0 (0%)	0 (0%)	2 (15%)
Death	3 (50%)	0 (0%)	1 (25%)	0 (0%)	4 (31%)
Death					
Early Neonatal death(< =7 days after birth)	2 (67%)	-	0 (0%)	-	2 (50%)
Infant death (>7 days after birth)	1 (33%)	-	1 (100%)	-	2 (50%)
Medical review required					
No	3 (3.0%)	1 (0.9%)	0 (0%)	1 (1.1%)	5 (1.3%)
Yes	98 (97%)	114 (99%)	65 (100%)	93 (99%)	370 (99%)
Body system category					

Cardiovascular	3 (3.0%)	1 (0.9%)	2 (3.1%)	0 (0%)	6 (1.6%)
Central Nervous System	13 (13%)	7 (6.1%)	7 (11%)	11 (12%)	38 (10%)
Digestive	17 (17%)	29 (25%)	9 (14%)	15 (16%)	70 (19%)
Immune	7 (6.9%)	8 (7.0%)	4 (6.2%)	6 (6.4%)	25 (6.7%)
Musculo-Skeletal	5 (5.0%)	2 (1.7%)	2 (3.1%)	2 (2.1%)	11 (2.9%)
Reproductive	1 (1.0%)	0 (0%)	0 (0%)	1 (1.1%)	2 (0.5%)
Respiratory	53 (52%)	68 (59%)	39 (60%)	59 (63%)	219 (58%)
Urogenital	0 (0%)	0 (0%)	1 (1.5%)	0 (0%)	1 (0.3%)
	HIV positive TdaP (N=40)	**HIV negative TdaP (N=50)**	**HIV positive Td (N=41)**	**HIV negative Td (N=50)**	**Overall (N=181)**
Infection	2 (2.0%)	0 (0%)	1 (1.5%)	0 (0%)	3 (0.8%)

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus. Percentages are column percentages and the denominators are the number of adverse events. There were no non-fatal unsolicited adverse events in infants leading to study withdrawal.

*Denominators are the number of participants in the study arm.

Table S7. Related unsolicited adverse events in mothers

ID	Study arm	HIV status	Severity/ Death	Body class system	International Classification of Diseases-11 clinical diagnosis	Days since first vaccination	Days since second vaccination
1	TdaP vaccine	HIV negative	Moderate	Central Nervous System	Dizziness unspecified	26 days	0 days

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus.

There were no related unsolicited adverse events in infants.

Table S8. Serious adverse events in mothers excluding deaths

ID	Study arm	HIV status	Severity	Serious adverse event type	Body class system	Causality	International Classification of Diseases-11 clinical diagnosis	Timing of start date
1	Td vaccine	HIV negative	Severe	Life threatening adverse event	Reproductive	Unrelated	Preterm labour without delivery	Between second vaccination and delivery

2	TdaP vaccine	HIV negative	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Urogenital	Unrelated	Infection of genitourinary tract in pregnancy	Between second vaccination and delivery
3	TdaP vaccine	HIV negative	Severe	Life threatening adverse event	Cardiovascular	Unrelated	Severe Preeclampsia	Between second vaccination and delivery
4	TdaP vaccine	HIV negative	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Infection	Unrelated	Malaria complicating pregnancy	Between first and second vaccination
5	TdaP vaccine	HIV negative	Severe	Life threatening adverse event	Cardiovascular	Unrelated	Severe Preeclampsia	Between first and second vaccination
6	TdaP vaccine	HIV negative	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Infection	Unrelated	Malaria complicating pregnancy	Between first and second vaccination
7	TdaP vaccine	HIV negative	Severe	Life threatening adverse event	Cardiovascular	Unrelated	Severe Preeclampsia	Between second vaccination and delivery

