
# NSW Metrics for Health and Medical Research, including Clinical Trials

## AU RED data collection and reporting instructions

NSW Office for Health and Medical Research

This document supplements the March 2016 document "Metrics for Health and Medical Research, including Clinical Trials" document, which detailed the strategic and site level performance and compliance metrics that will be collected by the Office for Health and Medical Research (OHMR) from NSW Public Health Organisations (PHOs) from July 2016 in accordance with the 2015 – 2017 Budget Supplementation – Research Governance Grant and the 2016/17 Service Agreement between LHD/SHN Chief Executives and the Ministry of Health. Additional information, such as performance thresholds and illustrations of measurement calculations, are provided in the March Metrics document.

Additionally, it outlines the AU RED data entry fields, requirements, definitions and other functionality that Local Health Districts (LHDs), Speciality Health Networks (SHNs) and NSW Ambulance will use to report metrics-related data to OHMR.

Please contact the Research Ethics and Governance Unit at researchethics@doh.health.nsw.gov.au with any questions about metrics data recording or reporting.

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**Version Control**

| **Version** | **Date** | **Purpose/Changes** | | |
|---|---|---|---|---|
| 1.0 | 16 June 2016 | Initial version | | |
| 1.1 | 5 August 2016 | *Section* | *Page* | *Change* |
| | | 2.2 | 9 | Note changed from "first reporting year/s" to "first reporting period/s" |
| | | 2.4 | 14 | SSA clock start date added to fields included in analysis |
| | | 2.6 | 18 | Deadlines for AU RED data entry changed to match those for metric 5 |
| | | 6.1 | 32 | "Application Clock Start Date" changed to "Initial Application Clock Start Date" |
| | | 6.1 | 33 | Additional detail added for HREC application "interim date of clock re-start definition" |
| | | 6.2 | 34 | "The date the SSA application is *received* will then be used to count the calendar days until authorization" changed to "The date the SSA application is *validated* will then be used to count the calendar days until authorization." |
| | | 6.2 | 34 | Paragraph added which starts "Research offices should develop their own procedures and materials…" |
| | | | | Other minor editorial changes. |
| 1.2 | 18 August 2016 | 6.1; 6.2.2 | 32; 36 | Signatures required on an SSA Application to be deemed valid by an RGO (Initial Application Clock Start Date) have been changed from "all investigators who will conduct research at the site; and the head of department (or divisional director or other authority) of each investigator at the site" to "all investigators who will conduct research at the site; and the head of department (or divisional director or other authority) of ***the Principal Investigator*** at the site." |
| 1.3 | 21 September 2016 | 7.1 | 39 | "Study state" changed to "HREC application study state" in the sentence "the user is NOT required to set the HREC application study state to 'Started'…" to provide further clarity on Work Area progress report alerts. |

| Version | Date | Purpose/Changes | | |
|---|---|---|---|---|
| | | *Section* | *Page* | *Change* |
| 1.3 | 21 September 2016 | 7.4 | 40 | The definitions of Study States "Finished" and "Closed at Site" were correct in the relevant metrics tables and in Table 2, Study State Definitions. However, references to these states were reversed in Section 7.4, and have been corrected. This includes:<br>• "Finished" was changed to "Closed at Site" in the sentence "At a minimum, OHMR will require institutions set the Study State to 'Closed at Site' at the SSA/site level when appropriate…"<br>• The following sentence was added: "The definition of 'Closed at Site' has been arbitrarily created to capture the date that a clinical trial is no longer enrolling participants at the study site, to set a date at which the enrolment target metric can be assessed."<br>• The subsequent sentence on the definition of "finished" was corrected to read: "The definition of 'finished' was created to capture the date that the last clinical trial participant has met the last study analysis endpoint."<br>• The following sentence was added to the second paragraph: "Sites may use this study state to inform metric 10, 'Reports of trial summary results (Summary Reports) for internally sponsored clinical trials in NSW posted publicly within 12 months of Study Completion.'" |
| 2.0 | 24 October 2016 | 2.2 | 12 | Current Decision was added to the list of fields that will be used to filter for metric 2 (so that only approved and authorised studies will be included; no substantive change) |
| | | 2.6 | 22 | The following instruction was added to the field "Maximum enrolment target per CTRA" - If there is no numeric maximum value, e.g. for competitive recruitment, please enter 9999. |
| | | 4.0 | 28 | Screenshots 1 and 2 were replaced to reflect the addition of the line "Please do not select the option 'to be documented/assessed/validated centrally" next to the valid reason drop down menus. |
| | | 5.3 | 31 | ACT was added to the list of states that participate in National Mutual Acceptance. |
| | | *Changes based on new Study State options* | | |
| | | 2.6 | 22 | "closed at site (end of enrolment period)" was renamed "closed to enrolment at site" |
| | | 2.7.3 | 25 | The definition of and use of Study State "closed but not archived" for final report tracking was added as the last paragraph. |
| | | 7.2 | 41 | The study state "closed but not archived" was added, "closed at site" was changed to "closed to enrolment at site (the values for any States previously-set to 'Closed at |

| Version | Date | Purpose/Changes | | |
|---|---|---|---|---|
| | | | | Site' will be retained)," and the distinction of Study State options for HREC versus SSA applications was added. |
| | | 7.4 | 42 | References to "closed at site" were changed to "closed to enrolment at site," and a sentence was added about the study state option "closed but not archived." |
| | | 7.4 | 44 | The new Study States were added to Table 2, Study State Definitions. |
| | | 7.4 | 45 | The new Study States were added to Figure 7, Application Status and Study State Continuum. |

# 1 Background and Overview

Delays in the clinical trial approval and enrolment process are often cited as contributing to a decline in Australia's clinical trial competitiveness, however this perception is difficult to verify without reliable data. The Office for Health and Medical Research (OHMR) has responded by implementing a number of reform initiatives which, it is hoped, will contribute to a significant and sustained improvement in NSW's ability to initiate and deliver health and medical research, including clinical trials. As part of this process, metrics will be utilised to measure the success of the reform agenda, and to help identify areas where there may be opportunities for process improvement.

## 1.1 Setting Objectives

In delivering Initiative 4 of the OHMR Reform Framework and Action Plan, the following objectives have been set so that all stakeholders understand OHMR's expectations and can work towards the same goals.

**Strategic objectives to position NSW as a preferred destination for clinical trials**

- To increase the number of commercial trials conducted in NSW
- To reduce the time taken to obtain research approvals (HREC & SSA)
- To increase the proportion of trials in NSW that enrol the agreed number of participants within the agreed timeframe

**Operational (performance) objectives relating to trial set-up and delivery at site**

- HREC - To continuously improve the quality of the HREC review and to reduce the time taken for ethical approval
- Governance - To continuously improve the quality of the SSA review and to reduce the time taken for site authorisation
- Governance - To improve trial delivery at the site by increasing the number of trials that enrol the agreed number of participants within the agreed timeframe
- To improve the quality and compliance of clinical trials conducted in NSW

## 1.2 Metrics Overview

A metric is defined as *any type of measurement used to gauge some quantifiable component of an entity's performance*. NSW research ethics and governance metrics will be collected initially using the Australian Research Ethics Database (AU RED). Two categories of metrics will be collected prospectively from July 2016:

1. **STRATEGIC METRICS**: Metrics used to capture a benchmark position and then periodic metrics so that the impact of reform initiatives can be quantified. These metrics will gauge progress towards meeting one of OHMR's main objectives to position NSW as a preferred destination to conduct commercial clinical trials. These metrics will be collected prospectively from July 2016.

2. **SITE LEVEL PERFORMANCE & COMPLIANCE METRICS**: Metrics used to drive internal process improvement and to identify organisations with exemplary or poor practice. Individual institutions may wish to use their Site Level Performance Metrics to advertise their competitive position or degree of improvement, in order to attract industry trials. These metrics will be collected prospectively from July 2016.

The seven metrics that OHMR will evaluate are outlined in section 2 below, along with instructions for the use of each AU RED field or function that will be used to inform that metric. These instructions should be used by the research office staff performing data entry and data verification/quality review to ensure the accuracy of the metrics, and to ensure that all data are reported consistently throughout the state.

Strategic Metrics 1 and 2 are not listed in the 2016/17 Service Agreements as they relate to state-wide objectives. These two metrics will be derived from data points collected for Performance/Compliance Metrics 3-7. Performance/Compliance Metrics 3-6 will be reported by institutions via AU RED (initially) to OHMR. These metrics will be used to calculate the related Monitoring Measures.

Metric 7 (monitoring measure 5) captures institutional progress reports on all authorised research projects received at least annually and at study close. These data will not be collected through AU RED; rather, each institution will provide a report to OHMR detailing the institution's compliance rates for interim and final reporting. The rationale and additional details for this metric are included in section 2.

Section 3 outlines four non-reportable quality and transparency metrics for internally-sponsored clinical trials, for optional use within an institution. These optional but valuable metrics may be collected and used by institutions to further research quality and transparency objectives in support of state-wide initiatives.

All metrics that measure application-review time durations account for clock starts and stops in order to exclude factors that are outside the control of HREC/governance staff; for example, the length of time it takes for the investigator/sponsor to fully address the queries raised by the approval body. There may be multiple requests for further information (clock stops) during the approval process; for example, if the investigator fails to address the HREC's or institution's feedback or if new information provided by the investigator generates additional queries.

## 1.3 AU RED Function Overview

Sections 4 – 7 provide supplementary instructions for the use of AU RED to provide the metrics data.

- Section 4 includes screenshots of **new data fields** that have been added to AU RED to collect information on clinical trial enrolment.
- Section 5 provides **definitions for drop-down options** of fields that are directly related to the analysis.
- Section 6 clarifies for the AU RED user the **meaning and derivation of each date and time** captured in AU RED, including those generated automatically in the system, and those that the user enters into "date-picker" fields. **Some changes to current data entry practice are outlined**, that may need to be implemented in accordance with future data collection.
- Finally, section 7 describes how the **Study State function** on the post-approval tab at both the HREC and the SSA level should be used to track the status of each clinical trial within the institution, which will in-turn inform OHMR when analysing data based on the status of a study (e.g. started, closed to enrolment at the site, temporarily halted).

# 2 Strategic and Performance Metrics to be Reported by Institutions

This section provides the AU RED data calculation parameters that OHMR will use to filter and analyse each metric. Each one is listed, along with its objectives and related monitoring measure per the Service Agreements, if relevant. The AU RED fields that will be accessed are also outlined, so that the user can ensure that the data for each study are accurately represented.

For definitions related to each field, see section 5 (drop down definitions), section 6 (clock and date definitions), and section 7 (Study State definitions).

