All vaccination complications per vaccination site and date of administration should be reported as one adverse event. Vaccination complications are disorders that occur after the injection of a substance with antigenic properties, administered to activate the immune system (i.e., Ad5/Placebo and N-803/Placebo for INT21-05-01), and include erythema, induration/swelling, life-threatening consequences, limiting self-care activities, lipodystrophy, necrosis, pain, and urgent intervention indicated. Itching and bruising at a vaccination site are also considered local vaccination complications. If itching or bruising at a vaccination site is accompanied by components of a vaccination complication as listed above, then all complications should be included as one adverse event. If itching or bruising at a vaccination site is the only complication reported at that vaccination site, then itching or bruising should be reported as a separate adverse event. This guide includes instructions and examples to assist with reporting vaccination complication adverse events for INT21-05-01.

Injury, poisoning and procedural complications					
CTCAE Term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
Vaccination complication	Mild pain; erythema 2.5-5cm; induration/swelling 2.5-5cm; does not interfere with activity	Moderate pain; Erythema 5.1-10 cm; Induration/swelling 5.1-10 cm; lipodystrophy; limiting instrumental ADL	Severe pain; Erythema > 10 cm; Induration/swelling > 10 cm; necrosis; limiting self care ADL	Life-threatening consequences; urgent intervention indicated	-
Definition: A disorder that occurs after the injection of a substance with antigenic properties, administered to activate the immune system.					
Navigational Note: For systemic vaccination complications, consider Immune system disorders: Allergic reaction or Anaphylaxis.					

Figure 1: Vaccination complications according to Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Refer to Table 8: Reactogenic Events Grading according to CTCAE v5.0 in the INT21-05-01 protocol for more information.

1. Definitions for the Adverse Events electronic Case Report Form (eCRF) in Medidata Rave

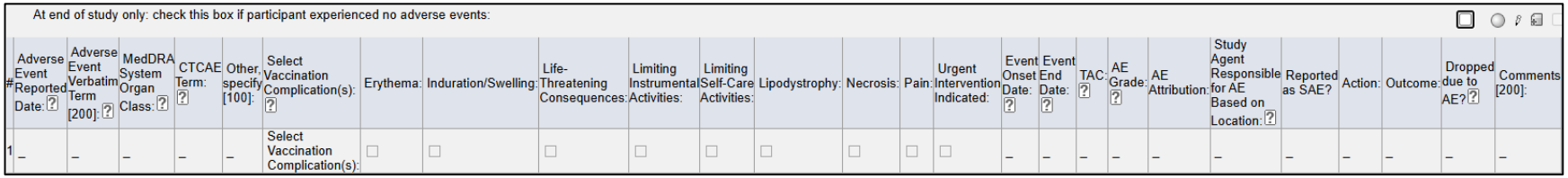

Figure 2: A blank Adverse Events eCRF in Medidata Rave.

- **Adverse Event Reported Date:** Enter the date the participant reported the adverse event to your site.
- **Adverse Event Verbatim Term:** Enter the specific complication(s), their respective measurements (if applicable), and the site of the complication(s) (e.g., Redness 3 cm, Swelling 3 cm, Abdomen).
- **MedDRA System Organ Class:** Select **"**Injury, poisoning and procedural complications."
- **CTCAE Term:** Select "Vaccination complication."
- **Other, Specify**: Leave this field blank.
- **Select Vaccination Complication(s) – Erythema, Induration/Swelling, Life-Threatening Consequences, Limiting Instrumental Activities, Limiting Self-Care Activities, Lipodystrophy, Necrosis, Pain, Urgent Intervention Indicated:** Check all that apply for the adverse event, regardless of the grade. These boxes should only be checked for adverse events where the CTCAE Term is "Vaccination complication."
- **Event Onset Date:** Enter the date when the first complication at the vaccination site began, regardless of the grade.
- **Event End Date:** Enter the date when all complications at the vaccination site resolved, regardless of the grade.
- **TAC:** Select the treatment assignment code (TAC) that was active at the time of the adverse event onset.
- **AE Grade:** Select the worst grade reached during the adverse event.
- **AE Attribution:** Select the attribution.
- **Study Agent Responsible for AE Based on Location:** Select the study agent responsible for the vaccination complication(s) based on location (e.g., "Ad5/Placebo" for thigh, "N-803/Placebo" for abdomen). This field should only be completed for adverse events where the CTCAE Term is "Vaccination complication."
- **Reported as SAE?:** Indicate if the adverse event was reported as a serious adverse event.
- **Action:** Select the action.

