Literature list – *Extended* IPU

Customer information

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Note: Whether references are given in British or American English depends on the original.

NEW New entries are highlighted by this icon.

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- The following list of research study publications is provided exclusively for scientific purposes.
- The studies may relate to the diagnostic use of the analytical parameters offered by Sysmex instruments. The diagnostic use is not validated by Sysmex and is therefore not in the scope of the Intended Purpose of the instruments. Details on the Intended Purpose can be found in the Sysmex Instructions For Use.
- Summaries of the study results are provided for convenience only and are not intended to convey any views of Sysmex on the study or the products used therein.
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- The information provided in the literature list is intended only for health care professionals.

Biomedical Validation

Based on the official recommendations of the ‘Groupe Francophone d'Hématologie Cellulaire’ (GFHC), the Biomedical Validation rule set supports in defining threshold values and different situations in which a blood smear review is desirable or RET reflex to explore RBC. It offers a standardised workflow for managing abnormal samples, so you can focus on the right results at the right time.

Genevieve F *et al*. (2014)

Smear microscopy revision - propositions by the GFHC.
Free online: feuillets de Biologie; LVI 317: 1.

Summary: The GFHC reviewed in detail the criteria used within the CBC to generate blood smears and has decided on a number of minimum recommendations, defining threshold values and various situations in which the blood smear review is desirable.

Cornet E *et al*. (2016)

Evaluation and optimization of the extended information process unit (E-IPU) validation module integrating the sysmex flag systems and the recommendations of the French-speaking cellular hematology group (GFHC).
Scand J Clin Lab Invest; 76(6): 465.

Summary: Using the biomedical validation criteria, 21.3% of samples triggered a smear review in this study cohort. Modification of four criteria by the authors reduced the number of smears from 21.3% to 15.0% without loss of clinical value.

Ronez E *et al.* (2017)

Usefulness of thresholds for smear review of neutropenic samples analyzed with a Sysmex XN-10 analyzer.
Scand J Clin Lab Invest; 77(6): 406.

Summary: A multi-centre study showed that 1031 smear reviews triggered by isolated neutropenic samples (NEUT# < 1.5 G/L) resulted in the detection of only one positive sample (containing blasts). The authors recommend using a lower cutoff of 1.0 G/L for smear review.

Paridaens H *et al*. (2019)

Can the 72-hour rule based on "Blast/Abn Lymph" flag on Sysmex XN-10 optimize the workflow in hematology laboratory?
Free online: Ann Biol Clin (Paris); 77(4): 422.

Summary: The authors verified GFHC rules for reducing unnecessary smears and even extended the rules for further smear reduction when using XN analysers. The very good sensitivity (93%) and specificity (94%) of the Blast/Abn Lympho? flag was confirmed in line with smear reduction of 5.7% and associated cost reduction.

CBC-O

CBC-O is a licence-based *Extended* IPU add-on, built on a proven algorithm aiming to support handling of samples with an increased MCHC by indicating the cause of interference and helping to resolve interfering conditions by using the RET channel.

Berda-Haddad Y *et al*. (2017)

Increased mean corpuscular haemoglobin concentration: artefact or pathological condition?
Free online: Int J Lab Hematol; 39(1): 32.

Summary: The use of the optical RBC parameters from the XN-Series saved time and helped in the determination of the cause of increased MCHC, in this study.

Nivaggioni V *et al*. (2022)

Detection of Southern Asian Ovalocytosis with Sysmex XN-10: A complement to the decision tree previously described.
Int J Hematol; 44(2): e84. (from *Extended* IPU 5.2 onwards)

Summary: The authors expanded the algorithm described in the Nivaggioni *et al*. 2020 publication with the addition of a step to detect Southeast Asian ovalocytosis (SAO) cases. All SAO samples were correctly classified using the Hypo-He/MicroR ratio, which achieved an AUC of 1.0.

