

Estimation of alert and change limits of haematological quantities and its application in the plausibility control

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ABSTRACT

Introduction: In the process of quality assurance of the measured values of the clinical laboratory, one of the purposes is to perform the *validation* of patients' measured values in the most objective way. This validation process is called *plausibility control* which may be defined as the set of procedures used to decide if a patient's measured value is valid according to established clinical and biological criteria.

The aim of this study is to propose a model to estimate alert and change limits of measured values of the blood cell count, to be applied to detect doubtful patients' measured values.

Methods: Some alert and change limits were estimated from the emergency laboratory database of the year 2010 using different percentiles. A verification of the suitability of the proposed model was also performed.

Results: Most of the fractions of the measured values excluded by the alert and change limits were according to the theoretical expected. The overall fraction of the number of doubtful clinical laboratory reports ranged between 0.6 and 47.6 %.

Conclusions: The proposed model helps, improves and standardizes the process of detection of doubtful measured values since they are produced objectively. These limits can also be configured in a laboratory information system letting the clinical laboratory professional staff to save time and efforts.

1. Introduction

In the clinical laboratory, different processes are involved to assure the quality of a clinical laboratory haematology report before releasing it to the requester: the visual inspection of the samples detects possible defects that make them unsuitable for the requested measurements in the pre-analytical phase; the internal quality control, the alarms of the measurement systems and the microscopic examination of stained blood film ensure the suitability in the analytical phase and the so-called “validation process” of measured values decides whether each clinical laboratory report may be issued (*validated*) or it should be retained for a more detailed final inspection (*doubtful* or *non validated*) in the post-analytical phase.

The visual inspection of the samples and the internal quality control are two well defined processes which have been standardized over time. In the same way, some scientific organizations have devoted their efforts to provide consensus rules for microscopic examination [1]. However, there are not guides or recommendations from a scientific or professional organisations providing information on how to conduct the validation process of patients’ measured values. Furthermore, despite all technological improvements, in many clinical laboratories this process is still performed in “manual” way by clinical laboratory specialised staff. So, every clinical haematology laboratory adapts this process in a particular way: some of them do not perform it because of its time consumption and its high costs of clinical laboratory specialised staff and some other, when performed, they do in a not standardized way. The lack of standardization of the validation process of patients’ measured values, performed by clinical laboratory specialised staff, has some disadvantages such as applying many subjective criteria and, consequently, having great interindividual variation, which degree depends on the experience of the mentioned professionals and the criteria used.

The *plausibility control* can be defined as the set of procedures used to decide if a patient’s measured value is valid or not according to clinical and biological criteria previously established [2]. This is a useful tool to detect doubtful measured values, which, despite of belonging to a series of measurements accepted by the internal quality control, can be erroneous and might be not detected by sample inspection, by the automated analysis or by the microscopic examination of stained blood film. The factors that may generate erroneous measured value are diverse: factors related to the sample (e.g. sample pertaining to another patient, sample collected from intravenous route), factors related to the measurement process (e.g. obstruction of the analyser, errors in manual transcription of measured values), and so on.

Probably, the most efficient way to eliminate the interindividual variation of the plausibility control of patients’ measured values is its computerization which, in addition, makes the process more efficient. In order to automate this process, some tools can be used to detect doubtful measured values: (i)

detection of measured values exceeding some alert limits, which define an interval where a large proportion of such a values can be expected to be found; (ii) detection of measured values which are not in agreement with the corresponding preceding one using a change limit (commonly called *deltacheck*); (iii) detection of patients' measured values which are not in agreement with measured values of other quantities obtained in the same sample [3]; and (iv) detection of measured values which are not consistent with the diagnosis, if known, or the origin of the request [2].

The alert limits are usually values far from the biological reference limits and can be set in different ways. Although there are not a lot of publications on this topic, and they mostly refer to biochemical quantities, there are some sources that have been used to set these limits: (i) unlikely limits (limits defining when a measured value has a very small or zero probability of corresponding to a patient), (ii) alarm or critical limits (limits indicating when a patient's measured value means an immediate danger to the patient), (iii) decision limits given by clinical practice guidelines and, finally, (iv) limits based on the clinicians opinion.

The change limits are those from which is considered that the change of a patient's measured value regarding the corresponding preceding one is suspected of being erroneous. There is not much literature on this subject. Several approaches have been used for this purpose: (i) data based on intraindividual (within-subject) biological variability [4], (ii) percentiles of the population distribution of the differences [5, 6, 7], or (iii) opinion of experts [8].