## 2.1 Data Entry Parameters and Deadlines

This section also includes the data reporting periods and AU RED data entry deadline for each measure, and the date parameters which determine whether or not an application needs to be data-entered according to the manual. As an example, to calculate metrics 1, 4 and 5, institutions are asked to enter data for applications *authorised* within the reporting period that meet certain filtering criteria. Therefore, the institution only needs to "back-enter" and/or quality-check data for applications that were authorised within the period, including relevant data points for those applications that may have occurred *before* the start of the reporting period. To illustrate:

- For period 1, Metric 4, "Date Valid SSA Application Received by the RGO to Site Authorisation" requires data entry in accordance with the manual, for all studies excluding LNR at the SSA level, that were authorised between 1 July – 31 December 2016.
- Per section 2, these data will also be analysed for date SSA application received, and all interim clock stop and re-start dates.
- For any relevant studies that fit within the reporting period, the institution will therefore need to "back-enter" and/or quality check all data in fields that indicate "date SSA application received," and all interim clock stop and re-start dates, that occurred before 1 July 2016.
- Sample: Greater-than-low-risk Study A was authorised at Site 101 on 4 July 2016. However, the SSA application was received on 3 May 2016, and the clock was stopped and re-started two times before 1 July. The institution must ensure that all dates for that application that occurred from 3 May 2016 are entered and accurate.

Data entry deadlines for metrics 1 and 2 are not provided, as there are no associated monitoring measures. However, these data will be collected by the completion of data entry for other metrics.

## 2.1 METRIC 1: Number of New Commercial Trials in NSW in the reporting period (state level)

Note: The first reporting period will provide the baseline data for comparison with future reporting periods.

**Associated monitoring measure:** none

**Objectives:**

1) To assess whether NSW is attracting more commercial trials
2) To increase the access to commercial trials for the NSW patient population

### Data Calculation Parameters

| All commercial clinical trials (excluding LNR) authorised within the reporting period at a NSW site | |
|---|---|
| **Period 1** | 1 July – 31 December 2016 |
| **Period 2** | 1 January – 30 June 2017 |

### Related AU RED Data fields

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| **Filtered by:** | | | |
| Study Type | **Included:**<br>Clinical trial (other); Clinical trial of a drug; Clinical trial of a device; Clinical trial of a drug and device; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – drug; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – device; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – drug and device<br>**Not included:**<br>Clinical research; Health Research/ Social Science; Other (please state) | HREC - Application References | |
| Application Type | **Included:**<br>Site Specific Assessment (duplicates removed)<br>**Not included:**<br>Application - Single Site; Application – Multi Site | Application References | |

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| LNR/non-LNR | **Included:**<br>No (HREC/LNR Reference number starts with HREC)<br>**Not included:**<br>Yes (HREC/LNR Reference number starts with LNR) | Set at HREC - New Application, which generates HREC/LNR Reference number | |
| Major Sponsor Type | **Included:**<br>Commercially Sponsored<br>**Not included:**<br>Collaborative Group; Investigator Initiated Group; Institution; Other | HREC - Application References | This field is answered by the HREC when setting up a new application for a non-LNR study. |
| Current Decision | **Included:**<br>Authorised; authorised with conditions; further information response authorised<br>**Not Included:**<br>Invalid application; not authorised; Request for further information/ modification; not requiring review by Research Organisation; further information response not authorised; further information response not complete | Meetings – Decisions | Current decision is auto-populated by any withdrawn status that is entered by the RED user, and, if there is no withdrawn status entered, by the last meeting decision (for HREC) or decision (for SSA) saved by the user. |
| Withdrawn Status | **Included:**<br>Not withdrawn or cancelled (default value)<br>**Not included:** Withdrawn by researcher; Withdrawn by Research Governance Officer; Cancelled as HREC application is Not Approved | Application – Withdraw/Cancel | |
| Date of Site Authorisation | Not applicable - date field | SSA - Meetings tab, clock stop | Must occur within the reporting period.<br><br>See clock definitions. |

## 2.2 METRIC 2: NSW HREC Submission Closing Date to First NSW Participant Enrolled (state level; with and without clock stops).

Note: The first reporting period will provide the baseline data for comparison with future reporting periods.

**Associated monitoring measure:** none

**Objectives:**

1) To reduce total time taken to obtain trial approvals/authorisations in NSW
2) To reduce the time to first participant enrolled
3) To identify bottlenecks outside the control of the HREC/Governance office

### Data Calculation Parameters

| All commercial clinical trials (excluding LNR) wherein the first NSW participant was enrolled within the reporting period | |
|---|---|
| **Period 1** | 1 July 2016 – 31 December 2016 |
| **Period 2** | 1 January 2017 – 30 June 2017 |

For applications/studies wherein the first NSW participant was enrolled within but submitted and/or approved before the reporting period, ensure submission and approval data are also appropriately entered.

### Related AU RED Data fields

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| **Filtered by:** | | | |
| Study Type | **Included:**<br>Clinical trial (other); Clinical trial of a drug; Clinical trial of a device; Clinical trial of a drug and device; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – drug; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – device; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – drug and device<br>**Not included:**<br>Clinical research; Health Research/ Social Science; Other (please state) | HREC - Application References | |

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| Application Type | **Included:**<br>For HREC data: Application – Single Site; Application – Multi Site<br>For site data: Site Specific Assessment | HREC - Application References | |
| LNR/non-LNR | **Included:**<br>No (HREC/LNR Reference number starts with HREC)<br>**Not included:**<br>Yes (HREC/LNR Reference number starts with LNR) | Set at HREC - New Application, which generates HREC/LNR Reference number | |
| Major Sponsor Type | **Included:**<br>Commercially Sponsored<br>**Not included:**<br>Collaborative Group; Investigator Initiated Group; Institution; Other | HREC - Application References | This field is answered by the HREC when setting up a new application for a non-LNR study. |
| Current Decision | **For HREC data:**<br>**Included:**<br>Approved<br>**Not Included:**<br>Not approved; Invalid application; not requiring review by HREC; further information/ modification requested; no opinion pending consultation with referee; invalid application<br>**For site data:**<br>**Included:**<br>Authorised; authorised with conditions; further information response authorised<br>**Not Included:**<br>Invalid application; not authorised; Request for further information/ modification; not requiring review by Research Organisation; further information response not authorised; further information response not complete | Meetings – Decisions | Current decision is auto-populated by any withdrawn status that is entered by the RED user, and, if there is no withdrawn status entered, by the last meeting decision (for HREC) or decision (for SSA) saved by the user. |
| **NEW FIELD:** Date first participant enrolled at site | Not applicable - date field | SSA - post approval tab, First Participant Enrolled | Must occur within the reporting period.<br><br>For metric calculation, the first (earliest) date for this field at any NSW site related to a single HREC applicaton will be used. |
| **Also included in analysis:** | | | |
| HREC application clock start date | Not applicable - date field | Applications - Checklist and Applications - Validate / Start screens | See clock definitions. |

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| (Interim) Clock stop and start dates | Not applicable - date field | Meetings – Application Decision and Clocks and correspondence tab | All included except the most recent (“final”) clock stop date. |
| (Final) Clock stop date | Not applicable - date field | Applications - Checklist and Applications - Validate / Start screens | The most recent clock stop date will be considered as the final clock stop date.<br><br>See clock definitions. |

## 2.3 METRIC 3: NSW HREC Submission Closing Date to NSW HREC Approval (Site level; with and without clock stops)*

**Associated monitoring measure:** 1 - Ethics applications involving more than low risk to participants approved by the reviewing HREC within 60 calendar days (%)

**Objective:** To assess the efficiency of the HREC's processes and to drive process improvement.

### Data Calculation Parameters and Deadlines

| All studies (excluding LNR) approved by the HREC with a final written notification date (final clock stop date) within the reporting period | | **Deadline for AU RED data entry** |
|---|---|---|
| **Period 1** | 1 July 2016 – 31 December 2016 | By 27 January 2017 |
| **Period 2** | 1 January 2017 – 30 June 2017 | By 28 July 2017 |

For studies approved within but submitted before the reporting period, ensure submission data are also appropriately entered.

### Related AU RED Data fields

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| **Filtered by:** | | | |
| Application Type | **Included:**<br>Application – Single Site; Application – Multi Site<br>**Not included:**<br>Site Specific Assessment | HREC - Application References | |
| LNR/non-LNR | **Included:**<br>No (HREC/LNR Reference number starts with HREC)<br>**Not included:**<br>Yes (HREC/LNR Reference number starts with LNR) | Set at HREC - New Application, which generates HREC/LNR Reference number | |
| Current Decision | **Included:**<br>Approved<br>**Not Included:**<br>Not approved; Invalid application; not requiring review by HREC; further information/ modification | Meetings – Decisions | Current decision is auto-populated by any withdrawn status that is entered by the RED user, and, if there is no withdrawn status entered, by the last meeting decision (for HREC) or decision (for SSA) saved by the user. |

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| | requested; no opinion pending consultation with referee; invalid application | | |
| (Final) Clock stop date | Not applicable - date field | Applications - Checklist and Applications - Validate / Start screens | See clock definitions.<br><br>Must occur within the reporting period.<br><br>The most recent clock stop date will be considered as the final clock stop date. |
| **Also included in analysis:** | | | |
| HREC application clock start date | Not applicable - date field | Applications - Checklist and Applications - Validate / Start screens | See clock definitions. |
| (Interim) Clock stop and start dates | Not applicable - date field | Meetings – Application Decision and Clocks and correspondence tab | All included except the most recent ("final") clock stop date. |

***** The monitoring measure will account for clock stops in accordance with the NHMRC Certification Handbook, which allows 60 calendar days for the ethical review of an application. Where a valid application is received, the clock starts on the submission closing date for the HREC meeting at which an application will be reviewed. The clock stops when a request for further information or clarification is requested from the applicant. The clock recommences when the requested information or clarification has been received. The clock is finally stopped when the HREC formally notifies the applicant of the final decision.

## 2.4 METRIC 4: Date Valid SSA Application Received by the RGO to Site Authorisation (site level; with and without clock stops)*

**Associated monitoring measure:** 2 - Site specific applications involving more than low risk to participants authorised within 30 calendar days (%)

**Objective:** To assess the efficiency of the site authorisation process and to drive process improvement.

### Data Calculation Parameters and Deadlines

| All studies (excluding LNR) authorised within the reporting period | | **Deadline for AU RED data entry** |
|---|---|---|
| **Period 1** | 1 July 2016 – 31 December 2016 | By 27 January 2017 |
| **Period 2** | 1 January 2017 – 30 June 2017 | By 28 July 2017 |

For applications authorised within but submitted before the reporting period, ensure submission data are also appropriately entered.