ID	Study arm	HIV status	Severity	Serious adverse event type	Body class system	Causality	International Classification of Diseases-11 clinical diagnosis	Timing of start date
8	Td vaccine	HIV negative	Severe	Life threatening adverse event	Cardiovascular	Unrelated	Severe Preeclampsia	Between second vaccination and delivery
9	Td vaccine	HIV negative	Severe	Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions	Digestive	Unrelated	Cholelithiasis with acute cholecystitis	After delivery
10	TdaP vaccine	HIV negative	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Urogenital	Unrelated	Infection of genitourinary tract in pregnancy	Between second vaccination and delivery
11	TdaP vaccine	HIV negative	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Infection	Unrelated	Malaria complicating pregnancy	Between first and second vaccination
12	TdaP vaccine	HIV positive	Severe	Important medical events based upon appropriate medical judgement	Cardiovascular	Unrelated	Anaemia complicating pregnancy	After delivery

13	TdaP vaccine	HIV positive	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Urogenital	Unrelated	Infection of genitourinary tract in pregnancy	Between second vaccination and delivery
14	TdaP vaccine	HIV positive	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Reproductive	Unrelated	Threatened abortion	Between second vaccination and delivery
15	TdaP vaccine	HIV positive	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Cardiovascular	Unrelated	Severe Preeclampsia	Between second vaccination and delivery

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus. The leading causes of serious adverse events for mothers were severe bladder infections, severe pre-eclampsia and malaria complicating pregnancy, these three accounted for 9 of the 16 events. Severe pre-eclampsia affecting fetus and newborn sepsis were the commonest reported infant serious adverse events.

Table S9. Serious adverse events in infants excluding deaths

ID	**Study arm**	**HIV status**	**Severity**	**Serious adverse event type**	**Body class system**	**Causality**	**International Classification of Diseases-11 clinical diagnosis**	**Days since delivery**

1	Td vaccine	HIV positive	Severe	Life threatening adverse event	Respiratory	Unrelated	Pneumonia	37 days
2	TdaP vaccine	HIV negative	Severe	Congenital anomaly/ birth defect	Digestive	Unrelated	Low anorectal malformation with fistula	0 days
3	Td vaccine	HIV negative	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Respiratory	Unrelated	Pneumonia	315 days
4	TdaP vaccine	HIV negative	Mild	Inpatient hospitalization or prolongation of existing hospitalization	Digestive	Unrelated	Diarrhoea	306 days
5	Td vaccine	HIV positive	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Digestive	Unrelated	Diarrhoea	300 days
6	Td vaccine	HIV positive	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Infection	Unrelated	Newborn sepsis	1 day
7	TdaP vaccine	HIV positive	Severe	Congenital anomaly/ birth defect	Cardiovascular	Unrelated	Congenital anomaly of great vessels	13 days
8	TdaP vaccine	HIV positive	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Infection	Unrelated	Newborn sepsis	1 day

9	TdaP vaccine	HIV positive	Severe	Inpatient hospitalization or prolongation of existing hospitalization	Infection	Unrelated	Newborn sepsis	96 days

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus.

Table S

10.Details relating to stillbirths and infant deaths

ID	Study arm	HIV status	Death category	Clinical detail relating to plausible causes	Body class system	Causality
1	TdaP vaccine	HIV negative	Macerated stillbirth	Severe preeclampsia affecting the fetus: mother developed high blood pressure reaching 161/109mmHg. This became complicated with intra-uterine fetal death.	Reproductive	Unrelated
2	TdaP vaccine	HIV negative	Fresh Stillbirth	Severe preeclampsia affecting the fetus: mother developed high blood pressure 176/107 mmHg. The mother delivered vaginally beyond 24 hours from time of admission based on a decision made by most senior obstetrician on duty. There were delays in decision making around time of delivery especially final decision for mother to have a vaginal delivery instead of c/section.	Reproductive	Unrelated
3	TdaP	Negative	Fresh Stillbirth	Severe obstructed labor: the mother transferred from the study area to her village due to COVID-19 related restrictions. Her village was more than six hours drive from study area. She got into labor and the district hospital where she reported was not in position to do the emergency caesarean section due to lack of resources. Mother was referred to the regional referral hospital in the region where she reached with severe obstructed labour and severe fetal distress. She was delivered of a fresh still birth.	Reproductive	Unrelated