- **Outcome:** Select the outcome.
- **Dropped due to AE?:** Indicate if the participant was taken off study due to the adverse event.

2. **Example: A TAC3 participant had their Day 0 vaccinations on 01 Jan 2025, their Week 4 vaccinations on 30 Jan 2025, and their Week 8 vaccinations on 27 Feb 2025.**

At end of study only: check this box if participant experienced no adverse events:

#	Adverse Event Reported Date:	Adverse Event Verbatim Term [200]:	MedDRA System Organ Class:	CTCAE Term:	Other, specify [100]:	Select Vaccination Complication(s):	Erythema:	Induration/Swelling:	Life-Threatening Consequences:	Limiting Instrumental Activities:	Limiting Self-Care Activities:	Lipodystrophy:	Necrosis:	Pain:	Urgent Intervention Indicated:	Event Onset Date:	Event End Date:	TAC:	AE Grade:	AE Attribution:	Study Agent Responsible for AE Based on Location:	Reported as SAE?	Action:	Outcome:	Dropped due to AE?	Comments [200]:
1	03 Jan 2025	Swelling 2 cm, Redness 8 cm, Bruising 1 cm, Left Thigh Proximal	Injury, poisoning and procedural complications	Vaccination complication	–	Select Vaccination Complication(s):	✓	✓								01 Jan 2025	15 Jan 2025	TAC3	2	Definite	Ad5/Placebo	No	Agent Dose Not Changed	Recovered/Resolved	No	–
2	03 Jan 2025	Bruising 3 cm, Abdomen	Injury, poisoning and procedural complications	Bruising	–	Select Vaccination Complication(s):										01 Jan 2025	04 Jan 2025	TAC3	1	Definite	–	No	Agent Dose Not Changed	Recovered/Resolved	No	–
3	04 Feb 2025	Swelling 12 cm, Redness 4 cm, Itching, Moderate Pain, Left Thigh Distal	Injury, poisoning and procedural complications	Vaccination complication	–	Select Vaccination Complication(s):	✓	✓						✓		2 Feb 2025	10 Feb 2025	TAC3	3	Definite	Ad5/Placebo	No	Agent Dose Not Changed	Recovered/Resolved	No	–
4	04 Feb 2025	Redness 3 cm, Swelling 4 cm, Abdomen	Injury, poisoning and procedural complications	Vaccination complication	–	Select Vaccination Complication(s):	✓	✓								3 Feb 2025	5 Feb 2025	TAC3	1	Definite	N-803/Placebo	No	Agent Dose Not Changed	Recovered/Resolved	No	–
5	04 Feb 2025	Itching, Right Thigh Distal	Skin and subcutaneous tissue disorders	Pruritus	–	Select Vaccination Complication(s):										2 Feb 2025	3 Feb 2025	TAC3	1	Probable	–	–	Agent Dose Not Changed	Recovered/Resolved	No	–
6	04 Mar 2025	Headache	Nervous system disorders	Headache	–	Select Vaccination Complication(s):										03 Feb 2025	03 Feb 2025	TAC3	1	Probable	–	No	Agent Dose Not Changed	Recovered/Resolved	No	–
7	04 Mar 2025	Mild Pain, Left Thigh Distal	Injury, poisoning and procedural complications	Vaccination complication	–	Select Vaccination Complication(s):								✓		28 Feb 2025	02 Mar 2025	TAC3	1	Definite	Ad5/Placebo	No	Agent Dose Not Changed	Recovered/Resolved	No	–

Figure 3: A completed Adverse Events eCRF in Medidata Rave.