### Related AU RED Data fields

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| **Filtered by:** | | | |
| Application Type | **Included:**<br>Site Specific Assessment<br>**Not included:**<br>Application - Single Site; Application – Multi Site | Application References | |
| LNR/non-LNR | **Included:**<br>No (SSA/LNR SSA Reference number starts with SSA/)<br>**Not included:**<br>Yes (SSA/LNR SSA Reference number starts with LNRSSA) | Set at New Application, which generates HREC/LNR Reference number and subsequent SSA/LNRSSA Reference number(s) | |
| Current Decision | **Included:**<br>Authorised; authorised with conditions; further information response authorised<br>**Not Included:**<br>Invalid application; not authorised; Request for further information/ modification; not requiring review by Research Organisation; further information response not authorised; further information response not complete | Meetings – Decisions | Current decision is auto-populated by any withdrawn status that is entered by the RED user, and, if there is no withdrawn status entered, by the last meeting decision (for HREC) or decision (for SSA) saved by the user. |

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| Date of Site Authorisation | Not applicable - date field | SSA - Meetings tab, clock stop | Must occur within the reporting period.<br><br>See clock definitions. |
| **Also included in analysis:** | | | |
| SSA clock start date | Not applicable - date field | SSA Applications - Validate / Start screen. | See clock definitions. |
| Date SSA application received | Not applicable - date field | SSA Applications - Checklist, and SSA Applications Validate / Start screens. Note: SSA valid letter uses date entered on Checklist screen. | See clock definitions. |
| (Interim) Clock stop and (re)start dates | Not applicable - date field | Meetings – Application Decision and Clocks and correspondence tab | See clock definitions. |

***** The monitoring measure will account for clock stops. The SSA application received date is the date the RGO or designee receives an SSA application from a researcher regardless of whether or not it is complete and/or deemed valid. The interim clock stop dates represent when a request for further information or clarification is requested from the applicant. The clock recommences (interim clock start dates) when the requested information or clarification has been received. The clock is finally stopped when the final SSA decision letter is provided to the site principal investigator (see clock definitions).

## 2.5 METRIC 5: Sites enrolling their first participant within 40 calendar days of Site Specific Authorisation

**Measures:**

Site Level: Proportion of commercial trials with at least one participant enrolled by Day 40 post Site Specific Authorisation
State Level: Proportion of sites with at least one participant enrolled by Day 40 post Site Specific Authorisation (derived by OHMR).

**Associated monitoring measure:** 3 - First participant enrolled to a commercial clinical trial by the site within 40 calendar days of site authorisation

**Objective:** To reduce the time taken to enrol first participant into commercial trials conducted in NSW.

### Data Calculation Parameters and Deadlines

| All commercial clinical trials (excluding LNR) authorised within the reporting period | | **Deadline for AU RED data entry** |
|---|---|---|
| **Period 1** | 1 July 2016 – 31 December 2016 | By 1 March 2017 |
| **Period 2** | 1 January 2017 – 30 June 2017 | By 1 September 2017 |

### Related AU RED Data fields

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| **Filtered by:** | | | |
| Study Type | **Included:**<br>Clinical trial (other); Clinical trial of a drug; Clinical trial of a device; Clinical trial of a drug and device; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – drug; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – device; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – drug and device<br>**Not included:**<br>Clinical research; Health Research/ Social Science; Other (please state) | Application References | |

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| LNR/non-LNR | **Included:**<br>No (SSA/LNR SSA Reference number starts with SSA/)<br>**Not included:**<br>Yes (SSA/LNR SSA Reference number starts with LNRSSA) | Set at New Application, which generates HREC/LNR Reference number and subsequent SSA/LNRSSA Reference number(s) | |
| Major Sponsor Type | **Included:**<br>Commercially Sponsored<br>**Not included:**<br>Collaborative Group; Investigator Initiated Group; Institution; Other | HREC - Application References | This field is answered by the HREC when setting up a new application for a non-LNR study. |
| Application Type | **Included:**<br>Site Specific Assessment<br>**Not included:**<br>Application – Single Site; Application – Multi Site | Application References | |
| Current Decision | **Included:**<br>Authorised; authorised with conditions; further information response authorised<br>**Not Included:**<br>Invalid application; not authorised; Request for further information/ modification; not requiring review by Research Organisation; further information response not authorised; further information response not complete | Meetings – Decisions | Current decision is auto-populated by any withdrawn status that is entered by the RED user, and, if there is no withdrawn status entered, by the last meeting decision (for HREC) or decision (for SSA) saved by the user. |
| Date of Site Authorisation | Not applicable - date field | SSA - Meetings tab, clock stop | Must occur within the reporting period.<br><br>See clock definitions. |
| **Also included in analysis:** | | | |
| Study State | Not applicable | SSA - post approval tab | Study state will be consulted and reported accordingly.<br><br>Please see definitions to ensure accurate representation. |
| **NEW FIELD:** Date first participant enrolled at site | Not applicable - date field | SSA - post approval tab, First Participant Enrolled | Defined as date first participant consented and screened, with eligibility verified. Often the date of randomisation, where applicable. |
| **NEW FIELD:** If first participant enrolled more than 40 calendar days after site authorisation, was there a valid reason for delay? | Not applicable: yes/no radio button field. | SSA - post approval tab, First Participant Enrolled | |

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| **NEW FIELD:** Valid reason for not enrolling within 40 days | **Included**:<br>All | SSA - post approval tab,<br>First Participant Enrolled | OHMR may issue queries for clarification of valid reason fields as needed. |
| **NEW FIELD:** Valid reason for not enrolling within 40 days comments box | Not applicable - free text field | SSA - post approval tab,<br>First Participant Enrolled | OHMR may issue queries for clarification of valid reason fields as needed. |

## 2.6 METRIC 6: Sites reaching or exceeding their agreed enrolment target as per contract

**Associated monitoring measure:** 4 - Actual participants enrolled to a commercial clinical trial project as a proportion of those initially agreed to be enrolled per the Clinical Trial Research Agreement (CTRA) minimum target (%)

**Objective:** To increase the number of commercial trials that achieve or surpass their enrolment target.

**Measures:**

Site Level: Proportion of trials reaching or surpassing their enrolment target at study closure
State Level: Proportion of trials reaching or surpassing their enrolment target at study closure (derived by OHMR)

### Data Calculation Parameters and Deadlines

| All commercial clinical trials (excluding LNR) closed to enrolment at the site between | | **Deadline for AU RED data entry** |
|---|---|---|
| **Period 1** | 1 July 2016 – 31 December 2016 | By 1 March 2017 |
| **Period 2** | 1 January 2017 – 30 June 2017 | By 1 September 2017 |

### Related AU RED Data fields

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| **Filtered by:** | | | |
| Study Type | **Included:**<br>Clinical trial (other); Clinical trial of a drug; Clinical trial of a device; Clinical trial of a drug and device; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – drug; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – device; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – drug and device<br>**Not included:**<br>Clinical research; Health Research/ Social Science; Other (please state) | Application References | |

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| LNR/non-LNR | **Included:**<br>No (SSA/LNR SSA Reference number starts with SSA/)<br>**Not included:**<br>Yes (SSA/LNR SSA Reference number starts with LNRSSA) | Set at New Application, which generates HREC/LNR Reference number and subsequent SSA/LNRSSA Reference number(s) | |
| Major Sponsor Type | **Included:**<br>Commercially Sponsored<br>**Not included:**<br>Collaborative Group; Investigator Initiated Group; Institution; Other | HREC - Application References | This field is answered by the HREC when setting up a new application for a non-LNR study. |
| Application Type | **Included:**<br>Site Specific Assessment<br>**Not included:**<br>Application – Single Site; Application – Multi Site | Application References | |
| Current Decision | **Included:**<br>Authorised; authorised with conditions; further information response authorised<br>**Not Included:**<br>Invalid application; not authorised; Request for further information/ modification; not requiring review by Research Organisation; further information response not authorised; further information response not complete | Meetings – Decisions | Current decision is auto-populated by any withdrawn status that is entered by the RED user, and, if there is no withdrawn status entered, by the last meeting decision (for HREC) or decision (for SSA) saved by the user. |
| Study State | **Included:**<br>Closed to enrolment at site<br>**Not included:**<br>All others | SSA - post approval tab | Study state may have been subsequently changed since it was set to "closed to enrolment at site". Data will be culled for all studies wherein Study State was designated "closed to enrolment at site" within the reporting period. |
| **Also included in analysis:** | | | |
| ***NEW FIELD:**<br>Minimum enrolment target per CTRA | Not applicable: numeric field | SSA - Application – Details screen | Maximum character limit: 4 |
| ***NEW FIELD:**<br>Maximum enrolment target per CTRA | Not applicable: numeric field | SSA - Application – Details screen | Maximum character limit: 4<br>If there is no numeric maximum value, e.g. for competitive recruitment, please enter 9999. |
| **REVISED FIELD:**<br>Actual enrolment at site by end of recruitment period/study closure | Not applicable: numeric field | SSA - Application – Details screen | Maximum character limit: 4 |

| AU RED field name | Drop down selections | Location | Notes |
|---|---|---|---|
| **NEW FIELD:** If did not meet minimum recruitment target, was there a valid reason for not doing so? | Not applicable: yes/no radio button field | SSA - Application – Details screen | |
| **NEW FIELD:** Valid reason for not reaching enrolment target | **Included**:<br>All | SSA - Application – Details screen | Do not complete field unless answer to "actual enrolment" is less than "minimum enrolment target per CTRA". |
| **NEW FIELD:** Valid reason for not reaching enrolment target comments | Not applicable: free text field | SSA - Application – Details screen | May select more than one option.<br><br>Do not complete field unless answer to "actual enrolment" is less than "minimum enrolment target per CTRA".<br><br>Must be completed if answer to "valid reason for not reaching enrolment target" is "other". |

***** The pre-existing AU RED field "targeted number of participants at this site" is automatically populated from the SSA Form Page 5 Question 5 when the Online Form is uploaded. This free-text field will not be included in analysis of this metric nor of the associated monitoring measure, as it may have been populated before the CTRA was finalised.

## 2.7 METRIC 7: Progress reports (including final progress reports) submitted by NSW PI/CPI to institution within the Required Timeframe (site level)

**Associated monitoring measure:** 5 - Progress reports on all authorised research projects received at least annually and at study close (%)

This metric will not be collected through AU RED. Each institution will provide a report to OHMR detailing the institution's compliance rates for annual/interim/final progress reporting.