The plausibility control of measured values should detect previously unnoticed errors produced in any process of the clinical laboratory [2] and should ensure the consistency of these values with the available clinical and biological information.

The aim of this article is to propose a model to estimate alert and change limits of the number concentration of erythrocytes, leukocytes and thrombocytes; number fraction of neutrophils, lymphocytes, monocytes, eosinophils and basophils; mass concentration of haemoglobin; volume fraction and entitic volume of erythrocytes (also known as PRC and MCV, respectively), to detect doubtful measured values in the plausibility control in an objective way.

2. Material and methods

In order to estimate the alert and change limits, measured values of each haematological quantity, from the year 2010 were taken from the database maintained in our emergency laboratory information system Omega 3000 (Roche Diagnostics España S.L., Sant Cugat del Vallès, Catalonia, Spain). The number of measured values obtained ranged between 89231 and 89786, depending on the quantity. In order to verify the suitability of the proposed model, another patients' measured values of each quantity, from the year 2011 were taken from the same data source. The number of measured values

obtained ranged between 38912 to 46003, depending on the quantity.

All quantities were measured in the emergency laboratory in an ABX Pentra 120 DX analyzer (Horiba Medical, Montpellier, France). Number concentrations of erythrocytes, thrombocytes and leukocytes in blood, volume fraction and entitic volume of erythrocytes in blood were measured using impedance whereas haemoglobin mass concentration was measured by the cyanmethemoglobin method, and differential leukocyte count was carried out using a flow cytochemistry method.

The differential leukocyte count was also carried out using microscopic examination of stained blood film when some suspect flags from automated analysis, specified by the manufacturer, appeared or when the consensus guidelines of the International Society for Laboratory Hematology indicated [1]. The smear, the stain and the microscopic examination of 100 leukocytes were carried out by some experienced technicians according to the standardized procedure in use in the laboratory [9].

The metrological characteristics of the measuring system were stable during the years 2010 and 2011 (no changes in the measurement system and in the measurement errors for each quantity, observed in external quality assessment schemes).

The selected alert limits were the percentiles that exclude 10 % or 1 % or 0.1 % or 0.01% of the patients' measured values and the change limits were the percentiles that exclude 10 % or 1 % or 0.1 % of the relative differences of patients' measured values. These percentiles were chosen in an arbitrary way but using professional consensus among the authors.

In order to define the alert limits, percentiles 5.00 and 95.00, 0.50 and 99.50, 0.05 and 99.95, and 0.005 and 99.995 of original data from the year 2010 were estimated. The percentiles estimated to define the change limits were 90.00, 99.00 and 99.90 from the same database and year.

In a manual 100 leukocytes differential counting, the number fraction of each type of leukocyte usually is expressed rounding to an integer. To estimate alert and change limits, these values were transformed by adding 0.5 to avoid giving biologically impossible measured values of 0 %.

All data were processed with the software SPSS v.17 (SPSS, Chicago, USA).

For each quantity, a change is the relative difference of a measured value with regard its preceding one. This relative difference (D), expressed in percent (%), is calculated taking into account the highest (x_h) and lowest (x_l) values [10]:

$$D = (x_h - x_l) / x_l \cdot 100 (\%)$$

In this way, from the year 2010, pairs of measured values of each haematological quantity from the same patient, were obtained. The pairs of measured values obtained ranged between 30917 and 31365, depending on the quantity.

To estimate change limits, measured values lower than the corresponding limit of detection have been transformed into the immediately preceding numerical measured value taking into account the number of digits used.

To estimate change limits, the selected time of searching back was one day.

For each haematological quantity, in order to verify the suitability of the estimated alert limits, the percent (%) of measured values from the year 2011 excluded by these limits was calculated. The same procedure was using the change limits.

The criteria applied to decide when a measured value is doubtful were the following: (i) for those measured values not having a preceding one, only the comparison with alert limits may produce doubtful measured values, obviously; (ii) for those measured values having a preceding one, only change limits are accepted to produce doubtful measured values.

For each quantity, the fractions (in %) of the number of measured values excluded by alert or change limits (doubtful measured values) were calculated applying together these limits to measured values from the year 2011. Since four alert limits and three different change limits have been estimated, twelve combinations giving twelve different possibilities were obtained.

In order to assess the real impact of the implementation of alert and change limits in the daily plausibility control, the overall fractions (in %) of the number of doubtful clinical laboratory reports, regardless of the quantity responsible of its exclusion, were also calculated.

