Medical Coverage Policy

Effective Date..... 5/20/2019
Next Review Date..... 5/15/2020
Coverage Policy Number 0538

Flow Cytometry

Table of Contents

Related Coverage Resources

Genetics

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Coverage Policy

Flow cytometry is considered medically necessary for the evaluation of any of the following:

- Hematopoietic/hematologic cancers
- Immunodeficiency disorders, including human immunodeficiency virus (HIV) and acquired immunodeficiency virus syndrome (AIDS)
- Paroxysmal nocturnal hemoglobinuria
- Gestational trophoblastic disease
- Transplantation

Flow cytometry for any other indication is considered not medically necessary.

Overview

This Coverage Policy addresses the indications for flow cytometry. Flow cytometry is a laboratory test used to separate, classify and count cells. It is clinically useful in the diagnosis and/or evaluation of hematopoietic cancers, human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), primary immunodeficiency disorders, molar pregnancies, paroxysmal hemoglobinuria and monitoring after transplantation.

General Background

A flow cytometer separates, classifies and counts cells that are suspended in a moving fluid medium as they pass through a beam of light. This method may be used to evaluate cells from blood, bone marrow, body fluids such as cerebrospinal fluid (CSF), or tumor tissue. Unlike other biochemical techniques, flow cytometry makes these multiparametric measurements on single cells as opposed to population measurements (National Institutes of Health, 2018).

Flow cytometry is an evolving laboratory test that measures cell surface antigen expression, also known as immunophenotyping. It is clinically useful for the diagnosis and prognosis of hematopoietic cancers, including lymphomas and leukemia, plasma cell neoplasms, myelodysplastic syndromes, myeloproliferative neoplasms, and certain anemias (Borowitz, 2014; Craig, 2008). Flow cytometry is commonly used to detect the presence of minimal residual disease and antigens used as therapeutic drug targets for cancer therapy. Professional society consensus support is noted in the National Comprehensive Cancer Network (NCCN®) Biomarker Compendium (2019) for certain cancer types as noted below in the Professional Societies/Organizations section.

Other uses of flow cytometry include monitoring lymphocyte populations, (e.g., T-cells, natural killer [NK] cells) in an individual with a primary immunodeficiency disorder or human immunodeficiency virus/acquired immunodeficiency syndrome [HIV/AIDs]) by tracking the number and ratio of antigen-specific T cells (CD4, CD8). CD4 T-cell counting in peripheral blood of HIV1 patients using flow cytometry is considered routine practice in clinical laboratories as an important tool in the management of HIV disease. Specifically, CD4 counts are used as a measure of the degree of immune deficiency, eligibility of HIV1 patients for antiretroviral treatment and to monitor immune restoration in an individual receiving antiretroviral therapy CD4 T-cell counting is a valuable tool for directing treatment against opportunistic infections (Kestens, 2017). It is also clinically useful to detect chimerism and rejection following transplantation and to monitor the toxicity or effectiveness of immunosuppressive therapy (Antin, 2001).

Flow cytometry is considered the most sensitive and informative assay available for diagnosis of paroxysmal nocturnal hemoglobinuria (PNH). It is considered the gold standard for identifying peripheral blood cells that are missing glycosyl phosphatidylinositol (GPI)–anchored proteins (National Organization for Rare Disorders [NORD], 2019; Borowitz, 2010; Parker, 2005).

Flow cytometry is considered a standard laboratory method to assess deoxyribonucleic acid (DNA) ploidy in gestational trophoblastic disease, including molar pregnancies; however, it is also proposed as a method to measure nuclear deoxyribonucleic acid (DNA) content (i.e., ploidy) and cell proliferation activity (i.e., S-phase fraction) for cancer in solid tumors (i.e., cancer in solid tumors). Correlation of ploidy and DNA activity with proliferation and aggressiveness of disease is primarily limited to retrospective, correlational studies. There are limited data in the published scientific literature to demonstrate improved health outcomes for this indication. Likewise, there is a lack of professional society consensus by way of published guidelines and recommendations for this purpose. The role of flow cytometry, including to determine ploidy and cell proliferation activity has not been established for cancer in solid tumors. Use of multiparametric flow cytometry in solid tumors is of ongoing research interest.