**Objective:** To improve compliance with study annual/interim/final progress reporting to the NSW institution.

### Data Calculation Parameters and Deadlines

| All authorised research projects (excluding LNR) where interim/final progress reports were expected to be received between | | **Deadline for data reporting to OHMR** |
|---|---|---|
| **Period 1** | 1 July 2016 – 30 June 2017 | By 28 July 2017 |

### 2.7.1. Progress Report Rationale

OHMR policy outlines roles and responsibilites for both HRECs and Research Governance Officers (RGOs), including the maintenance of oversight of approved/authorised research projects post-approval. Periodic and final status reports comprise one of several mechanisms for post-approval monitoring.

For clinical trials, the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guideline section 4.10 (Progress Reports) sets requirements for the provision of written summaries of trial status to the ethics committee annually, or more frequently, if requested by the ethics committee. For Public Health Organisations (PHO) hosting a trial site under a Site Specific Assessement (SSA), OHMR policy does not specify differences between Annual Progress Reports provided to an HREC, and those provided to an RGO to maintain oversight of authorised research projects.

### 2.7.2. Current Progress Report Policy Requirements

Section 12.8 – 12.10 of the HREC Executive Officers Operations Manual (GL2014_014), Annual Progress Reports, outlines processes wherein investigators submit annual progress reports to the reviewing HREC. Furthermore, "for a multi-centre research project Principal Investigators, at sites for which the HREC has given ethical and scientific approval, will submit annual progress reports to the Co-ordinating Investigator using the reporting template stipulated by the HREC. A copy of the report will be provided to the site Research Governance Officer by the Principal Investigator."

As well, per section 12.9 and 12.10, "For a multi-centre research project, the Co-ordinating Investigator will provide a copy of the HREC review outcome to the Principal Investigators involved in the project. Each Principal Investigator will provide a copy of this HREC correspondence to the site Research Governance Officer. The HREC will have the discretion to notify the review outcome directly to the Principal Investigators and Research Governance Officers, in which case the Coordinating Investigator will be informed of this action."

The Research Governance Officers Operations Manual (GL2010_015) notes that RGOs will maintain an oversight of authorised research projects through review of annual and final progress reports submitted by the Principal Investigator. For single centre projects, RGOs will work with the HREC to review the annual and final progress reports submitted by the Principal Investigator. For multi-centre projects, RGOs will review annual and final site progress reports submitted by the Principal Investigator. The Principal Investigator will also forward to the RGO any recommendations made by the HREC following review of these reports, unless the HREC elects to inform the RGO directly.

In complying with these policy requirements, RGOs may accept either an institution-specific progress report, a site-specific version of the HREC progress report, and/or a copy of the HREC progress report.

### 2.7.3. Progress Report Data Collection

To report these data to OHMR, institutions should first generate the number of research projects (greater than low risk) authorised at the site, wherein interim/final progress reports were expected within the reporting period. This figure will form the measure's denominator. If the institution has established an institutional progress report mechanism, the institution should then report on the number of these reports which were received within the expected reporting period.

If an institution is currently relying on the receipt of copies of HREC progress reports to fulfil the progress reporting requirement, the date a report is expected may be adjusted based on the HREC's reporting requirements. The institution should then report on the number of expected reports received within the reporting period, based on these adjustments. The institution may choose whether or not to also report to OHMR compliance with receipt of the HREC's review outcome.

Although a report on the timeliness of receipt of reports is not required at this time, an institution may also include this information in its report.

The study state "closed but not archived" has been added to the Post Approval tab at the SSA level, to indicate when the study has finished normally at the site, participants are no longer being treated or examined, but the documents are not yet archived. Institutions may use this study state to help inform the collection of final institutional progress reports, where applicable.

# 3 Non-Reportable Quality and Transparency Metrics for Optional Use within an Institution

Metrics 8 through 11 offer NSW institutions sponsoring clinical trials guidance to implement research quality and transparency metrics in support of state-wide initiatives for clinical trials.

The terminology and timepoints used align with those set out by the Alltrials campaign.

**Prospective Registration of Clinical Trials (Metric 8):** The International Committee of Medical Journal Editors (ICMJE) requires trial registration as a condition of the publication of research results generated by a clinical trial. Examples of registries include ClinicalTrials.gov, and the Australian New Zealand Clinical Trials Registry (ANZCTR). Registration of trials before they begin fulfils a number of purposes:

- It provides information to potential participants and referring clinicians
- It reduces publication bias and selective reporting
- It helps editors and others understand the context of trial results
- It helps HRECs determine the appropriateness of the trial

**Compliance with the SPIRIT Checklist for Clinical Trial Protocols (Metric 9):** The protocol of a clinical trial serves as the foundation for study planning, conduct, reporting, and appraisal. However, trial protocols and existing protocol guidelines vary in content and quality. The SPIRIT recommendations aim to facilitate the drafting of high-quality protocols. Adherence to the 33 Item SPIRIT Checklist also enhances the transparency and completeness of trial protocols for the benefit of key stakeholders including investigators, funders, sponsors, peer reviewers and HRECs.

**Publication of Summary Results (Metric 10):** Overall, only half of completed clinical and preclinical studies are reported. Publication of summary results reduces reporting biases and help researchers and policy-makers produce more reliable systematic reviews of the safety and effectiveness of medical interventions. Sponsors should ensure that summary results contain at least the items on a ClinicalTrials.gov results page (which includes summary participant information, protocol and amendments, summary results for pre-specified primary and secondary end points, details of adverse events and statistical analyses). An alternative template can be found in Appendix 1 of the AllTrials guidance.

**Full Study Reports for Non-commercial Clinical Trials (Metric 11):** For non-commercial trials, the common route to inform the research community of full trial methods and results is through publication in peer-reviewed scientific journals; however, many publications have documented deficiencies in the reporting of clinical trials. CONSORT is an initiative that was developed to improve the reporting of randomised controlled trials, enabling readers to understand a trial's design, conduct, analysis and interpretation and to assess the validity of its results.

## STUDY QUALITY AND TRANSPARENCY

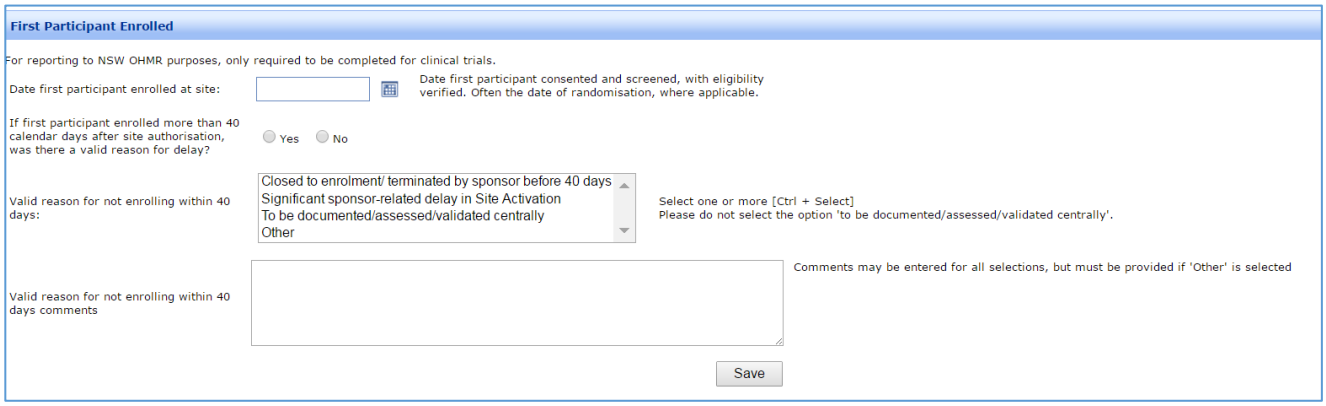
| | Metric Category & Description | Objective | Measure | Recommended Data Fields |
|---|---|---|---|---|
| **All Internally Sponsored Clinical Trials (except LNR)** | **8. Transparency:** Internally sponsored clinical trials in NSW that are registered on a publicly accessible database before the first participant is enrolled | To improve the transparency of internally sponsored NSW clinical trials through compliance with international trial registration requirements | Study Level: Proportion of internally sponsored NSW trials registered on a publicly accessible database before the first participant is enrolled | Available in AU RED:<br>• Study Type: All clinical trial options<br>• Major Sponsor Type (Institution)<br>• Date first participant enrolled<br><br>Other<br>• Date study registered on the chosen registry<br>• Valid reason for delayed registration |
| | **9. Quality/Transparency:** Protocols for internally sponsored clinical trials in NSW that comply with the 33-item SPIRIT checklist | To improve the quality of internally sponsored NSW clinical trial protocols through compliance with international standards | Site Level: Proportion of internally sponsored NSW trials with protocols that include all elements described in the SPIRIT checklist | Available in AU RED:<br>• Study Type: All clinical trial options<br>• Major Sponsor Type (Institution)<br><br>Other<br>• Protocol content assessed* as satisfactorily meeting the SPIRIT checklist (Y/N) |
| | **10. Transparency:** Reports of trial summary results (Summary Reports) for internally sponsored clinical trials in NSW posted publicly** within 12 months of Study Completion | To increase trial accountability and results uptake through improved compliance with international results reporting timelines | Study Level: Proportion of internally sponsored NSW trials that publish a Summary Report within 12 months of Study Completion | Available in AU RED:<br>• Study Type: All clinical trial options<br>• Major Sponsor Type (Institution)<br>• Date Study State becomes "Finished"<br><br>Other<br>• Summary Report posted publicly within the 12 month timeframe (Y/N)<br>• Valid reason for not meeting reporting requirements |
| | **11. Quality/Transparency:** Full reports of trial results (Final Study Reports) for internally sponsored clinical trials in NSW that comply with the 25-item CONSORT checklist or where applicable CONSORT Extensions | To facilitate the complete and transparent reporting of internally sponsored NSW Clinical Trials in compliance with international trial reporting recommendations | Site Level: Proportion of internally sponsored NSW trials that produce Study Reports that comply with the CONSORT Checklist (or where applicable, CONSORT Extension Checklists) | Available in AU RED:<br>• Study Type: All clinical trial options<br>• Major Sponsor Type (Institution)<br><br>Other<br>• Study Report received in the reporting year (Y/N)<br>• Study Report assessed*** as satisfactorily meeting the reporting requirements outlined the CONSORT checklist or CONSORT Extensions Checklist (Y/N) |

* It is suggested that in order to assess compliance with this metric, institutions develop/adopt a SPIRIT-compliant protocol template.
** The summary of results should be made publicly available at the same place where the trial was registered,e.g. ClinicalTrials.gov or ANZCTR, where summary results can be uploaded as a PDF.
***It is suggested that in order to assess compliance with this metric, researchers provide an annotated copy of the relevant Consort Checklist, which cross references to content within the Study Report.