4	TdaP vaccine	HIV positive	Early Neonatal death (< =7 days after birth)	Mother had a normal pregnancy and came to hospital in second stage of labour reporting history of precipitate labor, the mother was delivered within 31 minutes of arrival of a severely asphyxiated baby, APGAR 2/10, neonatal resuscitation efforts were futile.	Respiratory	Unrelated
5	TdaP vaccine	HIV negative	*Fresh Stillbirth	Clinical diagnosis of chorioamnionitis based on abnormal vaginal discharge and abdominal pain	Reproductive	Unrelated
6	TdaP vaccine	HIV negative	Fresh Stillbirth	Ascending infection – Endometritis, high vaginal swab analysis showed Gram positive diplococci, Gram negative rods	Reproductive	Unrelated
7	TdaP vaccine	HIV positive	Early Neonatal death (< =7 days after birth)	Baby was born with severe form of open spina bifida which was missed at the 19 weeks screening ultrasound, they were managed at the national specialized hospital by the paediatric neurology team but baby passed on within 24 hours of delivery	Central Nervous System	Unrelated
8	TdaP vaccine	HIV positive	Infant death (>7 days after birth)	Severe pneumonia and gastroenteritis in HEU infant: Mother had a successful pregnancy and delivery, baby was HIV exposed but uninfected. Baby had routine vaccinations however at 14 weeks of age, the mother reported that her baby was being treated for a short episode severe gastroenteritis and pneumonia in a private clinic, she was advised to immediately come to study site but baby was unresponsive and confirmed dead on arrival at study site.	Respiratory	Unrelated
9	Td vaccine	HIV positive	Infant death (>7 days after birth)	Bronchopneumonia in HEU infant	Respiratory	Unrelated

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus, HEU=HIV exposed uninfected infant

*The completed gestational age of the fetus was 24, this is below the age of fetal viability in Uganda, so would be considered an abortion in Uganda.

Table S

11. Geometric mean concentrations by study arm and HIV status in the modified intention-to-treat populations

	TdaP vaccine		**Td vaccine**	
	HIV positive (N=40)	**HIV negative (N=50)**	**HIV positive (N=41)**	**HIV negative (N=50)**
Anti-pertussis toxin IgG				
Baseline	10.7 (7.5, 15.3) [n=39]	10.7 (8, 14.2) [n=48]	12.3 (9.1, 16.8) [n=37]	10.7 (7.8,14.7) [n=48]
Second vaccination + 4 weeks	133.9 (91.4, 196.1) [n=40]	245.1 (167.8, 358) [n=46]	11.8 (8.6, 16.1) [n=38]	9 (6.5, 12.6) [n=46]
Maternal delivery	87.4 (55.1, 138.5) [n=37]	121.7 (79.4, 186.6) [n=42]	10.2 (7, 14.9) [n=36]	6.6 (4.5, 9.6) [n=38]
Infant delivery	114.7 (70.4, 186.8) [n=36]	169.7 (101.2, 284.5) [n=34]	11.9 (8.2, 17.4) [n=33]	7.9 (5.1, 12.2) [n=40]
Infant 18 weeks	16.8 (10.7, 26.1) [n=35]	23.5 (15.6, 35.3) [n=43]	87.6 (43.7, 175.6) [n=35]	141.1 (80.9, 246.1) [n=44]
Delivery to 18-week fold-change	0.14 (0.08, 0.25) [n=32]	0.13 (0.07, 0.24) [n=32]	6.55 (2.34, 18.34) [n=32]	18.82 (7.59, 46.63) [n=37]
Transplacental ratio	1.31 (1.17, 1.46) [n=36]	1.52 (1.2, 1.93) n=34]	1.31 (1.02, 1.67) [n=33]	1.09 (0.87, 1.37) [n=38]
Anti-filamentous hemagglutinin IgG				
Baseline	14.4 (9.5, 21.8) [n=39]	19.9 (15.4, 25.6) [n=48]	18.6 (13.5, 25.6) [n=37]	20.5 (15.8, 26.6) [n=48]
Second vaccination + 4 weeks	101.7 (65.3, 158.3) [n=40]	313.8 (236.5, 416.4) [n=46]	17.9 (13.3, 24.1) [n=38]	16.2 (12.6, 21) [n=46]