Literature Review
Borowitz (2014) notes the literature is confusing and contradictory regarding the use of flow cytometry to determine DNA ploidy and that the early promise of this measurement as an important diagnostic and prognostic marker in cancer has not been realized. Although some studies have demonstrated prognostic significance to measurements of ploidy, and especially S-phase fraction, in a number of tumors—most specifically bladder, prostate, and breast cancer—many studies conflict, and as a result, this technology has not been widely embraced in clinical oncology. DNA flow cytometry has largely been replaced by molecular prognostic markers. It is unlikely that these techniques will be adopted in routine clinical practice.

Ye et al. (2019) compared the ability of flow cytometry (FCM) and cytomorphology (CM) in detecting neuroblastoma cells in 21 patients with neuroblastoma metastasis. Bone marrow and effusion specimens were

analyzed by flow cytometry and cytomorphology. Cytomorphology detected three effusions not detected by flow cytometry. There was no significant differences between FCM and CM in the detection of NB cells in effusions ($p = 0.344$). Further studies are needed to demonstrate improved health benefit for the use of flow cytometry compared to conventional cytomorphology techniques.

Ludovini et al (2008) reported on a study evaluating the relationship between a panel of biological markers (p53, Bcl-2, HER-2, Ki67, DNA ploidy and S-phase fraction) and clinical-pathological parameters and its impact on outcome in non-small cell lung cancer (NSCLC). Tumor tissue specimens were collected from 136 consecutive patients with NSCLC following surgical resection. An immunocytochemical technique and flow cytometric DNA analysis were used to evaluate p53, Bcl-2, HER-2 and Ki67. Positivity of p53, Bcl-2, HER-2 and Ki67 was detected in 51.4 %, 27.9 %, 25.0 % and 55.8 % of the samples, respectively; 82.9 % of the cases revealed aneuploid DNA histograms and 56.7 % presented an S-phase fraction of more than 12 %. At uni-variate analysis, high Ki67 proved to be the only marker associated with disease-free survival ($p = 0.047$). After adjusting for stage, none of the examined immunocytochemical markers emerged as an independent factor for disease-free and overall survival; only pathological stage was identified as an independent prognostic factor for disease-free survival ($p = 0.0001$) and overall survival ($p = 0.0001$). The authors concluded the findings do not support a relevant prognostic role of immunocytochemical markers in NSCLC.

Dayal et al. (2013) published results of a retrospective correlational study reporting on the application of multiparameter flow cytometry and to examine the clinical and biomarker associations in 201 formalin-fixed, paraffin-embedded FFPE previously banked breast cancer specimens. Tumors were grouped into four categories based on the DNA index of the tumour cell population. Univariate statistical analysis demonstrated significant association with tumor category and prognosis in three of four tumor groups; however an independent association between tumor DNA content and overall survival was not confirmed by multivariate analysis. Further study is indicated before flow cytometry can be considered a standard clinical practice for the detection of breast cancer ploidy or DNA index.

Wolfson et al (2008) reported results of a retrospective study looking for possible associations between measurements of DNA index (DI), S-phase fraction (SPF), and tumor heterogeneity (TH) using flow cytometry in 57 patients with invasive cervical carcinoma. Patients had International Federation of Obstetrics and Gynecology Stages IB2 through IVB cervical carcinomas treated with definitive radiotherapy with or without concurrent chemotherapy. With a median follow-up of 3.7 years, there were no statistically significant associations by univariate analysis for DI, SPF, or TH and patient outcome or survival. The authors note additional studies are indicated to identify tumor biomarkers that could predict patients at risk for disseminated disease.

Davis et al. (2007) published international consensus recommendations regarding the use of flow cytometery for hematologic neoplasia. Uses recommended are cytopenias, elevated leukocyte count, identification of blasts in the marrow or peripheral blood, plasmacytosis or monoclonal gammopathy, tissue-based lymphoid neoplasia, lymph adenopathy, Staging disease to document the extent of involvement, Detecting potential therapeutic targets, assessment of response to therapy (e.g., minimal residual disease), documentation of progression or relapse, diagnosis of related disease (e.g., treatment-related or coincidental), documentation of disease acceleration, prognostication.