The criteria applied to consider the whole patients' clinical laboratory report as doubtful were, at least, one measured value of any quantity of the blood cell count excluded by alert or change limits.

3. Results

In all tables, haematological quantities are described using the traditional English acronyms but also according to the IUPAC-IFCC recommended syntax in which B means blood; Lkcs means leukocytes, num. means number, vol. means volume; c. means concentration and fr. means fraction [11]. Table 1 shows alert limits for all quantities estimated from original data of the year 2010, corresponding to percentiles 0.005, 0.05, 0.50, 5.00, 95.00, 99.50, 99.95 and 99.995, whereas Table 2 shows, for the same quantities and for the same year, the change limits of relative differences corresponding to percentiles 90.0, 99.0 and 99.9.

Table 1. Alert limits for each haematological quantity estimated with measured values from the year 2010.

Percentile	<i>RBC</i> (x10E12/L)	<i>Hb</i> (g/L)	<i>PRC</i> (1)	<i>MCV</i> (fL)	<i>Plt</i> (x10E9/L)	<i>WBC</i> (x10E9/L)	<i>Neu</i> (%)	<i>Lym</i> (%)	<i>Mono</i> (%)	<i>Eos</i> (%)	<i>Baso</i> (%)
$p_{0.005}$	0.9	25	0.088	52	<3	<0.2	0.5	0.5	0.2	0.1	0.1
$p_{0.05}$	1.3	38	0.121	59	<3	<0.2	2.2	1.5	0.5	0.1	0.1
$p_{0.50}$	1.9	58	0.179	68	13	0.4	13.5	2.5	1.1	0.3	0.1
$p_{5.00}$	2.5	78	0.239	81	69	3.7	49.6	4.5	2.8	0.5	0.1
$p_{95.00}$	5.1	155	0.470	103	448	19.5	90.3	38.5	12.5	4.9	1.5
$p_{99.50}$	5.8	172	0.522	114	746	38.6	94.4	68.5	31.1	10.6	4.2
$p_{99.95}$	6.6	188	0.572	126	1057	109.6	96.8	91.5	57.4	22.5	12.6
$p_{99.995}$	7.6	213	0.628	134	2027	275.1	98.5	98.5	82.1	48.7	34.1

RBC: B–Erythrocytes; num.c.; *Hb*: B–Haemoglobin; mass.c.; *PRC*: B–Erythrocytes; vol.fr.; *MCV*: B–Erythrocytes; entitic vol.; *Plt*: B–Thrombocytes; num.c.; *WBC*: B–Leukocytes; num.c.; *Neu*: Lkcs(B)–Neutrophils; num.fr.; *Lym*: Lkcs(B)–Lymphocytes; num.fr.; *Mono*: Lkcs(B)–Monocytes; num.fr.; *Eos*: Lkcs(B)–Eosinophils; num.fr.; *Baso*: Lkcs(B)–Basophils; num.fr.; *in parentheses*: units of measure; *p*: percentile having the order indicated by the subindex

Table 2. Change limits for each haematological quantity estimated with measured values from the year 2010.

Percentile	<i>DRBC</i> (%)	<i>DHb</i> (%)	<i>DPRC</i> (%)	<i>DMCV</i> (%)	<i>DPlt</i> (%)	<i>DWBC</i> (%)	<i>DNeu</i> (%)	<i>DLym</i> (%)	<i>DMono</i> (%)	<i>DEos</i> (%)	<i>DBaso</i> (%)
$p_{90.0}$	25.9	25.9	25.8	2.9	45.7	67.6	22.3	133.3	100.0	162.5	300.0
$p_{99.0}$	68.4	70.7	68.3	6.7	209.8	194.6	75.2	488.9	536.5	516.7	850.0
$p_{99.9}$	129.1	174.8	143.8	19.4	1269.0	606.3	473.1	1533.3	2085.5	1377.0	2150.0

Relative differences (D), in fraction (%), of: *DRBC*: B–Erythrocytes; num.c.; *DHb*: B–Haemoglobin; mass c.; *DPRC*: B–Erythrocytes; vol.fr.; *DMCV*: B–Erythrocytes; entitic vol.; *DPlt*: B–Thrombocytes; num.c.; *DWBC*: B–Leukocytes; num.c.; *DNeu*: Lkcs(B)–Neutrophils; num.fr.; *DLym*: Lkcs(B)–Lymphocytes; num.fr.; *DMono*: Lkcs(B)–Monocytes; num.fr.; *DEos*: Lkcs(B)–Eosinophils; num.fr.; *DBaso*: Lkcs(B)–Basophils; num.fr.; *p*: percentile having the order indicated by the subindex.

