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Conformity of Differential White Blood Cell (WBC) Examination Results on the Sysmex DI-60 And Sysmex XN-1000 at Prof. Dr. IGNG Ngoerah General Hospital, Denpasar, Bali

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ABSTRACT

Background: Sysmex DI-60 and Sysmex XN-1000 are automatic analyzers that can be used to check WBC differential counts. Ensuring the suitability of the WBC differential count results from the two tools can help in daily practice. **Objective:** Knowing the suitability of the WBC differential count examination results on the Sysmex DI-60 and Sysmex XN-1000. **Method:** Observational analytical research with a cross-sectional design. The data analyzed were differential WBC count data from samples of babies who underwent Complete Blood Count examinations on the Sysmex XN-1000 device and IT Ratio on the Sysmex DI-60 device without intervention (pre-classification results) at the Clinical Pathology Laboratory, Prof. Head overMarch 2023 – April 2023. **Results:** 81 samples were analyzed. The neutrophil value on the Sysmex DI-60 and Sysmex vs 34.15% ± 14.83%, median monocytes 4.00% (0.00-30.00)% vs 13.05% (1.30-34.40) %, median eosinophils 3.50% (0.00-31.00)% vs 3.75% (0.00-29.90)%, and median basophils 0.75% (0.00-16.00)% vs 0.30% (0, 00-2.90)%. The eosinophil variable did not show a significant difference between the results of the Sysmex DI-60 and Sysmex XN-1000 examinations (p=0.081). The results of the correlation analysis showed that there was a significant, strong, positive correlation between Sysmex DI-60 and Sysmex. Strong positive significance in the lymphocyte variable (r=0.818). However, no significant correlation basophil variable (r=0.044). Bland-Altman analysis shows that the most appropriate differential count examination is the eosinophil variable. **Conclusion:** Automatic WBC analyzers apply not only one examination method to detect WBC. The use of the Sysmex DI-60 and Sysmex XN-1000 provides automation for checking the WBC differential count with different working principles. In this study, there was only agreement between the differential count results for the eosinophil variable, so when operating these tools, intervention from a Clinical Pathologist was still required.

Key words: Differential Count, WBC, DI-60, XN-1000.

INTRODUCTION

Differential count White Blood Cells (WBC) is a commonly used hematological examination to provide important clinical information. The gold standard for examination is the manual counting of 200 cells each by two experts on peripheral blood smears stained with Romanowsky staining. Manual examination of peripheral blood smears for differential WBC count is very time-consuming, requires trained medical personnel, and is susceptible to inter-individual and intra-individual variability and variation, as well as cell distribution between slides. Technological developments have helped in developing automatic systems for analyzing cell morphology or automated morphological analysis systems.[1-3]

The Sysmex DI-60 system is a fully integrated cell image analyzer that can pre-classify WBC and can be used for differential WBC counts. Apart from the Sysmex DI-60, the Sysmex XN-1000 can also be used to carry out differential WBC count checks.[2,4] Sysmex DI-60 is an automated digital cell morphology system that uses artificial neural network technology to find, identify, and classify white blood cells and characterize red blood cells. This tool consists of an automated microscope that scans peripheral blood smears, a digital camera that captures images of all cellular and particulate material on the slide, and a computer that classifies each image using complex algorithms.

Sysmex DI-60 classifies WBCs as band neutrophils, segment neutrophils, lymphocytes, monocytes, eosinophils, basophils, promyelocytes, myelocytes, metamyelocytes, blasts, variant lymphocytes (or atypical lymphocytes), and plasma cells. "Unidentified" cells are a class of cells and objects that the system cannot identify.

Only some studies are comparing the performance of the two tools for examining WBC differential counts. Ensuring the suitability of the results of the WBC differential counts examination between the results of the two tools can help in daily practice.[2,4]

METHOD

This research is an observational analytical study, with a cross-sectional study design in the Clinical Pathology laboratory, Prof. Dr IGNG Ngoerah General Hospital, Denpasar, Bali, in the time March 2023 – April 2023. The data in this study are primary data from the WBC differential count results from 81 samples of babies who underwent Complete Blood Count examinations on the Sysmex XN-1000 device and IT Ratio on the Sysmex DI-60 device. The WBC differential count results used on the Sysmex DI-60 device are pre-classification results (no intervention

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was carried out). The differential WBC count analyzed in both tools is the variables neutrophils, lymphocytes, monocytes, eosinophils and basophils.

Excluded data are patients with a history of blood samples that were found to have clots and incomplete patient data.