Professional Societies/Organizations
National Cancer Institute ([NCI], 2018):

- Adult soft tissue sarcoma: The NCI notes flow cytometry is one of several techniques that may allow identification of particular subtypes within the major histologic categories
- Transitional cell cancer of the renal pelvis and ureter:
  - Regarding prognosis, DNA ploidy has not added significant prognostic information beyond that provided by stage and grade.
  - In metastatic disease, flow cytometry analysis identifies low-stage, low-grade tumors at high risk of recurrence by virtue of their aneuploidy histograms.
- Neuroblastoma: Regarding prognosis, low-risk tumors are hyperdiploid when examined by flow cytometry. In contrast, in high-risk neuroblastoma, tumors are near diploid or near tetraploid by flow cytometric measurement.

- Ovarian epithelial cancer: Ploidy may identify high risk in analysis of stage 1 and 2a tumors
- Prostate cancer: DNA ploidy is associated with outcome

The National Comprehensive Cancer Network (NCCN®) Biomarkers Compendium® (2019): The Compendium notes that flow cytometry may be used to assess the following hematologic lymphoid cancers:

- Acute lymphoblastic leukemia
- Chronic myeloid leukemia
- Lymphomas
- Hairy cell leukemia
- Myeloproliferative neoplasms
- Myelodysplastic disorders
- Multiple myeloma
- Systemic mastocytosis
- Waldenstrom's macroglobinemia

Flow cytometry is not mentioned in the Compendium as a laboratory method used for the diagnosis or management of solid tumors, including any of the following: bladder, brain, breast, colon, endometrium, gastric, kidney, lung, neuroblastoma, ovary, prostate or rectum.

International Bone Marrow Transplant Registry (IBMTR) and the American Society of Blood and Marrow Transplantation (ASBMT): Antin et al. (2001) published recommendations from a workshop at the 2001 Tandem Meetings of the IBMTR/ASBMT concerning the establishment of complete- and mixed-donor chimerism following allogeneic lymphohematopoietic transplantation and the role of flow cytometry in determining chimerisms of neutrophil, monocyte, and lymphocyte fractions.

Centers for Medicare & Medicaid Services (CMS)
National Coverage Determinations (NCDs): No NCD found.
Local Coverage Determination (LCD:

- Flow Cytometry (L34037). (2018). The LCD has the same scope as the Coverage Policy. Refer to the CMS LCD link in the reference section.
- Flow Cytometry (L34215). (2018). The LCD has the same scope as the Coverage Policy. Refer to the CMS LCD in the reference section.
- Flow Cytometry (L33661). (2018). The LCD has the same scope as the Coverage Policy. Refer to the CMS LCD link in the reference section.

Use Outside of the US: N/A

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
86355	B cells, total count
86356	Mononuclear cell antigen, quantitative (eg, flow cytometry), not otherwise specified, each antigen
86357	Natural killer (NK) cells, total count
86359	T cells; total count
86360	T cells; absolute CD4 and CD8 count, including ratio

86361	T cells; absolute CD4 count
86367	Stem cells (ie, CD34), total count
88182	Flow cytometry, cell cycle or DNA analysis
88184	Flow cytometry, cell surface, cytoplasmic, or nuclear marker, technical component only; first marker
88185	Flow cytometry, cell surface, cytoplasmic, or nuclear marker, technical component only; each additional marker (List separately in addition to code for first marker)
88187	Flow cytometry, interpretation; 2 to 8 markers
88188	Flow cytometry, interpretation; 9 to 15 markers
88189	Flow cytometry, interpretation; 16 or more markers