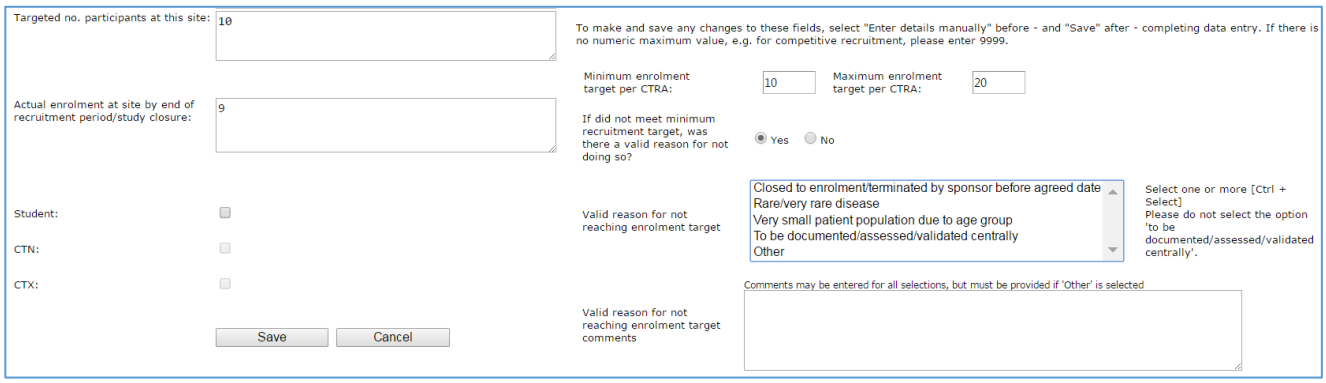
# 4 AU RED New Field Screenshots

The new fields added to AU RED to assist in the collection of data for metrics are available on the SSA Application – Post Approval tab, and the SSA Application – Details tab, as illustrated:

*Screenshot 1: First Participant Enrolled fields, SSA: Application - Post Approval tab*




*Screenshot 2: Enrolment targets, SSA: Application – Details tab*



# 5 AU RED Field Drop Down Definitions

## 5.1 Study Type

**Set by:** HREC staff
**Where:** New Application Tab, then Application References Tab
**When:** Upon starting a new application
**Editable:** Must be edited at HREC application level

As stated in section 2, metrics 1, 5 and 6 will be calculated for clinical trials only. All studies that meet the definition of clinical trial according to the table below must be coded as one of the following study types: Clinical trial (other); Clinical trial of a drug; Clinical trial of a device; Clinical trial of a drug and device; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – drug; First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – device; and, First Time In Human (FTIH) or First Time In Patients (FTIP) Clinical trial – drug and device.

The following study types will *not* be included in these metrics: Clinical research; Health Research/ Social Science; Other (please state).

To distinguish between a clinical trial and other types of clinical research, the definition of clinical research is also provided. Since clinical trials are a subset of clinical research, any clinical research study that also meets the definition of a clinical trial should be coded as one of the clinical trial study type options.

| Term | Definition |
|---|---|
| Clinical trial | A clinical trial is the name commonly given to research in which a therapeutic, preventive or diagnostic intervention is tested. It is a form of human research designed to find out the effects of an intervention, including a treatment or diagnostic procedure. A clinical trial can involve testing a drug, a surgical procedure, other therapeutic procedures (radiation therapy) and devices, a preventive procedure, or a diagnostic device or procedure.<br><br>Often a clinical trial will involve a new therapeutic drug or device i.e. a “therapeutic good” which is subject to the Therapeutic Goods Act, administered by the Therapeutic Goods Administration (TGA) under the CTN or CTX scheme.<br><br>According to the World Health Organisation (WHO), a clinical trial is 'Any research project that prospectively assigns human participants or groups to one or more health-related interventions to evaluate the effects on health outcomes.’ |
| Clinical research | Studies, including observational studies in the clinical setting, which are designed to understand, find and treat illnesses and other health issues. These studies involve a wide range of activities from genetics to assisting medical staff and patients to communicate better. Examples include finding how genetics leads to disease or finding the best ways to counsel people who have a genetic mutation that predisposes them to a certain disease such as cancer; and, the relationship between smoking and heart attacks. |

## 5.2 Major Sponsor Type

**Set by:** HREC staff
**Where:** New Application Tab, then Application References Tab
**When:** Upon starting a new application
**Editable:** Must be edited at HREC application level

A sponsor is the entity that takes overall responsibility for the conduct of a clinical trial and usually initiates, organises and supports the study.

These drop down definitions refer less to the roles and responsibilities of sponsors, and more to distinctions between types of organisation that act as a sponsor for a clinical trial.

| Major Sponsor Type | Definition |
|---|---|
| *To be included in the clinical trials metrics #1, #5, #6:* | |
| Commercially Sponsored | A for-profit company (e.g. pharmaceutical or device company) |
| *Will not be included in the clinical trials metrics:* | |
| Collaborative Group | An academic or other non-commercial collaborative or cooperative research group external to NSW Health |
| Institution | A government organisation such as a Local Health District. All institutions reporting metrics should be coded as this Major Sponsor Type. |
| Investigator Initiated Group | ***From 1 July, please do not use this field.***<br><br>Where the Co-ordinating Principal Investigator is an employee of a NSW Public Health Organisation (PHO), and is conducting the study as part of his/her employment, please select **'Institution.'**<br><br>In the rare case where an individual, such as a private medical practitioner, is the sponsor, please select **'Other.'** |
| Other | Is a sponsor that does not fall into the above classifications. |

## 5.3 Mode of HREC Review

**Set by:** HREC staff
**Where:** New Application Tab, then Application References Tab
**When:** Upon starting a new application
**Editable:** Must be edited at HREC application level

| Mode of HREC Review | Definition |
|---|---|
| Interstate Mutual Acceptance | (No longer a drop down option for new studies.)<br><br>Would have been selected when the application related to a multi-centre clinical trial to be conducted under the IMA scheme in two or more states (i.e. NSW, QLD, VIC), for which only one HREC review was required, which was approved before NMA was introduced on 1 November 2013. |
| National Mutual Acceptance | An application that relates to a multi-centre research study to be conducted in two or more states (i.e. NSW, ACT, QLD, SA, VIC), for which only one HREC review is required. NMA is established under the Memorandum of Understanding for Mutual Acceptance between NSW, ACT, QLD, SA & VIC and commenced on 1 November 2013. |
| State | Is the default value for the field. An application that is only taking place within NSW and is thus not a National Mutual Acceptance application. May also indicate a multi-site study that is taking place in NSW and a non-NMA jurisdiction, or a multi-site study that is taking place in NSW and other sites outside of Australia. |

## 5.4 Application Type

**Set by:** HREC staff
**Where:** New Application Tab, then Application References Tab
**When:** Upon starting a new application
**Editable:** No

| Application Type | Definition |
|---|---|
| Application - Single Site | Research to be conducted at one site only within the public health system, or at two or more sites under the jurisdiction of a single NSW Health HREC. |
| Application - Multi Site | Research to be conducted at more than one site, and within the jurisdiction of more than NSW Health HREC. |
| Site-Specific Assessment | The mechanism used by Public Health Organisations to determine the suitability of a research project to be conducted at a site, whether that project is multi-site or single-site. |

## 5.5 Application – Withdraw/Cancel tab

**Set by:** Research Governance Officer, HREC
**Where:** Application – Withdraw/Cancel Tab
**When:** As soon as application is withdrawn or cancelled
**Editable:** Not after study approved/authorised

| Options | Definition when pertaining to HREC application/entire study | Definition when pertaining to SSAs |
|---|---|---|
| Cancelled as HREC application is Not Approved | N/A | The SSA application is no longer under consideration for SSA authorisation, because the reviewing HREC did not approve the study. |
| Not Withdrawn or Cancelled | The application is under consideration for HREC review. This is the default value in AU RED. | The application is under consideration for SSA authorisation. This is the default value in AU RED. |
| Withdrawn by HREC co-ordinator | The HREC has removed the application from consideration before it has been granted a final decision. | N/A |
| Withdrawn by Research Governance Officer | N/A | The RGO has removed the application from consideration before it has been granted a final decision. |
| Withdrawn by researcher | The researcher (or sponsor, via the researcher) has removed the HREC application from consideration before it has been granted a final decision. | The researcher (or sponsor, via the researcher) has removed the SSA application from consideration before it has been granted a final decision. |

## 5.6 Valid reason for not enrolling within 40 days

**Set by:** Research Governance Officer
**Where:** Post Approval Tab, under First Participant Enrolled
**When:** As soon as information is available
**Editable:** Yes

| Valid Reason | Definition |
|---|---|
| Closed to enrolment/ terminated by sponsor before 40 days | Study closed to enrolment or terminated by the sponsor before 40 days from site authorisation. |
| Significant sponsor-related delay in Site Activation | Significant sponsor-related delay in Site Activation, wherein the sponsor notifies the site that clinical activities, including recruitment, can commence at the site. Examples include: overseas sponsor waiting for multiple site activation to plan travel to Australia; sponsor awaiting protocol amendment before activation; sponsor delay in drug shipment to site; unknown reason for delay on sponsor's end. |

| Valid Reason | Definition |
|---|---|
| To be documented/assessed/validated centrally | **Please do not use this drop-down type. It may be removed from AU RED in the future.** |
| Other | A valid reason for not enrolling within 40 days other than the provided drop-down options. Will be assessed by OHMR. |

## 5.7 Valid reason for not reaching enrolment target

**Set by:** Research Governance Officer
**Where:** Application – Details Tab
**When:** As soon as information is available/at study close
**Editable:** Yes

| Valid Reason | Definition |
|---|---|
| Closed to enrolment/terminated by sponsor before agreed date | Study closed to enrolment or terminated by sponsor before agreed completion date |
| Rare/very rare disease | Rare/very rare disease making enrolment difficult to predict up front |
| Very small patient population due to age group | Very small patient population due to age group to be treated, making enrolment difficult to predict up front |
| To be documented/assessed/validated centrally | **Please do not use this drop-down type. It may be removed from AU RED in the future.** |
| Other | A valid reason for not meeting enrolment target other than the provided drop-down options. Will be assessed by OHMR. |