Then, the collected data was subjected to descriptive analysis and through normality analysis and comparative analysis to see the difference in the mean or median differential count of WBC using the Sysmex DI-60 and XN-1000. The suitability test for the WBC differential count results was carried out using Bland-Altman analysis. The analysis results are significant if the p-value <0.05.

RESULTS

The results of this study showed that neutrophil values on the Sysmex DI-60 and Sysmex XN-1000 devices were 52.13% ± 18.27% vs. 45.00% (18.80-93.40) %, mean lymphocytes 21.06% ± 12.86% vs. 34.15% ± 14.83%, median monocytes 4.00% (0.00-30.00) % vs 13.05% (1.30-34.40)%, median eosinophils 3.50% (0.00-31.00)% vs 3.75% (0.00-29.90)%, and median basophils 0.75% (0.00-16.00)% vs 0.30% (0.00-2.90)% respectively (Table 1). Only the eosinophil variable showed no significant difference between the examination results using Sysmex DI and Sysmex XN-1000 (p=0.081) based on the Wilcoxon-Rank Test (Table 2).

Spearman correlation analysis showed a strong positive correlation between Sysmex DI-60 and Sysmex XN-1000 on neutrophil variables (r=0.857) and eosinophils (r=0.828), moderate positive correlation on monocyte variables (r=0.528) (p=0.000) (Table 3 and Figure 1). Pearson correlation analysis also showed a strong positive significant between Sysmex DI-60 and Sysmex XN-1000 on lymphocyte variables (r=0.818) (p=0.000), but no significant correlation was found on basophil variables (r=0.044) (p=0.699) (Table 3 and Figure 1).

Bland-Altman analysis showed that the mean bias value and limit of agreement (LOA) for the neutrophil variable was 4.49 (-14.22-23.20), followed by lymphocytes of -12, 99 (-29.78-3.80), monocytes by -7.80 (-17.3-1.70), eosinophils by 0.77 (-6.07-7.61), and basophils by 1.06 (-3.40-5.52) in both Sysmex DI-60 and Sysmex XN-1000 (Figure 2). These results indicate that the most suitable differential count examination is the eosinophil variable, with the lowest mean bias and LOA range compared to the other variables.

Table 1: Characteristics of the research sample.

Variable	Total (N=81)	p
Sysmex DI-60 (%)		
Neutrophils (Mean±SD)	52.13±18.27	0.200
Lymphocytes (Mean±SD)	21.06 ± 12.86	0.059
Monocytes, Median (Min-Max)	4.00 (0.00-30.00)	0,000*
Eosinophils, Median (Min-Max)	3.50 (0.00-31.00)	0,000*
Basophils, Median (Min-Max)	0.75 (0.00-16.00)	0,000*
Sysmex XN-1000 (%)		
Neutrophils, Median (Min-Max)	45.00 (18.80-93.40)	0.034*
Lymphocytes (Mean±SD)	34.15±14.83	0.079
Monocytes, Median (Min-Max)	13.05 (1.30-34.40)	0.009*
Eosinophils, Median (Min-Max)	3.75 (0.00-29.90)	0,000*
Basophils, Median (Min-Max)	0.30 (0.00-2.90)	0,000*

*Kolmogorov-Smirnov: data is not normally distributed if the p-value is less than 0.05

Table 2: Bivariate analysis of differential WBC count differences between Sysmex DI and Sysmex XN-1000.

Variable	Total (N=81)		p
	Sysmex DI-60	Sysmex XN-1000	
Neutrophils	52.13±18.27	45.00 (18.80-93.40)	0.000[a*]
Lymphocytes	21.06 ± 12.86	34.15±14.83	0.000[b*]
Monocytes	4.00 (0.00-30.00)	13.05 (1.30-34.40)	0.000[a*]
Eosinophils	3.50 (0.00-31.00)	3.75 (0.00-29.90)	0.081[a]
Basophils	0.75 (0.00-16.00)	0.30 (0.00-2.90)	0.000[a*]

[a]Wilcoxon-Rank Test; [b]Paired Sample-T Test; *Data differs significantly if the p-value is less than 0.05

Table 3: Correlation analysis.