Maternal delivery	66.4 (41.7, 105.7) [n=37]	210.9 (158.1, 281.4) [n=42]	18.8 (13.4, 26.3) [n=36]	16.5 (12.2, 22.2) [n=38]
Infant delivery	74.1 (44.3, 124.2) [n=36]	269.9 (186.5, 390.6) [n=34]	17.5 (11.6, 26.4) [n=33]	17.5 (12.5, 24.7) [n=40]
Infant 18 weeks	20.2 (15.4, 26.5) [n=35]	22.2 (17.1, 28.7) [n=43]	19.8 (14.2, 27.7) [n=35]	17.1 (12.8, 22.7) [n=44]
Delivery to 18-week fold-change	0.25 (0.13, 0.48) [n=32]	0.09 (0.07, 0.11) [n=32]	1.07 (0.59, 1.95) [n=32]	0.96 (0.59, 1.55) [n=37]
Transplacental ratio	1.13 (1, 1.29) [n=36]	1.22 (0.9, 1.66) [n=34]	0.94 (0.78, 1.14) [n=33]	1.02 (0.83, 1.24) [n=38]

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus.
Data presented are geometric means and 95% confidence intervals.

Table S

12. Geometric mean concentrations for anti-tetanus toxoid IgG concentrations by study arm and HIV status in the modified intentionto- treat populations

	TdaP vaccine		**Td vaccine**	
	HIV positive (N=40)	**HIV negative (N=50)**	**HIV positive (N=41)**	**HIV negative (N=50)**
Anti-tetanus toxoid IgG concentrations				
Infant delivery	4 (2, 8.02) [n=18]	6.46 (3.8, 11.01) [n=20]	4.27 (2.57, 7.1) [n=19]	8.1 (4.55, 14.43) [n=20]
Infant 18 weeks	1.19 (0.71, 2) [n=14]	1.34 (1.06, 1.71) [n=16]	1.16 (0.71, 1.88) [n=18]	1.75 (1.21, 2.54) [n=17]
Delivery to 18-week fold-change	0.3 (0.09, 1.01) [n=13]	0.16 (0.11, 0.24) [n=16]	0.26 (0.14, 0.51) [n=17]	0.17 (0.09, 0.31) [n=17]

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus.

Data presented are geometric means and 95% confidence intervals. Anti-tetanus toxoid IgG concentrations were only analysed for infants with blood samples available at delivery or 18-week visit.

13. Geometric mean ratios for anti-tetanus toxoid IgG concentrations in the modified intention-to-treat populations

	TdaP versus Td vaccine	**HIV-positive versus HIV-negative**

Table S

	HIV-positive	**HIV-negative**	**TdaP**	**Td vaccine**
Anti-tetanus toxoid IgG concentrations				
Infant delivery	0.94 (0.41, 2.13) [n=37]	0.80 (0.37, 1.70) [n=40]	0.62 (0.27, 1.43) [n=38]	0.53 (0.25, 1.11) [n=39]
Infant 18 weeks	1.03 (0.52, 2.05) [n=32]	0.77 (0.50, 1.18) [n=33]	0.88 (0.53, 1.49) [n=30]	0.66 (0.36, 1.19) [n=35]
Delivery to 18-week fold-change	1.13 (0.33, 3.91) [n=30]	0.95 (0.47, 1.96) [n=33]	1.86 (0.61, 5.67) [n=29]	1.57 (0.65, 3.77) [n=34]

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus.

Data presented are geometric means and 95% confidence intervals. Anti-tetanus toxoid IgG concentrations were only analysed for infants with blood samples available at delivery or 18-week visit.

	TdaP versus Td vaccine		**HIV-positive versus HIV-negative**		**p-value for interaction**
	HIV-positive	**HIV-negative**	**TdaP**	**Td vaccine**	