Additional publications

This article describes hyperleukocytosis as another reason for increased MCHC. The proposal can be added to *Extended* IPU on request.

Schillinger F *et al*. (2021)

Impact of hyperleucocytosis on erythrocytic parameters of cell blood count: management by Sysmex XN-10 RET analyzer.
Ann Biol Clin (Paris); 79(2): 181.

Summary: The study confirms the effect of hyperleukocytosis on RBC parameters. RBC and HCT are affected in lymphoid diseases (CLL, ALL). Haemoglobin is affected in myeloid diseases (CML, AML). Authors propose an algorithm to accurately correct the parameters based on the RET channel.

Intensive Care Infection Score (ICIS RUO*)

The ICIS RUO* can be integrated into the *Extended* IPU by a special licence. The research score is based on the differential count of white blood cells and red blood cell parameters from a routine blood count using the CBC, DIFF and RET channels.

**The product is released for research use only (RUO) which indicates that an in vitro diagnostic medical purpose has not been validated by the manufacturer. Health institutions that intend to use RUO product results for diagnostic purposes do so under their own responsibility and must observe the rules and regulations applicable in their region, such as Regulation (EU) 2017/746 (IVD-R) for the EU. Sysmex cannot support such diagnostic use.*

Nierhaus A *et al.* (2012)

Use of a Weighted, Automated Analysis of the Differential Blood Count to Differentiate Sepsis from Non-Infectious Systemic Inflammation: The Intensive Care Infection Score (ICIS).
Inflamm. Allergy Drug Targets 11(2):109-15.

Summary: The Intensive Care Infection Score RUO (ICIS RUO) consists of multiple differential blood count parameters and provides promising potential for reliably and swiftly discriminating sepsis from systemic inflammation (SIRS) in the first critical hours at the ICU, in this study.

Weimann K *et al.* (2015)

Intensive Care Infection Score--A new approach to distinguish between infectious and noninfectious processes in intensive care and medicosurgical patients.
J. Int. Med. Res. 43(3):435-51.

Summary: In this study, ICIS RUO showed better discriminatory power than CRP and PCT for differentiating between infected and non-infected ICU patients, especially in post-operative patients, and could therefore be useful as a decision-making aid for antibiotic treatment.

Van der Geest PJ *et al.* (2016)

The intensive care infection score - a novel marker for the prediction of infection and its severity.
Crit. Care 20(1):180.

Summary: ICIS RUO is potentially useful for the prediction of infections in critically ill patients and was shown to be non-inferior to CRP and PCT in this study.

NEW

Nacke N *et al.* (2025)

Exploring The Potential of The Intensive Care Infection Score in Antimicrobial Stewardship: A Case Report
A A Pract. 19(7):e02004

Summary: In a case series of three ICU patients, ICIS RUO* was used to retrospectively review antibiotic decisions.

- In the first case ICIS RUO* indicated a persistent infection and prompted therapy changes.
- In the second case it indicated ongoing infection despite declining CRP and PCT to guide treatment modification.
- In the third case an infection was ruled out despite elevated CRP and PCT.

The authors concluded that ICIS RUO* could support antimicrobial stewardship and infection management beyond conventional markers in critically ill patients.

NEW

Deniz E *et al.* (2025)

Intensive care infection score: ICIS dis-criminates between infected and uninfected critically ill patients in routine intensive care unit practice
Intensive Care Med Exp 13(1):58.

Summary: In a multicentre study of 115 ICU patients, ICIS RUO* (cut-off ≥ 3) outperformed CRP and PCT in distinguishing infection, with an AUC of 0.984, sensitivity of 90.7%, specificity of 97.5%, PPV of 98.6%, and NPV of 84.8%. The authors concluded that ICIS RUO* could support early infection assessment.

NEW

Vrbacký F *et al.* (2025)

Intensive Care Infection Score (ICIS) is an Early Marker for Infection in Time of Admission to Intensive Care Units
Int J Lab Hematol. 47(4):707-712.

