# Instructions for Building “Possible Side Effects” Tables for Informed Consent Forms

## Investigational Agents (Single Agents)

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Note to informed consent form authors: NCI uses CTCAE Scientific Terms when developing tables of possible side effects. The CTCAE Term has been translated into a lay term, known as an ‘Informed Consent Term’, for use in the Table of Possible Side Effects. A “lay translation spreadsheet” of CTCAE Terms and the respective ‘Informed Consent Term’ for each is available in the CTEP-Supported Trial Resources section of the DCTD website.

NCI uses the agent-specific CAEPR to determine what possible side effects should be included in the table. When custom-building a table of possible side effects, the Investigator’s Brochure, or other comprehensive resource, may be used.

1. Consult the NCI Scientific Term CTCAE[[1]](#footnote-1)-Informed Consent Term Spreadsheet for the ‘Informed Consent Term’ to be used for each possible side effect. Some side effects are conditions, such as ‘Reversible Posterior Leukoencephalopathy Syndrome’. When a side effect is a condition, a list of symptoms will be provided in the ‘Symptoms’ column.
2. A column titled ‘Directions’ has been included in the NCI Scientific Term CTCAE-Informed Consent Term Spreadsheet to give advice on describing possible side effects, when appropriate, including how to address related ‘Symptoms’.
3. When building a table of possible side effects, all relevant events listed in the NCI Scientific Term CTCAE-Informed Consent Term Spreadsheet should be included in the table, using the ‘Informed Consent Term’, and categorized under the appropriate ‘Common, Some May Be Serious’, ‘Occasional, Some May Be Serious’, and ‘Rare, and Serious’ frequency category.
4. The general layout of terms will be ‘Informed Consent Term’ followed by “which may cause” (when applicable) and then the symptoms listed in the ‘Symptoms’ column.
   1. Example: “abnormal heartbeat which may cause fainting”
5. The word “or” should be inserted at the end of a list of specific symptoms or organs.
   1. Examples:
      1. “which may cause belly pain, black tarry stool, or blood in vomit”
      2. “damage to the liver or lungs”
6. If an ‘Informed Consent Term’ applies to several different body sites, 2 or more, then the term in the General Lay Term (Roll-Up) column will be used.
   1. For example, for the ‘Informed Consent Terms’: “pain in belly”, “pain in the rectum”, and “pain in chest”, the General Lay Term (Roll-Up) term “pain” would be used in the table. All symptoms associated with the ‘Informed Consent Term’ should still be listed when the General Lay Term (Roll-Up) is used.
7. If the same ‘Informed Consent Term’ is listed for more than one CTCAE term, then the ‘Informed Consent Term’ should be removed from the less frequent category and placed in a more frequent category.
8. Certain CTCAE terms are really conditions and have symptoms that should always be listed with the ‘Informed Consent Term’. The ‘Symptom’ terms are listed on the NCI Scientific Term CTCAE-Informed Consent Term Spreadsheet in the ‘Symptoms’ column. The ‘Directions’ column will state which “symptoms cannot be omitted”.
   1. Example: The ‘Informed Consent Term’ for Allergic Reaction will always be listed as “allergies which may cause hives, low blood pressure, wheezing, or shortness of breath”.
9. If the same term is listed as both a Symptom and an ‘Informed Consent Term’, the Symptom should be omitted and the ‘Informed Consent Term’ used. Specifically, if an ‘Informed Consent Term’ is listed as a symptom in the ‘Common, Some May Be Serious’ category, and the same term is listed as an ‘Informed Consent Term’ in the ‘Occasional, Some May Be Serious’ category, the symptom in the ‘Common, Some May Be Serious’ category will be omitted and the ‘Informed Consent Term’ will be listed in the ‘Occasional, Some May Be Serious’ category.
   1. Example: If “High blood pressure which may cause headaches, tiredness, blurred vision” is listed in the ‘Common, Some May Be Serious’ category and the ‘Informed Consent Term’ “Tiredness” is listed in the ‘Occasional, Some May Be Serious’ category, the symptom “Tiredness” should be removed from the “High blood pressure…” description, leaving “High blood pressure which may cause headaches or blurred vision”. This approach avoids duplication but allows patients to know that “tiredness” may occur with or without high blood pressure.
10. If the CAEPR, or other resource, indicates “Infection”, and “Infection” includes all 75 infection sites under the INFECTIONS AND INFESTATIONS SOC, only the ‘Informed Consent Term’ “Infection” will be listed on the table of possible side effects. If a specific infection is indicated on the CAEPR or other resource, the corresponding ‘Informed Consent Term’, and the corresponding Symptoms, if applicable, can be listed on the table of possible side effects.
    1. When “Infection” and “Infection, especially when white blood cell count is low” are both listed in the CAEPR or other resource, “Infection” should be omitted so only “Infection, especially when white blood cell count it low” is listed in the table of possible side effects. If “Infection” is listed in the ‘Common, Some May Be Serious’ category and “Infection, especially when white blood cell count is low” is listed in the ‘Occasional, Some May Be Serious’ category, “Infection, especially when white blood cell count is low” should be listed in the ‘Common, May Be Serious’ category.
11. Guidelines for Internal bleeding, bleeding from multiple sites, vaginal bleeding, nose bleed, bleeding in testis, bleeding in the brain, and blood in urine:
    1. When both the ‘Informed Consent Term’ “Internal bleeding” and the ‘Informed Consent Term’ “blood in urine” are used in a table, follow the guidelines below:
       1. List Internal bleeding first.
       2. List all Symptoms associated with all internal bleeding ‘Informed Consent Terms’, omitting duplicates.
          1. Example: “Internal bleeding which may cause black, tarry stool or coughing up blood”
       3. Then add “blood in urine” to the symptoms following “internal bleeding which may cause …”
          1. Example: “Internal bleeding which may cause black, tarry stool, coughing up blood, or blood in urine”