Table S

Per-protocol analyses					

14. Sensitivity analyses of anti-pertussis toxin IgG concentrations

Maternal delivery	9.11 (5.00, 16.59) [n=70]	19.3 (10.8, 34.3) [n=78]	0.73 (0.38, 1.37) [n=76]	1.54 (0.91, 2.61) [n=72]	0.17
Infant 18 weeks	0.18 (0.07, 0.50) [n=47]	0.17 (0.08, 0.35) [n=68]	0.65 (0.32, 1.35) [n=61]	0.60 (0.22, 1.64) [n=54]	0.88
Sensitivity analyses in the modified intention-to-treat population					
Infant delivery adjusted for maternal age at enrolment, gestational age at delivery, and vaccination history	9.63 (5.04, 18.42) [n=69]	22.2 (11.4, 43.3) [n=74]	0.94 (0.43, 2.07) [n=70]	1.39 (0.77, 2.51) [n=73]	0.07
Infant 18 weeks					
Adjusted for gestational age at second vaccination	0.19 (0.08, 0.44) [n=70]	0.16 (0.08, 0.32) [n=87]	0.73 (0.40, 1.33) [n=78]	0.63 (0.27, 1.47) [n=79]	0.84

Table S

Adjusted for maternal age at enrolment, gestational age at delivery, vaccination history, and interval between infant wP first and second vaccinations, and interval between infant wP second and third vaccinations	0.25 (0.11, 0.60) [n=70]	0.17 (0.08, 0.34) [n=87]	0.64 (0.32, 1.28) [n=78]	0.60 (0.24, 1.50) [n=79]	0.58
Adjusted for gestational age at delivery	0.20 (0.09, 0.45) [n=70]	0.17 (0.08, 0.33) [n=87]	0.73 (0.40, 1.32) [n=78]	0.59 (0.25, 1.42) [n=79]	0.70
Adjusted for maternal age at enrolment, gestational age at delivery, and vaccination history	0.24 (0.10, 0.57) [n=70]	0.17 (0.08, 0.34) [n=87]	0.63 (0.32, 1.26) [n=78]	0.63 (0.26, 1.52) [n=79]	0.58
Adjusted for maternal age at enrolment, gestational age at delivery, vaccination history, and cord/neonatal venous blood concentrations on log_2 scale	0.58 (0.17, 1.91) [n=64]	0.31 (0.11, 0.88) [n=69]	0.75 (0.35, 1.60) [n=64]	0.66 (0.32, 1.38) [n=69]	0.33

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus; wP: whole-cell pertussis.

Data presented are geometric mean ratios and 95% confidence intervals. A geometric mean ratio of one indicates no difference. A confidence interval that lies completely to one side and not intersecting one indicates a significant difference in the geometric mean concentrations between the two study groups. P-values are from likelihood ratio tests for the interaction term between study arm and maternal HIV status.

15. Sensitivity analyses of anti-filamentous hemagglutinin IgG concentrations

	TdaP versus Td vaccine		**HIV-positive versus HIV-negative**		**p-value for interaction**
	HIV-positive	**HIV-negative**	**TdaP**	**Td vaccine**	
Per-protocol analyses					
Maternal delivery	3.67 (2.06, 6.55) [n=70]	13.2 (8.7, 20.0) [n=78]	0.33 (0.19, 0.56) [n=76]	1.17 (0.75, 1.84) [n=72]	<0.05
Infant 18 weeks	1.04 (0.62, 1.74) [n=47]	1.33 (0.87, 2.03) [n=68]	0.92 (0.59, 1.43) [n=61]	1.17 (0.71, 1.95) [n=54]	0.45
Sensitivity analyses in the modified intention-to-treat population					
Infant delivery adjusted for maternal age at enrolment, gestational age at delivery, and vaccination history	4.19 (2.10, 8.35) [n=69]	16.3 (9.8, 27.4) [n=74]	0.29 (0.14, 0.60) [n=70]	0.92 (0.54, 1.57) [n=73]	<0.05
Infant 18 weeks					
Adjusted for gestational age at second vaccination	1.07 (0.71, 1.63) [n=70]	1.30 (0.89, 1.91) [n=87]	0.94 (0.65, 1.36) [n=78]	1.16 (0.75, 1.79) [n=79]	0.44