Summary: In this cohort of 102 adult ICU patients (n=30 infected, n=72 non-infected), ICIS RUO* demonstrated a diagnostic performance for early infection detection at admission, with an AUC of 0.958, outperforming CRP, PCT and IL6. An ICIS RUO* cut-off of ≥4 provided a high sensitivity and specificity (93.3% and 84.2%, respectively). Infected patients had significantly higher levels of NEUT-SFL, NEUT#, HFLC#, and IG# ($p < 0.0031$).

Monocytosis Workflow Optimisation (MWO)

The MWO offers an evidence-based optional rule set embedded in the *Extended* IPU to distinguish reactive monocytosis from monocytosis of suspected malignant origin.

Schillinger F *et al*. (2017)

A new approach for diagnosing chronic myelomonocytic leukemia using structural parameters of Sysmex XN analyzers in routine laboratory practice.
Scand J Clin Lab Invest; 78(3): 159.

Summary: The study presents a score derived from Sysmex XN parameters that identifies possible CMML samples by excluding reactive monocytes. This reduces the smear review workload.

Additional publications

Below articles describe several applications of the mono-dysplasia score and a MDS score. The outcome of these publications are not part of the MWO add-on. The MDS score proposal can be added to *Extended* IPU on request.

Zhu J *et al*. (2019)

A hierarchical approach in the diagnostic workflow of chronic myelomonocytic leukemia: Pivotal role of the "Mono-dysplasia-score" combined with flow cytometric quantification of monocyte subsets.
Free online: Int J Lab Hematol; 41(6): 782.

Summary: The authors set up a workflow for monocytosis samples including mono-dysplasia score, smear review and flow cytometry. The proposed mono-dysplasia score was shown to be a valuable filter for reducing the number of smears without losing sensitivity for CMML suspicious samples.

Cornet E *et al*. (2024)

Applicability of mono dysplasia score on the new Sysmex XR analyzer range to predict diagnosis of chronic myelomonocytic leukaemia.
Int J Lab Hematol; 46:971-974.

Summary: A study of 316 patients with monocytosis showed that a mono-dysplasia score > 0.16 calculated on XR-Series could differentiate CMML samples (n=22) from reactive monocytosis cases (n=294) with an AUC of 0.994, sensitivity 100% and specificity of 95.2%.

Boutault R *et al.* (2018)

A novel complete blood count-based score to screen for myelodysplastic syndrome in cytopenic patients.
Br J Haematol; 183(5): 736.

Summary: The authors suggested an MDS-CBC multiparametric score as a screening tool for MDS patients by combining absolute neutrophil count (ANC), mean corpuscular volume (MCV), and median neutrophil complexity width of dispersion (NE-WX). The score had a sensitivity of 86% and a specificity of 88% in the leading cohort.

Zhu J *et al.* (2022)

Machine learning-based improvement of MDS-CBC score brings platelets into the limelight to optimize smear review in the hematology laboratory.
Free online: BMC Cancer; 22(1): 972.

Summary: A two-step algorithm, triggered by cytopenia, and utilising the MDS-CBC score and IPF, correctly separated myelodysplastic (MDS) samples (n=168) from other non-clonal cytopenic samples (n=357) with a sensitivity of 88.7% and a specificity of 95.8%. The algorithm had a 96.4% classification rate for MDS and 95.8% for the cytopenic controls in this study.

Podvin B *et al*. (2023)

A new combination of monocytic scores to support diagnosis of chronic myelomonocytic leukemia according to novel classifications.
Int J Lab Hematol; 45(5): 791.

Summary: A study of 76 patients with persistent monocytosis showed that a mono-dysplasia score > 0.16 and/or classical monocytes (MO1) > 94% could identify 46 out of 47 CMML samples (sensitivity 98%, specificity 79%, PPV: 88.5%, NPV: 95.8%) and differentiate them from reactive monocytosis (n=13) and other haemopathies (n=16).