# 6 AU RED Clock and Date Definitions

## 6.1 Definitions and origin of AU RED date markers and fields

Section 6 of the AU RED User Manual (Version 1.7) outlines instructions for registering, uploading, validating, and starting and stopping the clock for HREC and SSA applications. During these processes, AU RED generates some date/time datapoints automatically to capture *when* data were entered in the system (e.g. an audit trail). It also provides some date data entry fields wherein the user may manually enter a date to reflect a *process* that occurred outside of the AU RED system. This definitions table outlines both types of date fields as captured in AU RED, for HREC and SSA applications/studies. The figures below provide examples of each.

| | HREC | | SSA | |
|---|---|---|---|---|
| **Field** | **Definition for HREC application** | **Method of derivation** | **Definition for SSA application** | **Method of derivation** |
| Date Application Registered (same as Application Stub Created date) | Not applicable – reflective of a data entry process only. | AU RED user creates a "new" HREC application by selecting Application, New, enters information, and clicks the "Register Application" button. | Not applicable – reflective of a data entry process only. | AU RED user creates a "new" SSA application by selecting Application, New, enters the related HREC/LNR reference number, and clicks the "Register Application" button. |
| Date Application Received* | The date the HREC staff receives a NEAF application from a researcher, regardless of whether or not it is complete and/or deemed valid. | Under checklist tab, the date entered in the received date field when a AU RED user edits or checks in an "application," clicks "enter selected items," and fills out the resultant fields.<br><br>This field may be back-dated. | The date the RGO or designee receives an SSA application from a researcher regardless of whether or not it is complete and/or deemed valid. | Under checklist tab, the date entered in the received date field when an AU RED user edits or checks in an "SSA application," clicks "enter selected items," and fills out the resultant fields.<br><br>This field may be back-dated. |

| | HREC | | SSA | |
|---|---|---|---|---|
| **Field** | **Definition for HREC application** | **Method of derivation** | **Definition for SSA application** | **Method of derivation** |
| Date Checked In | Not applicable – reflective of a data entry process only. | Under checklist tab, the date the AU RED user imports a NEAF form, or the date the AU RED user selects the Application check box, selects "enter selected items" button, fills out the fields and clicks "save items." | Not applicable – reflective of a data entry process only. | Under checklist tab, the date the AU RED user imports an SSA form, or the date the AU RED user selects the SSA Application check box, selects "enter selected items" button, fills out the fields and clicks "save items." |
| Application Validation Date | Not applicable – reflective of a data entry process only. | On the Validate/Start tab, an AU RED user selects the Valid radio button under question 1. | Not applicable – reflective of a data entry process only. | On the Validate/Start tab, an AU RED user selects the Valid radio button under question 1. |
| Initial Application Clock Start Date | The submission closing date for the HREC meeting at which the ethics application is first considered.<br><br>Where a sub-committee meets to consider applications before they proceed to a full HREC meeting, the closing date for submissions for the sub-committee meeting should be entered as the start date. | The date an AU RED user enters under question 2 on the Validate/Start tab.<br><br>AU RED allows this to be back-dated, and it can be reset as needed. | The date on which an SSA application has been deemed valid by the RGO.*<br><br>This is the date the SSA has been received by the RGO and is confirmed to contain the following signatures: all investigators who will conduct research at the site; and the head of department (or divisional director or other authority) of the Principal Investigator at the site. | The date an AU RED user enters under question 2 under the Validate/Start tab.<br><br>AU RED allows this to be back-dated, and it can be reset as needed. |
| Meeting Date | The date that the HREC meets to consider the HREC application. | The date an AU RED user enters under Meeting, New. When an HREC application is subsequently assigned to this meeting, it assumes the meeting date set under New, Meeting. | Not applicable for SSA | Not applicable for SSA |

| | HREC | | SSA | |
|---|---|---|---|---|
| **Field** | **Definition for HREC application** | **Method of derivation** | **Definition for SSA application** | **Method of derivation** |
| Date Current Decision Recorded | Not applicable – reflective of a data entry process only. | The date the AU RED user clicks “save decision” under Meetings – Decisions tab, Edit Application Decision, Decision Info | Not applicable – reflective of a data entry process only. | The date the AU RED user clicks “save decision” under Meetings – Decisions tab, Edit Application Decision, Decision Info |
| [Final] Application Clock Stop Date*<br>(For SSA application, proxy for date of site authorisation, if approved) | Date on the final HREC decision letter that is provided to the investigator. | Under Meetings – Decisions tab, Edit Application Decision, Clocks and Correspondence, the date an AU RED user enters under Clock Actions, “stop clock by entering date in the text box below”. | Date on the final SSA decision letter that is provided to the site principal investigator.<br><br>This is the closest proxy in the system to date of site authorisation, if approved. | The date the RGO or designee enters on the SSA Meetings tab under “Once you have saved your decision you may stop the clock to complete the application.” |
| Interim date(s) of Clock Stop (post-initial application receipt) | Date(s) a written ”Request for Further Information" is provided to the investigator. | Under Meetings – Decisions tab, Edit Application Decision, Clocks and Correspondence, the date an AU RED user enters under Clock Actions, “stop clock by entering date in the text box below” . | Date(s) a written ”Request for Further Information” is provided to the investigator. | The stop clock date entered under the Applications – Meetings, after the user has saved the decision. |
| Interim date(s) of Clock re-start | Date(s) written response received from the investigator to a ”Request for Further Information”. If the response to a request for information is brought to a full HREC meeting, the clock re-start date should still reflect the date the response was received, not the closing date of the HREC meeting. | The date the AU RED user enters as the Received Date under Application – Checklist, when checking in a “response to request for further information” document. Note that there is no “clock start” button to activate in these instances. | Date(s) written response received from the investigator to a ”Request for Further Information”. | The date the AU RED user enters as the Received Date under Application – Checklist, when checking in a “response to request for further information” document. Note that there is no “clock start” button to activate in these instances. |

*Definitions will be changed in relevant policy documents.

## 6.2 SSA Application Received, Validated and Authorised Dates in AU RED

Data for metric 4, "Date Valid SSA Application Received by the RGO to Site Authorisation" and its associated monitoring measure "site specific applications involving more than low risk to participants authorised within 30 calendar days" is generated by filtering for projects authorised within the reporting period. The date the SSA application is *validated* will then be used to count the calendar days until authorization. It is still important for the AU RED user to log both receipt date and "validation" date appropriately. This process is outlined below. **Please note that this may differ from individual institution's current processes, and thus, although the differences may be minor, these instructions should be followed for all applications authorised as of 1 July 2016.**

Research offices should develop their own procedures and materials to encourage the submission of a complete SSA application. However, for the purposes of these metrics, an application must be accepted and the clock started upon receipt of a 'valid' application as defined in section 6.2.2. Furthermore, the office must determine an application's validity promptly upon receipt.

**Figure 1:** "Application stub created" date is automatically-generated when an AU RED user creates a "new" HREC or SSA application by selecting Application, New, enters information on the New Application tab, and clicks the "Register Application" button.

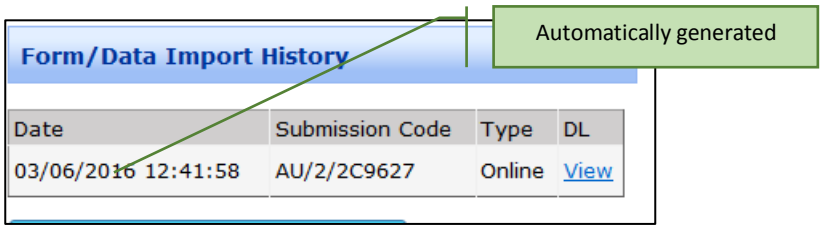



**Figure 2:** "Application made Valid from Invalid state" is automatically-generated when an AU RED user clicks the "valid" radio button in the system. It does not reflect the date a RGO deemed an SSA application to be valid:

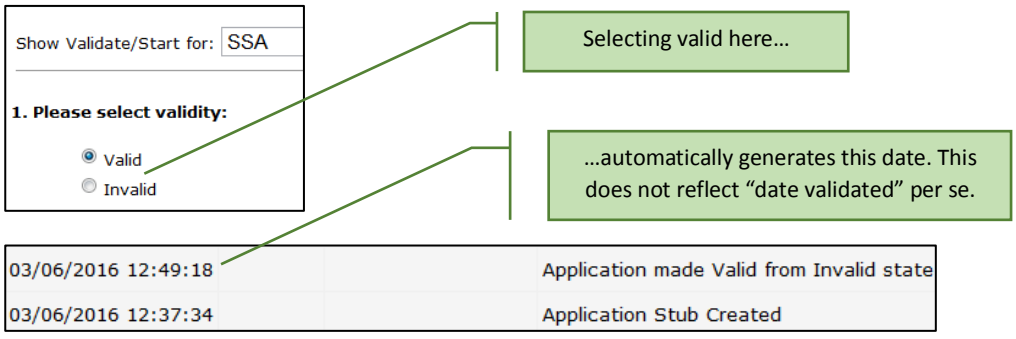
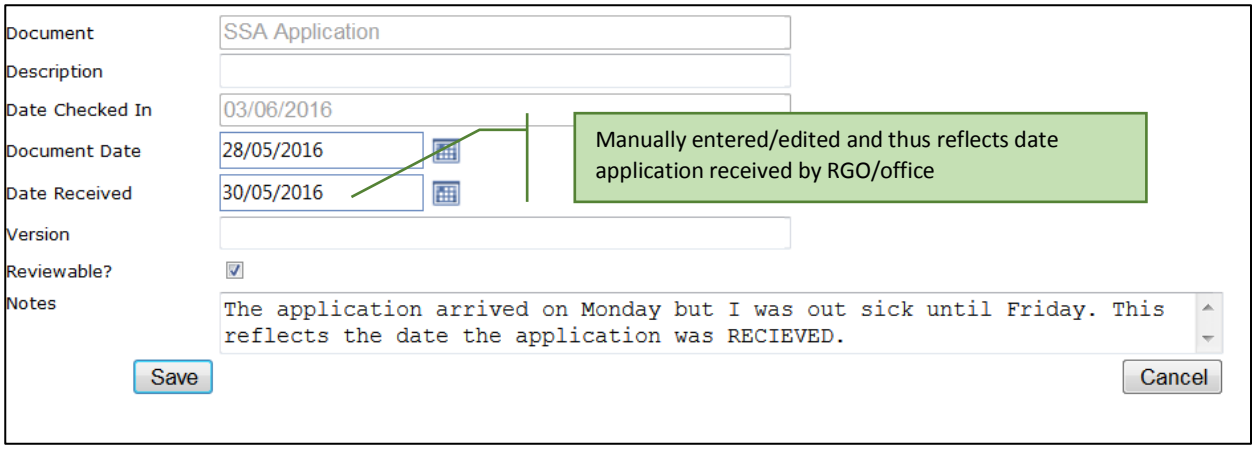