Adjusted for gestational age at delivery	1.00 (0.66, 1.53) [n=70]	1.30 (0.88, 1.91) [n=87]	0.90 (0.62, 1.31) [n=78]	1.17 (0.76, 1.82) [n=79]	0.35
Adjusted for maternal age at enrolment, gestational age at delivery, and vaccination history	0.96 (0.61, 1.50) [n=70]	1.31 (0.89, 1.95) [n=87]	0.92 (0.59, 1.42) [n=78]	1.10 (0.71, 1.71) [n=79]	0.29
Adjusted for maternal age at enrolment, gestational age at delivery, vaccination history,	1.00 (0.58, 1.72) [n=64]	0.63 (0.33, 1.21) [n=69]	1.06 (0.64, 1.75) [n=64]	1.02 (0.65, 1.60) [n=69]	0.45
and cord/neonatal venous blood concentrations on log_2 scale					
Adjusted for maternal age at enrolment, gestational age at delivery, vaccination history, and interval between infant wP vaccinations	1.03 (0.66, 1.61) [n=70]	1.31 (0.91, 1.90) [n=87]	0.92 (0.60, 1.43) [n=78]	1.01 (0.66, 1.56) [n=79]	0.34

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus; wP: whole-cell pertussis.

Data presented are geometric mean ratios and 95% confidence intervals. A geometric mean ratio of one indicates no difference. A confidence interval that lies completely to one side and not intersecting one indicates a significant difference in the geometric mean concentrations between the two study groups. P-values are from likelihood ratio tests for the interaction term between study arm and maternal HIV status.

16. P-values and beta coefficients in sensitivity analyses of anti-pertussis toxin IgG concentrations at infant 18 weeks post-delivery in the modified intention-to-treat population

Table S

	Main analysis model		Model 1		Model 2		Model 3		Model 4		Model 5	
	p-value	**10^{β}**	**p-value**	**10^{β}**	**p-value**	**10^{β}**	**p-value**	**10^{β}**	**p-value**	**10^{β}**	**p-value**	**10^{β}**
Study group (TdaP versus Td)	<0.001*	0.177	<0.001*	0.174	<0.001*	0.176	<0.001*	0.178	0.021*	0.411	<0.001*	0.179
Mother's HIV status (HIV-positive versus -negative)	0.122	0.666	0.111	0.657	0.115	0.661	0.182	0.686	0.142	0.654	0.185	0.684
Gestational age at second vaccination	-	-	0.269	0.944	-	-	-	-	-	-	-	-
Gestational age at delivery	-	-	-	-	0.231	1.014	0.209	1.014	0.015*	1.028	0.172	1.016
Mother's age	-	-	-	-	-	-	0.701	0.989	0.581	0.984	0.763	0.991
Previous vaccinations	-	-	-	-	-	-	0.472	0.666	0.228	0.483	0.495	0.678
Cord/neonatal venous blood concentrations on log2 scale	-	-	-	-	-	-	-	-	0.001*	0.787	-	-
Interval between first and second infant wP vaccinations	-	-	-	-	-	-	-	-	-	-	0.413	1.021
Interval between second and third infant wP vaccinations	-	-	-	-	-	-	-	-	-	-	0.926	0.998

Five sensitivity analysis models were fitted for which adjusted geometric mean ratios and 95% confidence intervals are presented in Table S12. This table presents the associated for type III p-values using likelihood-ratio chi-square tests from the models including the corresponding covariates.

*significant p-value at 5% significance level (<0.05)

17. P-values and beta coefficients in sensitivity analyses of anti-filamentous hemagglutinin IgG concentrations at infant 18 weeks postdelivery in the modified intention-to-treat population

	Main analysis model		Model 1		Model 2		Model 3		Model 4		Model 5	
	p-value	**10^{β}**	**p-value**	**10^{β}**	**p-value**	**10^{β}**	**p-value**	**10^{β}**	**p-value**	**10^{β}**	**p-value**	**10^{β}**
Study group (TdaP versus Td)	0.277	1.167	0.233	1.184	0.272	1.169	0.286	1.165	0.831	0.958	0.210	1.196
Mother's HIV status (HIV-positive versus -negative)	0.843	1.029	0.792	1.038	0.832	1.031	0.987	1.003	0.849	0.968	0.852	0.972
Gestational age at second vaccination	-	-	0.129	1.043	-	-	-	-	-	-	-	-
Gestational age at delivery	-	-	-	-	0.516	0.996	0.498	0.996	0.349	0.994	0.672	0.997
Mother's age	-	-	-	-	-	-	0.607	1.008	0.431	1.013	0.460	1.012
Previous vaccinations	-	-	-	-	-	-	0.795	0.923	0.317	0.71	0.885	0.957
Cord/neonatal venous blood concentrations on log2 scale	-	-	-	-	-	-	-	-	0.233	1.054	-	-
Interval between first and second infant wP vaccinations	-	-	-	-	-	-	-	-	-	-	0.081	1.024
Interval between second and third infant wP vaccinations	-	-	-	-	-	-	-	-	-	-	0.320	1.012