Bouriche L *et al.* (2023)

Detection of dysplasia in peripheral blood: Proposal of an algorithm to detect myelodysplastic syndromes and chronic myelomonocytic leukemias on a high-speed technical platform using the Sysmex XN™ analyser.
Int J Lab Hematol; 46(2): 286.

Summary: A decision tree utilising the MDS-CBC and mono-dysplasia scores had a 94.4% sensitivity and 91.4% specificity in identifying MDS (n=18) and CMML (n=18) samples within a cohort of 749. Routine implementation of the tree compared to using the recommended cytopenia or monocytosis criteria in over 25,000 samples significantly reduced the smear workload.

Podvin B *et al*. (2024)

Oligomonocytic chronic myelomonocytic leukemia is eligible to MDS-score and not Mono-dysplasia score.
Int J Lab Hematol; 46(5): 969-970.

Summary: In this letter to the editor the authors evaluated the MDS-score and the monodysplasia score in a small cohort (n=31) of oligomonocytic chronic myelomonoctic leukaemia (OM-CMML) patients and identified 90.0% as positive for the MDS score and 29.0% positive for the monodysplasia score.

RBC Defect Workflow Optimisation (RWO)

The RBC Defect Workflow Optimisation (RWO) add-on features an evidence-based rule set in the *Extended* IPU to support the identification of patients with hereditary RBC diseases and iron deficiency anaemia.

Nivaggioni V *et al*. (2020)

Use of Sysmex XN-10 red blood cell parameters for screening of hereditary red blood cell diseases and iron deficiency anaemia.
Free online: Int J Lab Hematol; 42(6): 697.

Summary: The authors propose a two-step algorithm, based on the XN RBC and reticulocyte parameters, to differentiate patients with a hereditary RBC disease from iron deficiency anaemia and other patients. The published flowchart recommends how to manage MCHC < 36.5 g/dL (22.7 mmol/L) samples in addition to the CBC-O application to assist the diagnosis of RBC diseases. Overall, it reaches a very good classification rate of 99.4%, confirmed by an external cohort.

Nivaggioni V *et al*. (2022)

Detection of Southern Asian Ovalocytosis with Sysmex XN-10: A complement to the decision tree previously described.
Int J Hematol; 44(2): e84.

Summary: The authors expanded the algorithm described in the Nivaggioni *et al*. 2020 publication with the addition of a step to detect Southeast Asian ovalocytosis (SAO) cases. All SAO samples were correctly classified using the Hypo-He/MicroR ratio, which achieved an AUC of 1.0.

Haemoglobin variants

Additional publications

According to various case reports over the past years, haemoglobin variants show a distinctive pattern in the WDF measurement channels of Sysmex XN and XR analysers. Below papers suggest rules to identify these kinds of samples. These rules are not embedded as a standard add-on in *Extended* IPU but can be implemented upon request.

Combaluzier S *et al.* (2023)

Detection of unstable haemoglobin variants with Sysmex XN-10.
Int J Lab Hematol; 45(2): e21.

Summary: WDF channel of XN analysers shows a decreased fluorescence signal in blood samples of patients with unstable haemoglobin variants causing an abnormal scattergram. The optimal threshold combination to specify unstable haemoglobin variants is LY-SFL < 42 and NE-SFL < 41.2 resulting in a sensitivity of 100% and specificity of 99.9%.

NEW

Bosma M *et al.* (2025)

Verification of an Algorithm for Detection of Unstable Haemoglobin Variants With Sysmex XN-10 Yielded a High Degree of False Positives

Int J Lab Hematol; 47(4):748-749.

Summary: The authors suggested modifying the algorithm for unstable haemoglobin variant identification by Combaluzier *et al.* (2023), recommending the addition of cut-offs of neutrophils > 0.5 × 10^9/L, lymphocytes > 0.1 × 10^9/L, and patient age > 30 days in order to gain specificity.