ICD-10-CM Codes	**Description**
A02.1	Salmonella sepsis
A07.2	Cryptosporidiosis
A07.3	Isosporiasis
A15.0-A19.9	Tuberculosis
A31.0	Pulmonary mycobacterial infection
A31.2	Disseminated mycobacterium avium-intracellulare complex (DMAC)
A31.8	Other mycobacterial infections
A81.2	Progressive multifocal leukoencephalopathy
B00.0	Eczema herpeticum
B00.1	Herpesviral vesicular dermatitis
B00.2	Herpesviral gingivostomatitis and pharyngotonsillitis
B00.89	Other herpesviral infection
B20	Human immunodeficiency virus [HIV] disease
B25.0-B25.9	Cytomegaloviral disease
B37.1	Pulmonary candidiasis
B37.81	Candidal esophagitis
B37.89	Other sites of candidiasis
B38.9	Coccidioidomycosis, unspecified
B39.2	Pulmonary histoplasmosis capsulati, unspecified
B39.3	Disseminated histoplasmosis capsulati
B39.4	Histoplasmosis capsulati, unspecified
B45.0-B45.9	Cryptococcosis
B58.2	Toxoplasma meningoencephalitis
B59	Pneumocystosis
B97.33	Human T-cell lymphotrophic virus, type I [HTLV-I] as the cause of diseases classified elsewhere
B97.34	Human T-cell lymphotrophic virus, type II [HTLV-II] as the cause of diseases classified elsewhere
B97.35	Human immunodeficiency virus, type 2 [HIV 2] as the cause of diseases classified elsewhere
C46.0-C46.9	Kaposi's sarcoma
C53.0-C53.9	Malignant neoplasm of cervix uteri
C58	Malignant neoplasm of placenta
C81.00-C81.99	Hodgkin lymphoma
C82.00-C82.99	Follicular lymphoma
C83.00-C83.99	Non-follicular lymphoma
C84.00-C84.99	Mature T/NK-cell lymphomas
C85.10-C85.99	Other specified and unspecified types of non-Hodgkin lymphomas
C86.0-C86.6	Other specified types of T/NK-cell lymphoma

C88.0-C88.9	Malignant immunoproliferative diseases and certain other B-cell lymphomas
C90.00-C90.32	Multiple myeloma and malignant plasma cell neoplasms
C91.00-C91.92	Lymphoid leukemia
C92.00-C92.92	Myeloid leukemia
C93.00-C93.92	Monocytic leukemia
C94.00-C94.82	Other leukemias of specified cell type
C95.00-C95.92	Leukemia of unspecified cell type
C96.0-C96.9	Other and unspecified malignant neoplasms of lymphoid, hematopoietic and related tissue
D39.2	Neoplasm of uncertain behavior of placenta
D45	Polycythemia vera
D46.0-D46.Z	Myelodysplastic syndromes
D47.01	Cutaneous mastocytosis
D47.02	Systemic mastocytosis
D47.09	Other mast cell neoplasms of uncertain behavior
D47.1	Chronic myeloproliferative disease
D47.2	Monoclonal gammopathy
D47.3	Essential (hemorrhagic) thrombocythemia
D47.4	Osteomyelofibrosis
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)
D47.Z2	Castleman disease
D47.Z9	Other specified neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue
D50.0	Iron deficiency anemia secondary to blood loss (chronic)
D50.8	Other iron deficiency anemias
D50.9	Iron deficiency anemia, unspecified
D51.0-D51.9	Vitamin B12 deficiency anemia, unspecified
D52.9	Folate deficiency anemia, unspecified
D53.0	Protein deficiency anemia
D53.1	Other megaloblastic anemias, not elsewhere classified
D53.8	Other specified nutritional anemias
D53.9	Nutritional anemia, unspecified
D56.0	Alpha thalassemia
D56.1	Beta thalassemia
D56.3	Thalassemia minor
D56.9	Thalassemia, unspecified
D57.00-D57.819	Sickle-cell disorders
D58.0	Hereditary spherocytosis
D58.2	Hereditary elliptocytosis
D58.9	Hereditary hemolytic anemia, unspecified
D59.0	Drug-induced autoimmune hemolytic anemia
D59.1	Other autoimmune hemolytic anemias
D59.2	Drug-induced nonautoimmune hemolytic anemia
D59.4	Other nonautoimmune hemolytic anemias
D59.5	Paroxysmal nocturnal hemoglobinuria [Marchiafava-Micheli]
D59.6	Hemoglobinuria due to hemolysis from other external causes
D59.8	Other acquired hemolytic anemias
D59.9	Acquired hemolytic anemia, unspecified
D60.1-D60.9	Acquired pure red cell aplasia (erythroblastopenia)
D61.01-D61.9	Other aplastic anemias and other bone marrow failure syndromes
D62	Acute posthemorrhagic anemia
D63.0-D63.8	Anemia in chronic diseases classified elsewhere
D64.0-D64.9	Other anemias
D65	Disseminated intravascular coagulation [defibrination syndrome]

