**Transfusion-associated circulatory overload**

**(TACO; 2017 proposed reporting criteria)**

**Transfusion-associated acute lung injury (TRALI)**

**Transfusion-associated dyspnoea (TAD)**

**Other transfusion reaction**

**Definitions for use in validation phase 2, autumn 2017**

*International Society of Blood Transfusion*

*Working Party on Haemovigilance*

*in collaboration with*

*The International Haemovigilance Network*

*and AABB*

This document is for use in the Autumn 2017 validation of the revised TACO reporting criteria and combines the following definitions:

1. TACO reporting criteria (draft)
2. TRALI (ISBT, 2013)
3. TAD (ISBT, 2011/2013)
4. “Other”

**The proposed TACO surveillance reporting criteria represent a revision of the previous international TACO definition published by the International Society for Blood Transfusion Haemovigilance working party and International Haemovigilance Network:**

<http://www.isbtweb.org/fileadmin/user_upload/Proposed_definitions_2011_surveillance_non_infectious_adverse_reactions_haemovigilance_incl_TRALI_correction_2013.pdf>

1. **Transfusion-associated circulatory overload (TACO)**

**Proposed standard reporting criteria (2017)**

**Context**

* The term transfusion-associated circulatory overload or TACO indicates that there is a *temporal* association with blood transfusion. The imputability, the *causal* contribution of the transfusion, is assessed separately.
* Certain clinical conditions, e.g. cardiovascular, renal, pulmonary diseases and severe anemia, are risk factors for TACO. These conditions do not preclude a diagnosis of TACO.
* Other fluids given before or around the time of the transfusion contribute to and can exacerbate the fluid challenges posed by transfusion. The volume of transfused products may constitute only a percentage of fluids administered overall.
* Patients with TACO cardinally manifest respiratory system-related signs and symptoms such as tachypnea, dyspnea, and decreased oxygen saturations, typically occurring during or within 12 hours of transfusion.
* Close monitoring of the patient and the vital signs during transfusion are important; review of vital sign values/net fluid balance for at least 24 hours prior to the transfusion of the unit identified with the reaction may be of value.
* An increase of blood pressure and tachycardia may be warning signs; appropriate clinical management may prevent development of TACO.
* Radiographic chest imaging of adequate quality at the time of the reaction is an important means of gaining diagnostic information and should be considered. However, cases without chest imaging may be reported as TACO providing other features are present.

Patients with TACO may experience an increase in body temperature. An increase of body temperature should be investigated according to protocol and clinical judgement. Increased body temperature does not exclude TACO if the reporting criteria are met.

Patients receiving ventilatory support: In ICU patients who may be receiving varying degrees of PEEP (positive end expiratory pressure) ventilatory support, pulmonary oedema may be difficult to diagnose at higher PEEP settings with TACO becoming apparent only if PEEP settings are reduced or ventilation is discontinued.

**TACO reporting criteria\***

Patients classified with a **TACO (surveillance diagnosis)** should have acute or worsening respiratory compromise during or up to 12 hours after transfusion and should exhibit two or more of the criteria below:

* **Evidence of acute or worsening pulmonary oedema based on:**
	+ **clinical physical examination (see Note 1), *and/or***
	+ **radiographic chest imaging and/or other non-invasive assessment of cardiac function e.g. echocardiogram (see Note 2)**
* Evidence for cardiovascular system changes not explained by the patient’s underlying medical condition, including development of tachycardia, hypertension, jugular venous distension, enlarged cardiac silhouette and/or peripheral oedema(see Note 3)
* **Evidence of fluid overload including any of the following: a positive fluid balance; response to diuretic therapy combined with clinical improvement; and change in the patient’s weight in the peri-transfusion period (see Note 4)**
* Elevation in B type natriuretic peptide (NP) levels (e.g., BNP or NT-pro BNP) to greater than 1.5 times the pretransfusion value. A normal post-transfusion NP level is not consistent with a diagnosis of TACO; serial testing of NP levels in the peri-transfusion period may be helpful in identifying TACO.

**\***These criteria establish a surveillance definition based on a complete description of an event, including information that becomes available well after onset. This is for reporting and tracking purposes and the criteria do not constitute clinical diagnosis for the purpose of real-time clinical interventions.

