SOP # 001

SOP Title:	QUALITY CONTROL/QUALITY ASSURANCE
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1.0 Purpose

The objective of this Standard Operating Procedure (SOP) is to describe the methods for Quality Control (QC)/Quality Assurance (QA) for identification and annotation of clinical studies compiled on HemOnc.org, for maintenance of the HemOnc.org website, and for the creation of the HemOnc ontology.

2.0 Scope

This SOP pertains to all clinical studies described on HemOnc.org, to the general maintenance and upkeep of the website, and to all content within the derivative HemOnc ontology.

3.0 Responsibilities

The Editor-in-Chief and Deputy Editor are responsible for ensuring that requirements of this SOP are met.

4.0 Procedures

4.1 Screening for trials

To identify new regimens and study references for inclusion on HemOnc.org, we undertake several parallel screening methods. These are described in further detail here and the frequency is summarized in Table 1 below:

4.1.1 Review of PubMed

4.1.1.1 *[Annually]* PubMed search for ("Phase 3" OR "Phase III") AND "neoplasms"[MeSH Terms]

4.1.1.2 *[Ongoing; Reviewed Monthly]* PubMed email alert for "Clinical Trial, Phase III "[Publication Type] AND "Neoplasms"[Mesh]

4.1.2 Review of select publications:

4.1.2.1 *[Quarterly]* Review of the entire Table of Contents (eTOC) of the following "top-tier" general medical and hematology/oncology journals:

- JAMA
- The Lancet
- The New England Journal of Medicine
- Annals of Oncology Official journal of the European Society for Medical Oncology (ESMO)
- Blood Official journal of the American Society of Hematology (ASH)
- JAMA Oncology
- Journal of Clinical Oncology Official journal of the American Society of Clinical Oncology (ASCO)
- The Lancet Haematology
- The Lancet Oncology

4.1.2.2 *[Biennally]* Review of all freely available Cochrane Library Reviews under the topics "Cancer" and "Blood disorders"

4.1.3 Review of additional key sources:

4.1.3.1 *[Monthly]* Review of submitted feedback containing any missing studies obtained via the RedCap linked on HemOnc.org homepage

4.1.3.2 *[Quarterly]* Review of all studies cited on the FDA drug label ("package insert") section 14 (CLINICAL STUDIES) for all antineoplastic agents with new approvals and/or new indications

4.1.3.3 *[Annually]* Review of all non-active interventional phase 3 clinical trials registered on clinicaltrials.gov

4.1.3.4 *[Biennally]* Review of all ASCO, ESMO, and NCCN clinical practice guidelines

4.1.4 Input from Editorial Board members:

4.1.4.1 *[Once, at the time of Onboarding]* For the assigned page, perform the following tasks:

- Review the relevant content for any important missing trials and/or references which should be added
- Suggest new subsections/treatment scenarios (e.g., based on mutations, clinical scenario) to group regimens/references under
- Suggest useful links to websites, tools, or additional references for a disease type
- Review the disease page(s) for outdated regimens which should be moved to "historical" pages

4.1.4.2 *[Quarterly]* Solicitation of new addition requests as well as suggestions for guidelines or regimens that can be moved to a historical status via a REDCap form

Table 1: Frequency at which trial screening procedures are executed.

	Frequency			
Screening Procedure	**Biennially**	**Annually**	**Quarterly**	**Monthly**
Review of PubMed				
PubMed search		X		
PubMed e-mail alerts				X
Review of select publications				
Top-tier Journals			X	
Cochrane Library Reviews	X			
Additional Review				
Review of REDCap feedback survey				X
FDA drug labels			X	
ClinicalTrials.gov		X		
Guidelines	X			
Editorial Members				
Suggested additions			X	

4.2 Prioritization

Because HemOnc.org is a voluntary effort driven by the contributors, it is not possible to add every study describing every treatment regimen, in anything close to real time. Priority is on randomized studies, but we do add high-quality non-randomized studies (or even retrospective case series) if they are used in practice. What follows is the prioritization list for adding new regimens to HemOnc.org. This prioritization schedule will be revisited from time to time and updated as required.

For each category, priority would be given to those studies published in top-tier journals and then those published in other journals (see Sources).

For all RCTs, annotation should be performed of both the Control arms of RCTs reported by the paper describing these regimens, if they are described in sufficient detail, as well as the experimental arms of RCTs reported by the paper describing these regimens, if they have statistically superior findings.

Note: On a case-by-case basis, we add regimens/references which only have been presented in abstract form if they are practice-changing or anticipated to lead to FDA approval.

4.2.1 Regimens described in registration studies (FDA has priority; other approval agencies are considered) whether they are randomized or not. However, if a product is approved and labeled based on both randomized and non-randomized studies, the priority will be to add the randomized studies.