D66	Hereditary factor VIII deficiency
D67	Hereditary factor IX deficiency
D68.0	von Willebrand's disease
D68.1	Hereditary factor XI deficiency
D68.2	Hereditary deficiency of other clotting factors
D68.311	Acquired hemophilia
D68.51	Activated protein C resistance
D68.52	Prothrombin gene mutation
D68.59	Other secondary thrombocytopenia
D68.61	Antiphospholipid syndrome
D68.62	Lupus anticoagulant syndrome
D68.69	Other thrombophilia
D68.8	Other specified coagulation defects
D68.9	Coagulation defect, unspecified
D69.1	Qualitative platelet defects
D69.2	Other nonthrombocytopenic purpura
D69.3	Immune thrombocytopenic purpura
D69.41	Evans syndrome
D69.42	Congenital and hereditary thrombocytopenia purpura
D69.49	Other primary thrombocytopenia
D69.51	Posttransfusion purpura
D69.59	Other secondary thrombocytopenia
D69.6	Thrombocytopenia, unspecified
D69.8	Other specified hemorrhagic conditions
D69.9	Hemorrhagic condition, unspecified
D70.0-D70.9	Neutropenia
D71	Functional disorders of polymorphonuclear neutrophils
D72.0-D72.9	Other disorders of white blood cells
D73.0-D73.9	Diseases of spleen
D75.0-D75.9	Other and unspecified diseases of blood and blood-forming organs
D76.1-D76.3	Other specified diseases with participation of lymphoreticular and reticulohistiocytic tissue
D80.0-D80.9	Immunodeficiency with predominantly antibody defects
D81.0-D81.9	Combined immunodeficiencies
D82.0-D82.9	Immunodeficiency associated with other major defects
D83.0-D83.9	Common variable immunodeficiency
D84.0-D84.9	Other immunodeficiencies
D86.0	Sarcoidosis of lung
D86.1	Sarcoidosis of lymph nodes
D86.2	Sarcoidosis of lung with sarcoidosis of lymph nodes
D86.85	Sarcoid myocarditis
D89.0-D89.9	Other disorders involving the immune mechanism, not elsewhere classified
E34.0	Carcinoid syndrome
E85.0-E85.9	Amyloidosis
E88.01	Alpha-1-antitrypsin deficiency
E88.02	Plasminogen deficiency
E88.09	Other disorders of plasma-protein metabolism, not elsewhere classified
G93.49	Other encephelopathy
I88.0-I88.9	Nonspecific lymphadenitis
I89.1	Lymphangitis
I89.8	Other specified noninfective disorders of lymphatic vessels and lymph nodes
I89.9	Noninfective disorder of lymphatic vessels and lymph nodes, unspecified
J15.3	Pneumonia due to streptococcus, group B