**Notes**

1. **Clinical findings could include crackles on lung auscultation, orthopnea and cough, cyanosis and decreased oxygen saturation values in the absence of other specific causes.**
2. **Diagnostic radiographic imaging**

**Findings consistent with pulmonary oedema from circulatory overload could include presence of new or worsening pleural effusions,** progressive lobar vessel enlargement, peribronchial cuffing, bilateral Kerley lines, alveolar oedema with nodular areas of increased opacity and/or **cardiac silhouette enlargement.**

1. **Blood pressure monitoring**

**Often the arterial pressure is raised, often with widened pulse pressure; however hypotension** may be a presenting feature, e.g. in patients in a state of acute cardiac collapse.

B**lood pressure should be monitored especially if multi-unit transfusions are given.**

1. **Change in the patient’s weight**

Typically the patient’s weight will increase. However there may be a decrease following diuretic therapy.

**Imputability**

The imputability, the *causal* contribution of the transfusion, is assessed separately.

1. **Transfusion-related acute lung injury (TRALI)**

In patients with no evidence of acute lung injury (ALI) prior to transfusion, TRALI is diagnosed if a new ALI is present (all five criteria should be met):

* Acute onset
* Hypoxemia

o Pa02 / Fi02 < 300 mm Hg or

o Oxygen saturation is < 90% on room air or

o Other clinical evidence

* Bilateral infiltrates on frontal chest radiograph
* No evidence of left atrial hypertension (i.e. circulatory overload)
* No temporal relationship to an alternative risk factor for ALI, during or within 6 hours of completion of transfusion.

Alternate risk factors for ALI are:

* Direct Lung Injury

o Aspiration

o Pneumonia

o Toxic inhalation

o Lung contusion

o Near drowning

* Indirect Lung Injury

o Severe sepsis

o Shock

o Multiple trauma

o Burn injury

o Acute pancreatitis

o Cardiopulmonary bypass

o Drug overdose

It has been suggested by the Toronto TRALI Consensus Panel to add a category of *possible*

*TRALI* that would have the same definition as TRALI except for the presence of a temporal

relationship to an alternative risk factor for ALI (as described above). In such a circumstance

TRALI should be indicated with a *possible* imputability to transfusion.

TRALI is therefore a clinical syndrome and neither presence of anti-HLA or anti-HNA

antibodies **in donor(s)** nor confirmation of cognate antigens **in recipient** is required for

diagnosis.

1. **Transfusion associated dyspnea (TAD)**

TAD is characterized by respiratory distress within 24 hours of transfusion that does not meet

the criteria of TRALI, TACO, or allergic reaction. Respiratory distress should be the most

prominent clinical feature and should not be explained by the patient’s underlying condition

or any other known cause.

1. **“Other”**

For the purposes of the Phase 2 validation exercise, please classify case examples which do not fit in the above categories of reactions as “other”.

**Background information about the TACO revision and 2017 validation**

**Rationale for the revision**

At the Amsterdam meeting of the ISBT haemovigilance working party (2013), a number of members requested revision of the TACO definition. Notably, strict application of the definition leads to non-acceptance of cases which would be accepted as TACO by clinicians and by some haemovigilance systems.

A first revised version was circulated in December 2014 and tested by contributors from haemovigilance systems in several countries and continents by applying it to their own cases. This definition was found to be more inclusive than the 2011 version but limited by the weight placed on enlargement of the cardiac silhouette and increase of BNP – both are often not investigated or not recorded in haemovigilance reports.

The revision group recognises that the chief priority is to adopt standard reporting criteria which will enable professionals to raise awareness of TACO and lead to improved reporting, research and reduction of transfusion complications. The revision group includes representatives from AABB, and this opens possibilities for harmonisation. In future, the criteria may need to be adjusted in the light of accumulating evidence.

**The revision group** (listed alphabetically)

Chester Andrzejewski, Paula Bolton-Maggs, Sharran Grey, Kevin Land, Harriet Lucero, Mark Popovsky, Philippe Renaudier, Pierre Robillard, Matilde Santos, Martin Schipperus, Dafydd Thomas, Barbee Whitaker, Johanna Wiersum-Osselton (convenor).