4.2.2 Clinically relevant regimens, evaluated in fully enrolling phase III RCTs (including trials not specified as phase III but having a statistical power of 90% or greater):

4.2.3 Clinically relevant regimens, evaluated in randomized phase II RCTs or incompletely enrolled phase III RCTs (e.g., those closed early due to poor accrual

4.2.4 Clinically relevant regimens, evaluated in non-randomized trials

4.2.5 Clinically relevant regimens, evaluated in case series

4.2.6 Clinically relevant regimens, evaluated in retrospective studies

4.2.7 Clinically relevant regimens, published in conference proceedings (see Sources):

4.2.7.1 Evaluated in fully enrolling phase III RCTs (including trials not specified as phase III but having a statistical power of 90% or greater

4.2.7.2 Evaluated in randomized phase II RCTs or incompletely enrolled phase III RCTs (e.g., those closed early due to poor accrual

4.2.7.3 Evaluated in non-randomized trials

4.2.7.4 Evaluated in case series

4.2.7.5 Evaluated in retrospective studies

4.3 Quality Assurance Checks

4.3.1 Wiki Maintenance Reports

[Quarterly] To ensure the functionality of the Wiki itself, several maintenance reports are generated and reviewed, as described below.

4.3.1.1 Broken redirects

4.3.1.2 Dead-end pages

4.3.1.3 Double redirects

4.3.1.4 Long pages

4.3.1.5 Oldest pages

4.3.1.6 Pages with the fewest revisions

4.3.1.7 Pages without language links

4.3.1.8 Protected pages

4.3.1.9 Protected titles

4.3.1.10 Short pages

4.3.1.11 Uncategorized categories

4.3.1.12 Uncategorized files

4.3.1.13 Uncategorized pages

4.3.1.14 Uncategorized templated

4.3.1.15 Unused categories

4.3.1.16 Unused files

4.3.1.17 Unused properties

4.3.1.18 Unused templates

4.3.1.19 Wanted categories

4.3.1.20 Wanted files

4.3.1.21 Wanted pages

4.3.1.22 Wanted properties

4.3.1.23 Wanted templates

4.3.2 Ontology Generation

[Quarterly] During the process of transforming the HTML website content to the structured OMOP-conformant ontology, several automated QA routines are executed to identify any inconsistencies or errors in the underlying data. This includes the following routines:

4.3.2.1 Determine whether the de-duplicated OMOP concept table has non-unique concept codes.

4.3.2.2 Check that the OMOP concept table has all unique concept codes.

4.3.2.3 Check that there are no concept self-referrals except for preceding/subsequent relationships.

4.3.2.4 Review concepts with the same concept name and different concept codes.

4.3.2.5 Check that there is no instantiated modality by the name of "Other therapy"

4.3.2.6 Generate an enumerated list of concept-relationship-concept triples and review for non-allowed triples.

4.3.2.7 Generate a list of concepts that have no relationships

4.3.2.8 Generate a table of regimens and their components for manual review of potential duplicates

4.3.2.9 Check for incorrectly instantiated modalities

4.3.2.10 Generate a table with study, reference, PMID, PMCID, URL, and NCT code to review for missing data

4.3.3 Additional Checks

[Quarterly] Several additional QA checks are performed periodically to ensure the functionality and quality of the Wiki, as described below.

4.3.3.1 Confirm that external links to original manuscripts are working as expected

4.3.3.2 Confirm that internal wiki links are functional

4.3.3.3 Add content to pages categorized as stubs

4.3.3.4 Define regimens that are categorized as regimen stubs

4.3.3.5 Add missing pages to the wiki in cases where the link exists, but the page does not exist

4.3.3.6 Verify unverified dosing information

4.3.3.7 Monitor the REDCap feedback survey dashboard for new entries from users

4.3.3.8 Monitor HemOnc.org email and feedback form linked from the homepage

5.0 Sources

Knowledge aggregation sites such as HemOnc.org could not exist without primary sources. We access primary sources through a variety of means, including subscription to eTOCs, conference proceedings, and customized e-mail alerts through PubMed and other

sources. This is a list of the sources that we use most frequently; decisions on whether to include treatment regimens are informed by our eligibility criteria.

5.1 "Top-tier" general medical journals

- *JAMA*
- *The Lancet*
- *The New England Journal of Medicine*

5.2 "Top-tier" hematology/oncology journals

- *Annals of Oncology* Official journal of the European Society for Medical Oncology (ESMO)
- *Blood* Official journal of the American Society of Hematology (ASH)
- *JAMA Oncology*
- *Journal of Clinical Oncology* Official journal of the American Society of Clinical Oncology (ASCO)
- *The Lancet Haematology*
- *The Lancet Oncology*

5.3 Other hematology/oncology journals

- *Blood Advances*
- *British Journal of Haematology* Official journal of the British Society for Haematology
- *Cancer* Published on behalf of the American Cancer Society (ACS)
- *Clinical Cancer Research*
- *Clinical Lymphoma, Myeloma & Leukemia*
- *Haematologica* Journal of the European Hematology Association (EHA)
- *Journal of Hematology & Oncology* Official journal of the Chinese American Hematologist and Oncologist Network
- *Journal of the National Cancer Institute*
- *Leukemia*
- *Leukemia & Lymphoma*
- *Seminars in Oncology*

5.4 Conference proceedings

- ASCO Annual Meeting Proceedings
- ASH Annual Meeting Abstracts
- EHA Abstract Book

- ESMO Scientific Meeting Reports

5.5 E-mail Alerts

- ASH Practice Updates
- FDA Oncology Drug Approvals
- Research to Practice

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