J15.4	Pneumonia due to other streptococci
J90	Pleural effusion, not elsewhere classified
J91.0	Malignant pleural effusion
J91.8	Pleural effusion in other conditions classified elsewhere
J94.0	Chylous effusion
M02.30-M02.39	Reiter's disease
O01.0-O01.9	Hydatidiform mole
O02.0	Blighted ovum and nonhydatidiform mole
O98.711-O98.719	Human immunodeficiency virus [HIV] disease complicating pregnancy, childbirth, and the puerperium
R59.0-R59.9	Enlarged lymph nodes
R64	Cachexia
R75	Inconclusive laboratory evidence of human immunodeficiency virus [HIV]
R76.9	Abnormal immunological finding in serum, unspecified
T86.00-T86.09	Complications of bone marrow transplant
T86.10-T86.19	Complications of kidney transplant
T86.20-T86.298	Complications of heart transplant
T86.30-T86.39	Complications of heart-lung transplant
T86.40-T86.49	Complications of liver transplant
T86.5	Complications of stem cell transplant
T86.810-T86.819	Complications of lung transplant
T86.850-T86.859	Complications of intestine transplant
T86.890	Other transplanted tissue rejection
T86.891	Other transplanted tissue failure
T86.892	Other transplanted tissue infection
T86.898	Other complications of other transplanted tissue
Z21	Asymptomatic human immunodeficiency virus [HIV] infection status
Z48.21-Z48.298	Encounter for aftercare following organ transplant
Z52.001	Unspecified donor, stem cells
Z52.011	Autologous donor, stem cells
Z52.091	Other blood donor, stem cells
Z52.3	Bone marrow donor
Z52.4	Kidney donor
Z52.6	Liver donor
Z52.89	Donor of other specified organs or tissues
Z76.82	Awaiting organ transplant status
Z85.6	Personal history of leukemia
Z85.71	Personal history of Hodgkin lymphoma
Z85.72	Personal history of non-Hodgkin lymphomas
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues
Z94.0	Kidney transplant status
Z94.1	Heart transplant status
Z94.2	Lung transplant status
Z94.3	Heart and lungs transplant status
Z94.4	Liver transplant status
Z94.81	Bone marrow transplant status
Z94.82	Intestine transplant status
Z94.83	Pancreas transplant status
Z94.84	Stem cells transplant status
Z94.89	Other transplanted organ and tissue status

References

1. American Cancer Society (ACS). Gestational trophoblastic disease. ©2019 American Cancer Society, Inc. Accessed Feb 1, 2019. Available at URL address: https://www.cancer.org/cancer/gestational-trophoblastic-disease/about/what-is-gtd.html

2. Antin JH, Childs R, Filipovich AH, Giralt S, Mackinnon S, Spitzer T, et al. Establishment of complete and mixed donor chimerism after allogeneic lymphohematopoietic transplantation: recommendations from a workshop at the 2001 Tandem Meetings of the International Bone Marrow Transplant Registry and the American Society of Blood and Marrow Transplantation. Biol Blood Marrow Transplant. 2001;7(9):473-85.

3. Borowitz MJ. Flow cytometry in oncologic diagnosis. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastn MB, Tepper JE, editors. Abeloff's clinical oncology, 5th ed. Livingstone, an imprint of Elsevier, Inc. Philadelphia, 2014.

4. Borowitz MJ, Craig FE, Digiuseppe JA, Illingworth AJ, Rosse W, Sutherland DR, et al. Guidelines for the diagnosis and monitoring of paroxysmal nocturnal hemoglobinuria and related disorders by flow cytometry. Cytometry B Clin Cytom. 2010 Jul;78(4):211-30.

5. Cancer.net. Lymphoma-Non-Hodgkin. Accessed Feb 6, 2019. Available at URL address: https://www.cancer.net/cancer-types/lymphoma-non-hodgkin/view-all

6. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determinations (LCD) Flow cytometry. (L34215). 2018. Accessed Feb 2, 2019. Available at URL address: https://www.cms.gov/medicare-coverage-database/indexes/lcd-alphabetical-index.aspx?Cntrctr=373&ContrVer=1&CntrctrSelected=373*1&DocType=Active%7cFuture&s=All&bc=AggAAAQAAAAA&

7. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determinations (LCD) Flow cytometry. (L34215). 2018. Accessed Feb 2, 2019. Available at URL address: https://www.cms.gov/medicare-coverage-database/indexes/lcd-alphabetical-index.aspx?Cntrctr=373&ContrVer=1&CntrctrSelected=373*1&DocType=Active%7cFuture&s=All&bc=AggAAAQAAAAA&

8. Centers for Medicare and Medicaid Services (CMS). Local Coverage Determinations (LCD) Flow cytometry. (L33631). 2018. Accessed Feb 2, 2019. Available at URL address: https://www.cms.gov/medicare-coverage-database/indexes/lcd-alphabetical-index.aspx?Cntrctr=373&ContrVer=1&CntrctrSelected=373*1&DocType=Active%7cFuture&s=All&bc=AggAAAQAAAAA&

9. Craig FE, Foon KA. Flow cytometric immunophenotyping for hematologic neoplasms. Blood. 2008 Apr 15;111(8):3941-67. doi: 10.1182/blood-2007-11-120535. Epub 2008 Jan 15.