**Figure 3:** The "date received" entered under Application – Checklist can be manually entered (or updated, if generated at time of import), to reflect the date it arrived at the office, NOT the date it was imported into the system:

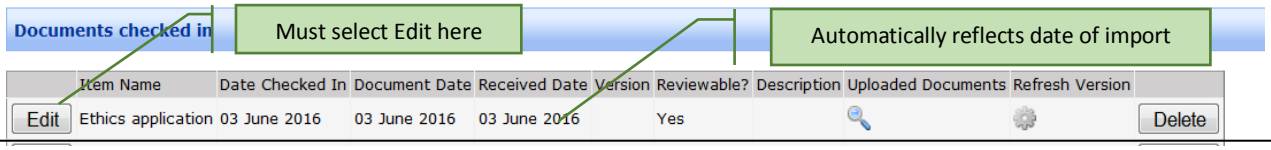



### 6.2.1. When is an application "received?"

The date in the footer of a NEAF or SSA application reflects the date a researcher generates a submission code in Online Forms, which is not necessarily the date that the researcher emails, posts or delivers the application to the HREC or Research Office for consideration. Similarly, the field "Date Application Registered" that is retrieved under AU RED's application search page merely reflects the date the AU RED user selects Application, New, enters information on the New Application tab, and clicks the "Register Application" button. It does not reflect the date the application arrives at the office.

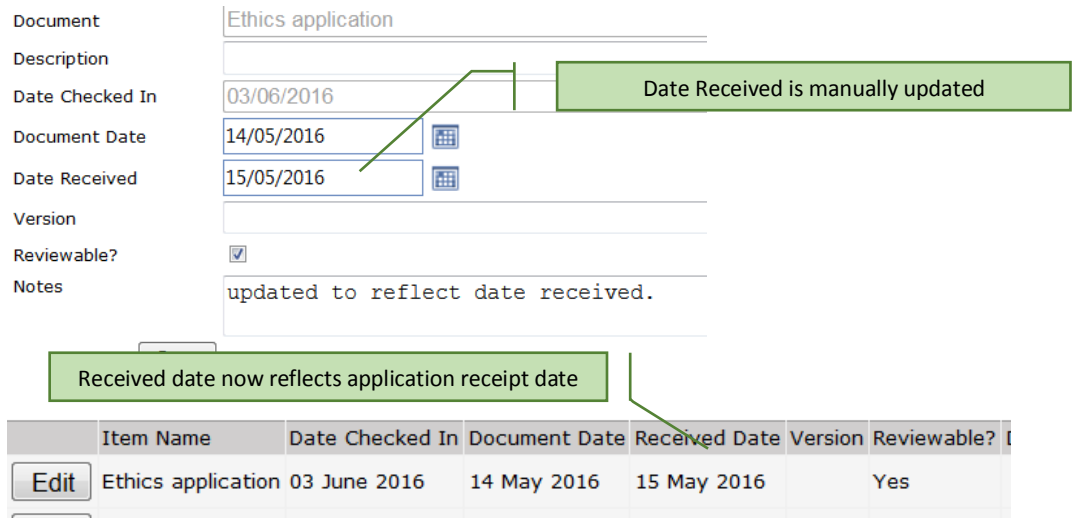
Since AU RED automatically checks-in imported NEAF and SSA applications, it also creates an automatic application "received" date at that time. This date reflects when the AU RED user uploads Online Form Data on the Application – Details page. This may or may not be different from the "Registered date." Since the date the Online Forms data are imported does not necessarily reflect the date the application was received at the office, the user must manually edit the Received Date of the application on the Application – Checklist page. To do so, click the Edit button on the Application – Checklist page:

**Figure 4:**




The user should then manually change the Date Received to reflect, for HREC applications, the date the HREC staff received the NEAF from a researcher, whether or not it is complete and/or deemed valid. For SSA applications, the user should edit the Date Received to reflect the date the RGO or designee receives an SSA application from a researcher, whether or not it is complete and/or deemed valid. The document dates may also need to be manually updated.

**Figure 5:** Manual update of "Date Received"




### 6.2.2. When is an application "validated?" Change in SSA Clock Start Date

Per Figure 2, AU RED's Validation Date does not reflect the date an RGO deemed an SSA application to be valid. In order to record that date in AU RED, for all SSA applications greater than low risk authorised as of 1 July 2016, **please ensure the SSA application Clock Start Date reflects the date on which the SSA application is deemed valid by the RGO.** The date an SSA application is deemed valid should be the date that the SSA has been received by the RGO and is confirmed to contain the following signatures: all investigators who will conduct research at the site; and, the head of department (or divisional director or other authority) of the Principal Investigator at the site.

Institutions may choose whether or not to implement this new definition for LNR SSA applications authorised as of 1 July 2016. To ensure data on all SSA applications that were authorised before this date remain comparable between institutions, please do not modify pre-existing entries based on the new clock start date definition.

NSW policy documents for research governance do not currently define application validation. The application assessment process outlines per policy (e.g. GL2010_015 Operations Manual: Research Governance Officers, section 4.10), shall occur after the application form is deemed valid, and comprises part of the assessment process. The relevant policy documents will be updated accordingly.

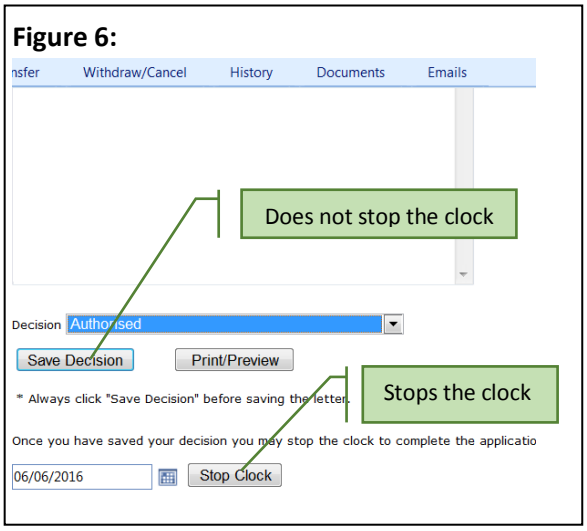
### 6.2.3. What is the final SSA clock stop? Change in AU RED definition

Like metric 4, data for metrics 1 and 5 are generated by filtering for projects authorised within the reporting period. Since there is no meeting date for SSA applications and there is no datapoint in AU RED that specifically reflects the date an SSA application was deemed authorised, for all SSA applications greater than low risk authorised as of 1 July 2016, please set the final clock stop date of an SSA application as the date on the final SSA decision letter that is provided to the site principal investigator.

Please note this is a change from the definition of SSA Clock End Date provided in previous documentation, which was the "date on which the Chief Executive or delegate has granted approval for a research project to commence at a site."

To ensure accurate data reporting, AU RED users must remember to stop the clock to represent this date, on the SSA Meetings tab under "Once you have saved your decision you may stop the clock to complete the application." Solely clicking the "Save Decision" button does not stop the clock:

**Figure 6:**




Institutions may choose whether or not to implement this new definition for LNR SSA applications authorised as of 1 July 2016. However, to ensure data on all SSA applications that were authorised before this date remain comparable between institutions, please do not modify pre-existing entries based on the new stop clock date definition.

# 7 Use of AU RED Post Approval Tab Study State

The AU RED Post Approval Tab for both HREC and SSA applications offers Study State fields wherein the user may track changes in the study after approval/authorisation until the end of its lifecycle.

This section clarifies the use of Study State to assist institutions in improving data quality and accuracy whilst also informing processes such as progress and final reporting.

## 7.1 What is Study State?

In AU RED, study state refers to the status of a health or medical research study at any timepoint after it has received HREC approval (for HREC application functionality) or site authorisation (for SSA application functionality). As an example, the status of a study that begins enrolling participants changes – at a minimum – from "not started" to "started." Similarly, the status of a study that receives ethical approval but does not progress to enrolment changes from "not started" to "abandoned" or "terminated."

HREC progress report alerts are scheduled from any HREC application that is "approved." The user is NOT required to set the HREC application study state to "Started" in order for Work Area progress report alerts to commence. Institutional (SSA) progress report alerts are currently not available in AU RED.

## 7.2 How is Study State different from Withdrawn/Cancelled Status?

Whereas Study State represents a study's status after it has been approved, the "withdraw/cancel" tab under "Application" reflects an application's status before it has been reviewed. Furthermore, in AU RED, an HREC application can be withdrawn, but only an SSA application can be cancelled. However, the AU RED field "current decision" as available under Applications – Search reflects and is populated by data from the "Withdraw/Cancel" tab and from the Post-Approval tab – Study State.

Table 1 illustrates the differences between Withdrawn/Cancelled status and Study State.

*Table 1: Study State versus Withdrawn/Cancelled Status*

| | Withdraw/Cancel options | Study State Options (see Table 2 for definitions of each) |
|---|---|---|
| For HREC applications/studies | • Not withdrawn or cancelled (default value)<br>• Withdrawn by Researcher<br>• Withdrawn by HREC Co−ordinator | • Abandoned<br>• Closed and Archived<br>• Finished<br>• Halted temporarily<br>• Not started<br>• Restarted<br>• Started<br>• Suspended<br>• Terminated |
| For SSA applications/studies | • Not withdrawn or cancelled (default value)<br>• Withdrawn by researcher<br>• Withdrawn by Research Governance Officer<br>• Cancelled as HREC application is Not Approved | • Abandoned<br>• Closed but not archived<br>• Closed and Archived<br>• Closed to enrolment at Site*<br>• Finished<br>• Halted temporarily<br>• Not started<br>• Restarted<br>• Started<br>• Suspended<br>• Terminated |

*the values for any studies previously-set to "Closed at Site" will be retained

## 7.3 How is Study State for HREC applications linked to Study State for SSA Applications?

Currently, AU RED does not change Study State of an HREC application based on a Study State change of an SSA application, and vice versa. Therefore, HREC and SSA Study States must be managed

independently. (An AU RED user can only view the SSA application post-approval tab after the SSA application has been authorised.)

In theory, SSA Study State for a single-site study approved by its "local" HREC may be managed within the same office. However, SSA applications wherein the approving HREC is not internal are reliant on real-time communication with the study sponsor, Coordinating Principal Investigator, and/or local Principal Investigative team.