Sysmex DI-60	r	p
Sysmex XN-1000		
Neutrophils	0.857	0.000a*
Lymphocytes	0.818	0.000b*
Monocytes	0.528	0.000a*
Eosinophils	0.828	0.000a*
Basophils	0.044	0.699a

[a]Spearman; [b]Pearson; *Statistically significant difference if the p-value is less than 0.05

DISCUSSION

The Sysmex DI-60 automated digital cell morphology system provides complete automation of the manual WBC differential count process.[5] The Sysmex DI-60 consists of a scanning microscope with two magnifications (10x and 100x), intermediate optical switching (1.0x and 0.5x), a digital camera, and a computer system with software (version 6.0) that identifies and classifies cells.[4] Research using the Sysmex XN-1000 revealed that the tool works by analyzing blood cells using the principle of flow cytometry-based optical measurement.[6] Previous studies for WBC differential count examination with Sysmex DI-60 had a high overall sensitivity for neutrophils, lymphocytes, basophils, blasts, and nucleated erythrocytes (range, 86.5 -95.8%), and relatively low for monocytes, eosinophils, IG, and others (range, 52.6–66.6%). The study revealed that the difference in WBC between Sysmex DI-60 and manual counting did not show a significant difference, especially for neutrophils and lymphocytes.[4] A study revealed that examination using Sysmex XN-1000 in the pediatric population showed that Sysmex XN-1000 had high sensitivity in blast identification.[7] Strong correlations were observed for differential and absolute count results for neutrophils, lymphocytes, eosinophils and monocytes compared with manual examination.[8]

In this research, only the eosinophil variable showed that there was no significant difference between the results of the WBC differential count using Sysmex DI-60 and Sysmex XN-1000 (p=0.081). Different results were obtained in a study that compared the analysis of Sysmex DI-60, which had carried out WBC classification; Sysmex XN-1000 and Sysmex DI-60 pre-classification results showed differences in mean WBC differential count analysis. So, it is necessary to classify WBC cells on the Sysmex DI-60 tool to increase its accuracy.[2]

This study showed a strong positive correlation between Sysmex DI-60 and Sysmex XN-1000 on neutrophil variables (r=0.857) and eosinophils (r=0.828), but had a moderate positive correlation on monocyte variables (r=0.528) (p=0.000). Pearson correlation analysis also showed a significant strong positive between Sysmex DI-60 and Sysmex XN-1000 on the lymphocyte variable (r=0.818) (p=0.000), but no significant correlation was found on the basophil variable (r=0.044) (p=0.699). Another study assessing the correlation of WBC differential counts after cell classification on the Sysmex DI-60 (corrected and confirmed by laboratory experts) compared to the Sysmex XN-20 showed r values >0.9 for neutrophils (r=0.90), eosinophils (r=0.96), and lymphocytes (r=0.93), but not for monocytes (r=0.75), and basophils (r=0.43). A low correlation coefficient was observed for basophils due to their low numbers in most samples.[1]

The test of the suitability of the results of the WBC differential counts examination between the Sysmex DI-60 and Sysmex XN-