10. Davis BH, Holden JT, Bene MC, Borowitz MJ, Braylan RC, Cornfield D, et al. 2006 Bethesda International Consensus recommendations on the flow cytometric immunophenotypic analysis of hematolymphoid neoplasia: medical indications. Cytometry B Clin Cytom. 2007;72 Suppl 1:S5-1

11. Dome JS, Rodriguez-Galindo C, Spunt SL, Santan VM. Pediatric solid tumors. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastn MB, Tepper JE, editors. Abeloff's clinical oncology, 5th ed. Livingstone, an imprint of Elsevier, Inc. Philadelphia, 2014.

12. Izadi-Mood N, Sarmadi S, Tayebivaljozi R, Mohammadi-Zia F, Farhadi M. Flow Cytometric DNA Analysis and Histopathologic Re-Evaluation of Paraffin Embedded Samples from Hydatidiform Moles and Hydropic Abortions. Int J Fertil Steril. 2015 Oct-Dec;9(3):322-8. Epub 2015 Oct 31.

13. Kestens L, Mandy F. Thirty-five years of CD4 T-cell counting in HIV infection: From flow cytometry in the lab to point-of-care testing in the field. Cytometry B Clin Cytom. 2017 Nov;92(6):437-444.

14. Ludovini V, Pistola L, Gregorc V, Floriani I, Rulli E, Di Carlo L, et al. Biological markers and DNA flow cytometric analysis in radically resected patients with non-small cell lung cancer. A study of the Perugia Multidisciplinary Team for Thoracic Tumors. Tumori. 2008 May-Jun;94(3):398-405.

15. Mandy FF, Nicholson JK, McDougal JS; CDC. Guidelines for performing single-platform absolute CD4+ T-cell determinations with CD45 gating for persons infected with human immunodeficiency virus. Centers for Disease Control and Prevention. MMWR Recomm Rep. 2003 Jan 31;52(RR-2):1-13. Accessed Feb 6, 2019. Available at URL address: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5202a1.htm

16. National Cancer Institute (NCI). Accessed Feb 6, 2019. Available at URL address: https://www.cancer.gov/

17. National Institutes of Health (NIH).National Institute of Environmental Health Sciences. August 8, 2018. Accesed Feb 6, 2019. Available at URL address: https://www.niehs.nih.gov/research/atniehs/facilities/flowcytometry/index.cfm

18. National Organization for Rare Disorders {NORD). Paroxysmal nocturnal hemoglobinuria. 2019. Accessed Feb 5, 2019. Available at URL address: https://rarediseases.org/rare-diseases/paroxysmal-nocturnal-hemoglobinuria/

19. Niemann I, Petersen LK, Hansen ES, Sunde L. Predictors of low risk of persistent trophoblastic disease in molar pregnancies. Obstet Gynecol. 2006 May;107(5):1006-11.

20. Parker CJ. Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria. Hematology Am Soc Hematol Educ Program. 2016 Dec 2;2016(1):208-216.

21. Pincus MR, Lifshitz MS, Bock JL. Flow cytometry. In: McPherson RA, Pincus MR, editors. Henry's clinical diagnosis and management by laboratory methods, 23rd ed. Elsevier, Inc. New York;2017.

22. Wolfson AH, Winter K, Crook W, Krishan A, Grigsby PW, Markoe AM, et al. Are increased tumor aneuploidy and heightened cell proliferation along with heterogeneity associated with patient outcome for carcinomas of the uterine cervix? A combined analysis of subjects treated in RTOG 9001 and a single-institution trial. Int J Radiat Oncol Biol Phys. 2008 Jan 1;70(1):111-7.

23. World Health Orgnization (WHO). Core medical equipment information. Cytometer. 2011. Accessed Feb 1, 2019. Available at URL address: https://www.who.int/medical_devices/innovation/cytometer.pdf

24. Ye W, Wang J, Li W, Shen H. Comparative Analysis of Flow Cytometry and Cytomorphology for Neuroblastoma Cell Detection in Effusion and Bone Marrow Specimens. Fetal Pediatr Pathol. 2019 Jan 22:1-7.