AU RED provides some functionality to help manage Study State changes through the following Work Area alerts:

- If the Study State for a HREC application is set to either "Halted Temporarily", "Finished", "Suspended" or "Terminated", an alert (for the RGO's information) will appear on the Work Area-SSA screen for all associated SSA applications.
- If the Study State for an HREC application is set to 'Finished', an alert will appear in the Work Area called "reminder for summary of final report" twelve months later.
- Another alert section on the Work Area-Application screen ("Applications with SSAs whose study state was modified within last 'x' days"), enables HREC Co−ordinators to view the study state of any SSAs linked to HREC applications registered with their committee.
- If the study state for an HREC application is set to "Abandoned", "Finished", "Closed and Archived" or "Terminated", it clears all Work Alerts for the study at the HREC application level but does not clear work alerts for any related SSA applications. If the study state for an SSA application is set to any of these values, it clears all Work Alerts for the study at the SSA application level, but does not clear work alters for the parent HREC application.
- If the study state for an HREC application is set to "Halted Temporarily" at the HREC application level, HREC summary progress report notifications are suspended.

## 7.4 How is Study State related to the OHMR Research and Governance Metrics?

For the collection of OHMR metrics, the Study State definitions in table 2 refer specifically to clinical trials. At a minimum, OHMR will **require institutions set the Study State to "Closed to enrolment at Site" (previously, "Closed at Site") at the SSA/site level** when appropriate, to help calculate metric 6/monitoring measure 4, "actual participants enrolled to a commercial clinical trial project as a proportion of those initially agreed to be enrolled…" The definition of "Closed to enrolment at Site" has been arbitrarily created to capture the date that a clinical trial is no longer enrolling participants at the study site, to set a date at which the enrolment target metric can be assessed.

The definition of "finished" was created to capture the date that the last clinical trial participant has met the last study analysis endpoint. Please note that this timepoint is most often referred to as "completed" in most international definitions documents, and will likely be appropriately named in the upcoming Research Ethics and Governance Information System (REGIS ). Sites may use this study state to inform metric 10, "Reports of trial summary results (Summary Reports) for internally sponsored clinical trials in NSW posted publicly within 12 months of Study Completion." Study state option "closed but not archived" was added to help sites calculate site final progress report deadlines, where

applicable.  Other Study State selections may be used to inform metric 5, monitoring measure 3 (enrolment within 40 days).

Figure 7, Application Status and Study State Continuum, visually plots Study State options throughout the lifecycle of the study.  It also illustrates the difference between application status (e.g. withdrawn, cancelled), and study state.

***Table 2: Study State Definitions***

*Before study start:*

| **Not started** | **Abandoned** | **Started** |
|---|---|---|
| No clinical activities involving participants (including participant recruitment) have commenced. This is the default state for all applications in AU RED. | The application has been approved/authorised, but it has been determined that the project will never commence at the study site.<br><br>**Note:** Per GL2010_014, a final report will be submitted if a project is abandoned. | The sponsor has notified the site that clinical activities, including recruitment, can commence at the site. In industry, this is sometimes referred to as "green light" or "site activation."<br><br>**Note:** HREC progress reports alerts are scheduled from any HREC application that is "approved." The user is not required to set the study state to "Started" in order for Work Area progress report alerts to commence. |

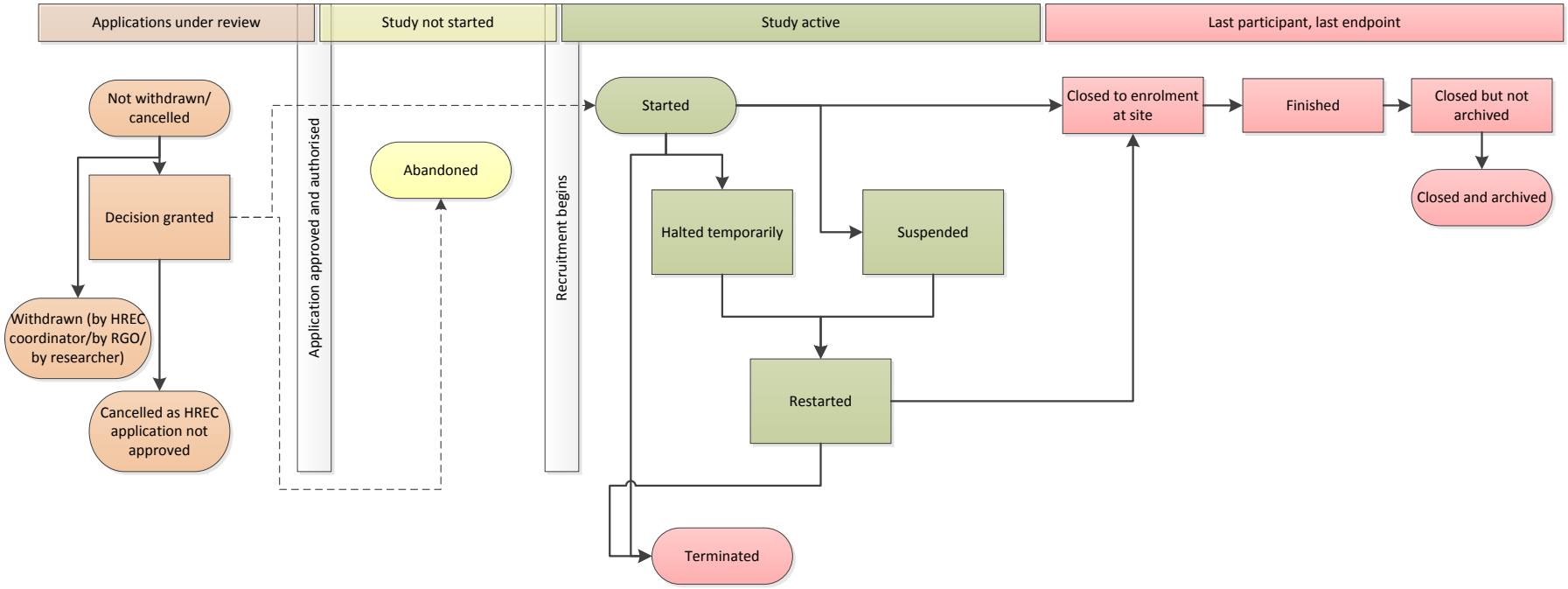
*Once study has started:*

| **Halted temporarily** | **Suspended** | **Restarted** | **Terminated** |
|---|---|---|---|
| After study start but before study close, study activity has been temporarily stopped for any reason other than HREC (ethical) suspension. | After study start in at least one site but before study close, the HREC will suspend approval if it deems the research is not, or cannot be, conducted in accordance with the approval or that the rights, safety or welfare of participants may be compromised. Suspension can relate to some or all project activities, and certain aspects of the protocol will continue to ensure participant safety. | Study activity has resumed at least at one of the study sites, after it was halted temporarily or suspended. | After study start but before study close, discontinuation of a research project by **the investigator or sponsor, wherein activity will not resume.** Possible reasons include: ethical, safety, financial or other grounds. Will never progress to "finished," "closed at site" or "closed and archived."<br><br>**Note:** Per GL2010_014, a final progress report will be submitted if a study is terminated. |

*Once last participant has met last endpoint:*

| **Finished** | **Closed to enrolment at site** | **Closed but not archived** | **Closed and archived** |
|---|---|---|---|
| This is referred to as "completed" in most international definitions documents.<br><br>When the last participant has met the last study analysis endpoint. When reached at a single site study, this is likely the time point when data analysis can begin. When reached at the last site in a multi-site study, this is likely the time point when data analysis can begin. Participants may still be undergoing follow-up visits. | For the OHMR metrics, this status is to be selected at the SSA level when the study is closed to enrolment/ recruitment at the site.<br><br>The values for any studies previously-set to "closed at site" will be retained. | The study has finished normally at the site, participants are no longer being treated or examined, but the documents are not yet archived. | The study has finished normally at the site, participants are no longer being treated or examined, and the study documents have been archived. |

**Figure 7:** Application Status and Study State Continuum



# APPENDIX 1: TERM DEFINITIONS

| | |
|---|---|
| **Clinical Trial Research Agreement (CTRA)** | Clinical Trial Research Agreement (usually a standard template hosted by Medicines Australia) between Sponsor and Institution |
| **Contract Research Organisaton (CRO)** | A Contract Research Organization (CRO) is an organization that provides support to the pharmaceutical, biotechnology, and medical device industries in the form of research services outsourced on a contract basis. |
| **Coordinating Principal Investigator (CPI)** | The individual who takes overall responsibility for the research project and submits the project for scientific and ethical review. The CPI is responsible for ongoing communication with the HREC and passing on any outcomes from this to the Principal Investigators. |
| **Date first participant enrolled at site** | Date first participant consented and screened, with eligibility verified. Often the date of randomisation, where applicable. |
| **Internally Sponsored Clinical Trial** | A clinical trial where a NSW institution has accepted the role of sponsor |
| **Progress Reports** | A report provided to the institution to enable appropriate study oversight |
| **Final Progress Report** | A report provided to the HREC at the time of Study Close |
| **Registry** | A structured online system, such as ClinicalTrials.gov, that provides the public with access to summary information about ongoing and completed clinical studies. |
| **Site Initiation Visit (SIV)** | The on-site/telephone meeting designed to prepare the study team for conducting the study. |
| **Sponsor** | An individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.<br>For non-commercial trials, the sponsor is often the employer of the Co-ordinating Principal Investigator. |
| **Final Study Report** | A full study report of trial results detailing methods, analysis, results and conclusions of a clinical trial and complying with the CONSORT Statement (or when applicable, CONSORT Extensions). |
| **Summary Results Report** | A report of clinical trial summary results posted publicly where the trial was registered (or if not possible within the registry, in another location) within one year of the completion of the trial.<br>Reports of clinical trial summary results should at least contain the items on a clinicaltrials.gov results page. |
| **The CONSORT Statement** | An evidence-based, minimum set of recommendations for reporting randomized trials. It offers a standard way for authors to prepare reports of trial findings, facilitating their complete and transparent reporting, and aiding their critical appraisal and interpretation. |
| **The SPIRIT Statement** | The SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials): An international initiative that aims to improve the quality of clinical trial protocols by defining an evidence-based set of items to address in a protocol. Provides high-quality standards for trial protocols, helping to streamline their development and reporting. |
| **Trial Registration** | The process of submitting and updating summary information about a clinical study protocol, from its beginning to end, to a structured, Web-based registry that is accessible to the public, such as ClinicalTrials.gov. |