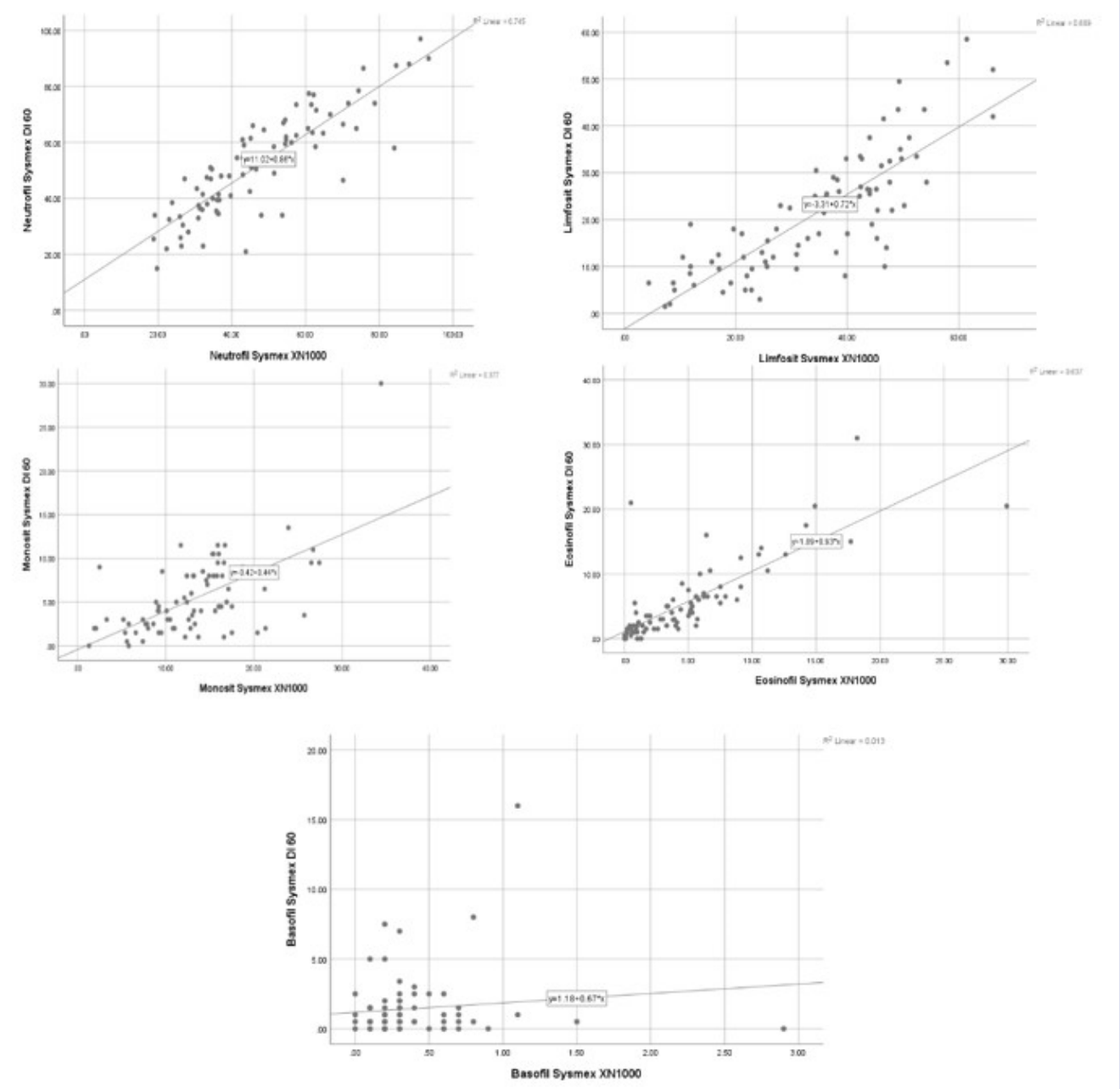

Figure 1: Results of Spearman and Pearson correlation scatter plot analysis.

1000 tools with the Bland-Altman test was based on the mean bias value. The limits of agreement (LOA) showed that the most suitable WBC differential count examination among the five variables analyzed was only the eosinophil variable with the lowest mean bias and the narrowest LOA range compared to other variables. This can theoretically be caused by differences in methods (working principles) in determining differential count WBC on the two tools, and on the Sysmex DI-60 tool, the results of differential count WBC used in this study are the results of pre-classification or no manual intervention/ classification by clinical pathologists so that many cells are included in the unidentified category, which cannot be classified by the tool as in Figure 1 (attachment). The existence of conformity in the results of eosinophil examination is theoretically caused by eosinophils, which have a distinctive morphology, are slightly larger than neutrophils, and have bright orange-red granules that can be easily recognized by imaging on DI-60 with the Feature Extraction method for cell grouping based on shape, color, granule, and vacuole detection. Likewise, the Sysmex XN-1000 tool with the fluorescent flow cytometry method uses forward scattered light to determine cell size and side scattered light to see the internal structure of cells, such as the shape of the nucleus and the presence of granules from cells in detecting eosinophils.[9] Another study assessing the agreement of Sysmex DI-60 results against flags generated from XN-20 to detect abnormal cells showed that the positive percent agreement (PPA) of Sysmex DI-60 for the flags "NRBC (Nucleated Red Blood Cells) Present," "IG (Immature Granulocytes) Present," and "Left Shift?" were 82.9%, 79.5%, and 82.7%, respectively. In contrast, the flags for "Blasts?" and "Atypical Lympho?" were 46.8% and 30.9%, so considering the accuracy of Sysmex DI-60, manual peripheral blood smear review remains necessary, especially for abnormal cells.[10]