    2. For the terms associated with General Lay Term “Bleeding from multiple sites” and the ‘Informed Consent Terms’ “bleeding in the testis”, “bleeding in the brain”, “vaginal bleeding”, “nose bleeds”, follow the guidelines below:
       1. List “Bleeding from multiple sites” first.
       2. Certain types of bleeding have been identified as non-roll-up terms. These are: “vaginal bleeding”, “nose bleed”, “bleeding in the brain”, and “bleeding in testicles”. The non-roll-up bleeding terms should be listed individually after “Bleeding from multiple sites”.
          1. Example: “Bleeding from multiple sites including the vagina, testis, or brain”
       3. List all associated Symptoms at the end.
          1. Example: “Bleeding from multiple sites including the brain which may cause headaches or confusion”
12. All ‘Informed Consent Terms’ associated with the General Lay Term (Roll-Up) “blockage of internal organs” will only be listed if their associated symptoms have not been already listed.
    1. Examples:
       1. If “blockage of the liver” is the ‘Informed Consent Term’ and the associated Symptom “which may cause belly pain” is already listed, “blockage of the liver” will be omitted.
       2. If “blockage of the airway which may cause shortness of breath” and “blockage of the lungs which may cause shortness of breath” are listed, the terms would be rolled up to “blockage of internal organs which may cause shortness of breath.” If all associated symptoms have already been included, “blockage of internal organs” will be omitted.
13. All ‘Informed Consent Terms’ associated with the General Lay Term (Roll-Up) “sores in internal organs” will only be listed if their associated symptoms have not been already listed.
    1. Examples:
       1. If “sores in rectum” is the ‘Informed Consent Term’ and the associated Symptom “which may cause rectal pain” is omitted because “pain or rectal pain” is already listed, “sores in rectum” will also be omitted.
       2. If “sores in rectum which may cause pain” and “sores in stomach which may cause pain” are listed, the terms would be rolled up to “sores in internal organs which may cause rectal pain or belly pain”. If the symptoms “rectal pain and belly pain” are already listed, “sores in internal organs” will be omitted.
14. When the term “swelling of the body” is listed as an ‘Informed Consent Term’ in one category, the symptom “swelling” can be omitted from other frequency categories.
15. When the ‘Informed Consent Term’ is “blank - abnormal laboratory result” or “blank - patient would not perceive,” nothing needs to be included in the table of possible side effects.
16. When “heart failure”, “heart stops beating”, and “heart attack” are listed in the same frequency category, list them on the same line, followed by relevant Symptoms.
17. If the phrase “in children” or “in children or adolescents” is at the beginning of an ‘Informed Consent Term’, the term only needs to be included if the study includes children or adolescents.
18. Informed Consent Terms that are italicized on the NCI Scientific Term CTCAE – Informed Consent Term Spreadsheet can be listed on the same line, if they are listed under the same ‘CTCAE SOC’.
19. ‘Informed Consent Terms’ that do not have any associated Symptoms can be listed on the same line, if they pertain to the same ‘CTCAE SOC’.
    1. The following is a sampling of terms that can be combined because they pertain to the same CTCAE SOC:
       1. Abnormal XXX
          1. Example:“Abnormal menstrual period” and “abnormal sexual function” can be combined to say: “abnormalmenstrual period, sexual function”
       2. Blood clots which may cause XXX
          1. Example: “Blood clots which may cause bleeding” and “blood clots which may cause belly pain” can be combined to say “blood clots which may cause bleeding or belly pain”.
       3. Blurred vision
          1. Example: “Blurred vision” and “blurred vision which may cause blindness” can be combined to say “blurred vision which may cause blindness”.
       4. Dry XX
          1. Example: “Dry mouth”, “dry eye” and “dry skin” can be combined to say “dry mouth, eye or skin”.
       5. In children and adolescents: XXX
          1. Example: “In children and adolescents: decreased height” and “in children and adolescents: different lengths between arms or legs” can be combined to say “in children and adolescents: decreased height or different lengths between arms or legs”.
       6. Inability to XX
          1. Example: “Inability to absorb food” and “inability to control bowel movements” can be combined to say “inability to absorb food or control bowel movements”.
       7. Loss of XX
          1. Example: “Loss of bone tissue” and “loss of some or all of the nails” can be combined to say “loss of bone tissue or some or all of the nails”.
       8. Stiff XX
          1. Example: “Stiff neck” and “stiff back” can be combined to say “stiff neck or back”.
       9. Swelling and redness of XX
          1. Example: “Swelling and redness at the site of the medication injection” and “swelling and redness of the eye” can be combined to say “swelling and redness of the eye or at the site of the medication injection”.
20. These guidelines have been developed in order to create a systematic and consistent approach to developing risk profiles for investigational agents. While ‘Informed Consent Terms’ from different SOCs are listed on separate lines, an Investigator may modify the risk profile by listing related risks on the same line or, alternatively, listing some risks on separate lines.

## Rules for Regimens:

1. Tables of Possible Side Effects will be developed in the future for commonly used, standard regimens.
2. Overlapping toxicities between or among Tables for regimens will not be omitted, as it is important to indicate the potential increase in toxicity when new agents or therapies are combined with standard regimens.
3. Investigational agents will always have a separate risk profile so that patients can understand the potential additional toxicity that results from the investigational agent.

1. Refers to the current version of CTCAE available online in the CTEP-Supported Trial Resources section of the DCTD website. [↑](#footnote-ref-1)