**Validation Protocol (Synopsis; May 2017)**

**Abstract**

Harmonised and standardised surveillance case definitions of adverse transfusion reactions are paramount for meaningful and accurate data reporting and analyses. On-going review of these definitions is necessary to ensure their continuing clinical validity and applicability to haemotherapy monitoring and for enhancing patient safety. This protocol describes a two-stage validation study for evaluating a draft revision of the reporting criteria (definition) for surveillance purposes for Transfusion-Associated Circulatory Overload (TACO). Phase I consists of review of the draft among contributors from various haemovigilance systems in several countries and continents with their subsequent testing of it by applying it to cases derived from their own institutions using a Working Party derived Evaluation Tool. In Phase II individuals will be solicited and asked to classify a set of case vignettes (descriptions) using the proposed draft criteria and the Evaluation Tool. The main objective of the study is to analyse the validity of the revised TACO reporting criteria (definition) for haemovigilance surveillance purposes.

# Study Aims

Objectives of this study include:

* To develop a database of pulmonary transfusion reactions for definition validation purposes.
* To assess if the revised definition will distinguish between TACO and other acute pulmonary reactions, identify true TACO cases, and evaluate whether the revised definition will adequately define/classify clinical cases that were reported to national haemovigilance systems as TACO and accepted as TACO according to each system’s evaluation procedures.
* To incorporate the feedback obtained via case evaluations using and assessing the proposed TACO standard definition for surveillance of non-infectious pulmonary adverse transfusion reactions1 for clarity and applicabilityby users from (inter)national haemovigilance systems.
* To recommend changes to achieve harmonised adverse reaction definitions.
1. **Scope and method**

This validation study is conducted to test the validity of the proposed TACO surveillance definition (reporting criteria).

In Phase I, the participants will classify 10 clinical cases previously reported and endorsed as TACO in their own system using the draft revised criteria for TACO. Additionally, 2 cases previously classified as TRALI, 2 cases previously classified as TAD and 1 unclassifiable pulmonary case will be assessed and classified using the ISBT revised criteria1.

In Phase II, 26 real life acute pulmonary transfusion reaction case vignettes will be distributed, participants will classify these cases as TACO (or not TACO) independently.

This validation study will be conducted in the setting of haemovigilance surveillance systems. It is important to note that the criteria establish a surveillance definition based on a complete description of an event, including information that becomes available well after suspected reaction onset and extending into the post transfusion period. The criteria do not constitute a clinical diagnosis for the purpose of real-time clinical interventions.

# Analysis Plan

* Phase I

The revised TACO reporting criteria will be provided to the participating HV systems throughout the world. Participants will be asked to reclassify 10 cases of TACO, 2 case of TRALI, 2 cases of TAD and another unclassified case with significant pulmonary features from reports within their haemovigilance system, based on the revised definition for TACO and current ISBT definitions for other adverse transfusion reactions. The level of agreement between their system classification and reclassification based on revised definition, and sensitivity of the TACO criteria to recognise cases accepted by haemovigilance systems as TACO will be analysed. The result will measure how well the revised definition will accurately classify TACO cases. The participants will have the option to submit the actual case reports for consideration for use in Phase II.

* Phase II

From the bank of cases, 26 cases will be selected with proportional distribution of pulmonary adverse reaction categories based on data from several haemovigilance systems2-5. Participants will be provided with the cases and asked to complete the assessment form. The results will be represented by histograms and cross tabulation tables. The agreement level between participants and experts can be measured by Cohen’s kappa coefficient. Participants’ comments will be reviewed by the revision group to assess whether these indicate need for clarification of items in the reporting criteria.

These results will provide a synopsis on the effectiveness and accuracy of the definitions and its ability to distinguish between TACO and other acute pulmonary reactions

Participants will be acknowledged in the presentations arising from this work. It is the intention is to submit a manuscript for publication based on the activity.

# Literature

* + - 1. ISBT,<http://www.isbtweb.org/fileadmin/user_upload/Proposed_definitions_2011_surveillance_non_infectious_adverse_reactions_haemovigilance_incl_TRALI_correction_2013.pdf>

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5. TRIP 2015 Annual Hemovigilance Report, Extended Version (2016), www.tripnet.nl