- **Log line 1:** At the phone call on 03 Jan 2025 after the Day 0 vaccinations, the participant reported several vaccination complications at the left thigh proximal site. All complications, including bruising, are reported as one adverse event. The Select Vaccination Complication(s) checkboxes for Erythema and Induration/Swelling are checked. 8 cm of redness makes this adverse event a grade 2. The swelling resolved on 05 Jan 2025, the redness resolved on 15 Jan 2025, and the bruising resolved on 06 Jan 2025. The Event End Date is 15 Jan 2025, since this is the date when all complications at the vaccination site resolved. The Study Agent Responsible for AE Based on Location is Ad5/Placebo, since the complications were on the left thigh.
- **Log line 2:** At the phone call on 03 Jan 2025 after the Day 0 vaccinations, the participant also reported bruising on the abdomen. Since bruising was the only complication at this site at this time, it is reported as a separate adverse event where the MedDRA System Organ Class is “Injury, poisoning and procedural complications,” and the CTCAE Term is “Bruising.” The Select Vaccination Complication(s) checkboxes and Study Agent Responsible for AE Based on Location field are left blank.
- **Log line 3:** At the phone call on 04 Feb 2025 after the Week 4 vaccinations, the participant reported several vaccination complications at the left thigh distal site. All complications, including itching, are reported as one adverse event. The Select Vaccination Complication(s) checkboxes for Erythema, Induration/Swelling, and Pain are checked. 12 cm of swelling makes this adverse event a grade 3. The swelling resolved on 08 Feb 2025, the redness resolved on 10 Feb 2025, and the itching and moderate pain resolved on 09 Feb 2025. The Event End Date is 10 Feb 2025, since this is the date when all complications at the vaccination site resolved. The Study Agent Responsible for AE Based on Location is Ad5/Placebo, since the complications were on the left thigh.
- **Log line 4:** At the phone call on 04 Feb 2025 after the Week 4 vaccinations, the participant also reported several vaccination complications on the abdomen. All complications are reported as one adverse event. The Select Vaccination Complication(s) checkboxes for Erythema and Induration/Swelling are checked. 4 cm of swelling makes this adverse event a grade 1. The redness and swelling resolved on 05 Feb 2025. The Event End Date is 05 Feb 2025, since this is the date when all complications at the vaccination site resolved. The Study Agent Responsible for AE Based on Location is N-803/Placebo, since the complications were on the abdomen.
- **Log line 5:** At the phone call on 04 Feb 2025 after the Week 4 vaccinations, the participant also reported itching at the right thigh distal site. Since itching was the only complication at this site at this time, it is reported as a separate adverse event where the MedDRA System Organ Class is “Skin and subcutaneous tissue disorders,” and the CTCAE Term is “Pruritus.” The Select Vaccination Complication(s) checkboxes and Study Agent Responsible for AE Based on Location field are left blank.
- **Log line 6:** At the phone call on 04 Mar 2025 after the Week 8 vaccinations, the participant reported a headache. Headache is not considered a vaccination complication. It is reported as an adverse event where the MedDRA System Organ Class is “Nervous system disorders,” and the CTCAE Term is “Headache.” The Select Vaccination Complication(s) checkboxes and Study Agent Responsible for AE Based on Location field are left blank.
- **Log line 7:** At the phone call on 04 Mar 2025 after the Week 8 vaccinations, the participant also reported mild pain at the left thigh distal site. Pain was the only complication at this site at this time. The Select Vaccination Complication(s) checkbox for Pain is checked. Mild pain makes this adverse event a grade 1. The Study Agent Responsible for AE Based on Location is Ad5/Placebo, since the complication was on the left thigh.