Five sensitivity analysis models were fitted for which adjusted geometric mean ratios and 95% confidence intervals are presented in Table S13. This table presents the associated for type III p-values using likelihood-ratio chi-square tests from the models including the corresponding covariates.

18. Immunogenicity values for cord blood samples taken at delivery for stillborn babies excluded from the modified intention-to-treat analysis

Study arm	**HIV-status**	**Anti-pertussis toxin IgG concentrations**	**Anti-filamentous hemagglutinin IgG concentrations**

Table S

TdaP vaccine	HIV negative	0.477	0.903
TdaP vaccine	HIV negative	1.146	1.230

TdaP: tetanus-diphtheria-pertussis vaccine; Td: tetanus-diphtheria vaccine; HIV: Human Immunodeficiency Virus.

Data presented are log10 transformed values. Anti-tetanus toxoid IgG concentrations were not analysed for the two stillborn babies with cord blood samples at delivery.

Table S19: Serum Bactericidal assay description

Serum bactericidal assays were performed based on the method previously described.[1] Briefly, frozen aliquots of mid-exponential phase bacteria grown in THIJS medium[2] supplemented with 0.75 mM heptakis-(2,6-di-O-methyl)-β-cyclodextrin (Daito Pharmaceutical Company) were warmed at 37°C for 30 min prior to the assay.

Two-fold serial dilutions of heat-inactivated (56°C for 30 min) serum samples were performed in HBSS and 0.5% BSA in 20 µl final volume in a microplate. *B. pertussis* B1917 (10 µl) diluted in the same buffer to 8 x 10^4 CFU/mL and 10 µl of IgG- and IgM-depleted human plasma,[3] were added in each well. After 2 h incubation at 37°C with shaking at 900 rpm, 10 µl from each well was plated onto blood charcoal agar (Oxoid) using the tilt method and then incubated for five days at 35°C.

Colonies were counted and interpolated reciprocal titres were assigned as the serum dilution that gives 50% survival compared to the complement only CFU count. Heat-inactivated 1st WHO International Standard pertussis antiserum (NIBSC 06/140) was included in every plate as a control. A value of 4 was arbitrarily reported when no titre could be assigned using the first dilution (1:8).

References:

1. Lesne, E., et al., *Acellular pertussis vaccines induce anti-pertactin bactericidal antibodies which drives the emergence of pertactin-negative strains.* Frontiers in Microbiology, 2020. **11**: p. 2108.
2. Thalen, M., et al., *Rational medium design for Bordetella pertussis: basic metabolism.* Journal of biotechnology, 1999. **75**(2-3): p. 147-159.
3. Alexander, F., et al., *Generation of a universal human complement source by large-scale depletion of IgG and IgM from pooled human plasma.* Bacterial Vaccines: Methods and Protocols, 2022: p. 341-362.

20: Description of the in-house multiplex assay used to measure Tetanus Toxoid specific serum IgG

An in-house Multiplex assay was used to measure TT-specific serum IgG as described below.

MagPlex microspheres (Luminex DiaSorin, Italy) were conjugated to tetanus toxoid (191B, List Biological Laboratories, Campbell, United-States). Serum samples were diluted to 1:100, 1:1000 and 1:10.000, next to a curve prepared from the Pertussis Antiserum WHO International standard (1:60 dilution and 3-fold serial dilution, NIBSC 06/140, UK).

Serum and microspheres were incubated two hours at 300rpm, and R-Phycoerythrin-conjugated goat anti-human IgG secondary antibody (1:200, 50ul/well, 109-115-098, Jackson ImmunoResearch, Ely, UK) was added for 30 minutes at 300 rpm. Plates were read with Bio-Plex 200 (Bio-Rad, Hercules, UnitedStates).