Table 3 and Table 4 show, respectively, the fraction (in %) of data of the year 2011 excluded by alert limits and change limits.

Table 3. Fraction (in %) of the number of measured values for each haematological quantity from the year 2011 excluded by alert limits.

	<i>RBC</i> (%)	<i>Hb</i> (%)	<i>PRC</i> (%)	<i>MCV</i> (%)	<i>Plt</i> (%)	<i>WBC</i> (%)	<i>Neu</i> (%)	<i>Lym</i> (%)	<i>Mono</i> (%)	<i>Eos</i> (%)	<i>Baso</i> (%)
Excluded by $p_{5.00}$ and $p_{95.00}$	8.09	9.94	10.01	8.11	9.97	10.57	9.70	7.47	10.42	5.96	5.79
Excluded by $p_{0.50}$ and $p_{99.50}$	0.86	1.06	1.12	0.61	0.93	1.02	1.13	0.85	1.01	0.73	0.73
Excluded by $p_{0.05}$ and $p_{99.95}$	0.08	0.09	0.11	0.07	0.14	0.38	0.17	0.11	0.05	0.03	0.09
Excluded by $p_{0.005}$ and $p_{99.995}$	0.01	0.01	0.04	0.02	0.05	0.28	0.01	0.003	0.002	0.003	0.01

RBC: B–Erythrocytes; num.c.; *Hb*: B–Haemoglobin; mass c.; *PRC*: B–Erythrocytes; vol.fr.; *MCV*: B–Erythrocytes; entitic vol.; *Plt*: B–Thrombocytes; num.c.; *WBC*: B–Leukocytes; num.c.; *Neu*: Lkcs(B)–Neutrophils; num.fr.; *Lym*: Lkcs(B)–Lymphocytes; num.fr.; *Mono*: Lkcs(B)–Monocytes; num.fr.; *Eos*: Lkcs(B)–Eosinophils; num.fr.; *Baso*: Lkcs(B)–Basophils; num.fr.; *p*: percentile having the order indicated by the subindex.

Table 4. Fraction (in %) of the number of measured values for each haematological quantity from the year 2011 excluded by change limits.

	<i>DRBC</i>	<i>DHb</i>	<i>DPRC</i>	<i>DMCV</i>	<i>DPlt</i>	<i>DWBC</i>	<i>DNeu</i>	<i>DLym</i>	<i>DMono</i>	<i>DEos</i>	<i>DBaso</i>
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
Excluded by $p_{90.0}$	9.83	9.68	9.93	5.55	9.22	10.05	10.52	10.03	11.63	9.95	10.23
Excluded by $p_{99.0}$	0.63	0.66	0.73	0.80	0.85	1.14	0.95	0.82	1.03	1.06	1.70
Excluded by $p_{99.9}$	0.07	0.03	0.12	0.03	0.02	0.12	0.09	0.07	0.13	0.09	0.28

Relative differences (*D*) of: *DRBC*: B–Erythrocytes; num.c.; *DHb*: B–Haemoglobin; mass c.; *DPRC*: B–Erythrocytes; vol.fr.; *DMCV*: B–Erythrocytes; entitic vol.; *DPlt*: B–Thrombocytes; num.c.; *DWBC*: B–Leukocytes; num.c.; *DNeu*: Lkcs(B)–Neutrophils; num.fr.; *DLym*: Lkcs(B)–Lymphocytes; num.fr.; *DMono*: Lkcs(B)–Monocytes; num.fr.; *DEos*: Lkcs(B)–Eosinophils; num.fr.; *DBaso*: Lkcs(B)–Basophils; num.fr.; *p*: percentile having the order indicated by the subindex.

Table 5 shows, for all the quantities studied, the fraction (in %) of the number of doubtful measured values of the year 2011 detected applying both alert and change limits. All fractions (in %) are expressed regarding to the total number of measured values studied.

Table 5. Fraction (in %) of the number of doubtful measured values for each haematological quantity found applying alert and change limits to measured values, having or not a preceding one, from the year 2011.