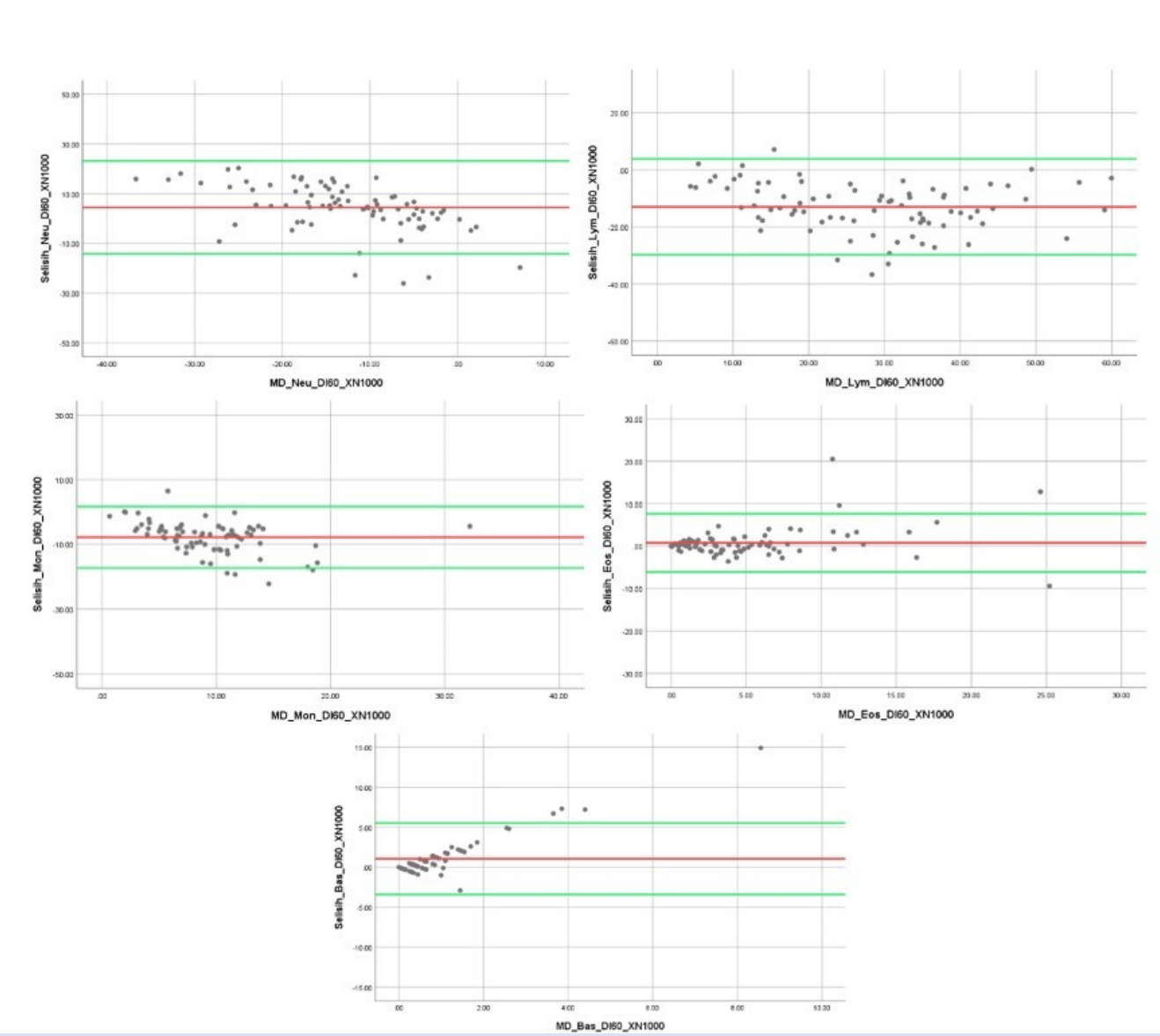

Figure 2: Bland-Altman suitability test results from checking the WBC differential count between the Sysmex DI-60 and Sysmex XN-1000.

CONCLUSION

This research shows that there is a strong correlation between the two analyzers on the neutrophil, eosinophil, and lymphocyte variables and a moderate correlation on the monocyte variable and no significant correlation was found on basophils. The results of the suitability test show that the most suitable WBC differential count examination is the eosinophil variable with the lowest mean bias and LOA range.

The automatic WBC analyzer applies not only one method to detect differential WBC count. The use of the Sysmex DI-60 and Sysmex XN-1000 tools provides complete automation, such as the manual WBC differential count process with different working principles. The automated system for counting blood cells through cell morphology analysis is expected to contribute to increasing the efficiency of routine hematology analysis. Still, it requires intervention to carry out manual classification on the Sysmex DI-60 instrument and peripheral blood smears by Clinical Pathologists.

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None

CONFLICTS OF INTEREST

None

ETHICS STATEMENT

This research has received ethical approval from the Research Ethics Commission of the Faculty of Medicine, Udayana University Number: 575/UN14.2.2.VII.14/LT/2023.

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