Alert and change limits applied	<i>RBC</i>	<i>Hb</i>	<i>PRC</i>	<i>MCV</i>	<i>Plt</i>	<i>WBC</i>	<i>Neu</i>	<i>Lym</i>	<i>Mono</i>	<i>Eos</i>	<i>Baso</i>
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
AL1 or CL1	9.14	10.60	10.39	7.54	9.32	9.73	10.07	10.08	10.89	7.61	7.40
AL1 or CL2	5.95	7.22	7.16	5.82	6.43	6.65	6.77	6.92	7.21	4.56	4.47
AL1 or CL3	5.76	7.01	6.95	5.55	6.15	6.29	6.47	6.66	6.90	4.23	3.99
AL2 or CL1	4.07	4.23	4.34	2.45	3.83	4.12	4.43	4.42	4.75	3.98	4.05
AL2 or CL2	0.89	1.09	1.11	0.73	0.94	1.02	1.13	1.26	1.08	0.93	1.12
AL2 or CL3	0.69	0.88	0.90	0.46	0.66	0.67	0.83	1.00	0.77	0.59	0.63
AL3 or CL1	3.47	3.43	3.55	2.05	3.28	3.74	3.71	3.64	4.06	3.45	3.58
AL3 or CL2	0.28	0.30	0.33	0.33	0.39	0.65	0.41	0.48	0.39	0.40	0.65
AL3 or CL3	0.09	0.08	0.11	0.07	0.11	0.30	0.11	0.22	0.08	0.06	0.16
AL4 or CL1	3.42	3.37	3.50	2.01	3.21	3.69	3.63	3.46	4.03	3.42	3.51
AL4 or CL2	0.23	0.23	0.27	0.29	0.32	0.60	0.33	0.30	0.36	0.37	0.58
AL4 or CL3	0.03	0.02	0.06	0.03	0.03	0.24	0.03	0.04	0.05	0.03	0.1

(Table 5 continued on next page)

(Table 5 continued) RBC: B–Erythrocytes; num.c.; Hb: B–Haemoglobin; mass c.; PRC: B–Erythrocytes; vol. fr.; MCV: B–Erythrocytes; entitic vol.; Plt : B–Thrombocytes; num.c.; WBC : B–Leukocytes; num.c.; Neu: Lkcs(B)–Neutrophils; num.fr.; Lym: Lkcs(B)–Lymphocytes; num.fr.; Mono: Lkcs(B)–Monocytes; num.fr.; Eos: Lkcs(B)–Eosinophils; num.fr.; Baso: Lkcs(B)–Basophils; num.fr.; Alert limits (AL) corresponding to: AL1: $p_{5,00}$ and $p_{95,00}$; AL2: $p_{0,50}$ and $p_{99,50}$; AL3: $p_{0,05}$ and $p_{99,95}$; AL4: $p_{0,005}$ and $p_{99,995}$; Change limits (CL) corresponding to: CL1: $p_{90,0}$; CL2: $p_{99,0}$; CL3: $p_{99,9}$

Table 6 shows, for all the quantities studied, the fraction (in %) of the number of doubtful clinical laboratory reports of the year 2011 detected applying both alert and change limits.

Table 6. Fraction (in %) of the number of doubtful clinical laboratory reports found applying alert and change limits.

	AL1 or CL1	AL1 or CL2	AL1 or CL3	AL2 or CL1	AL2 or CL2	AL2 or CL3	AL3 or CL1	AL3 or CL2	AL3 or CL3	AL4 or CL1	AL4 or CL2	AL4 or CL3
Excluded (%)	47.6	32.8	30.4	22.1	7.3	4.8	18.4	3.5	1.1	17.9	3.1	0.6

Alert limits (AL) corresponding to: AL1: $p_{5,00}$ and $p_{95,00}$; AL2: $p_{0,50}$ and $p_{99,50}$; AL3: $p_{0,05}$ and $p_{99,95}$; AL4: $p_{0,005}$ and $p_{99,995}$; Change limits (CL) corresponding to: CL1: $p_{90,0}$; CL2: $p_{99,0}$; CL3: $p_{99,9}$

4. Discussion

There are many clinical laboratories around the world producing daily by thousands of patients' measured values of haematological quantities which are subject to a validation process performed by clinical laboratory specialised staff. This process is difficult and time consuming, so many laboratories cannot afford to carry it out. On the other hand, its subjectivity and interindividual variation make this process less efficient than it could be. As an alternative, computerization of the plausibility control could conduce to a final inspection of those haematological laboratory reports containing doubtful patients' measured values, and to deliver automatically to the requester those considered acceptable according to unambiguous defined rules. For these haematology laboratories, the computerized plausibility control allows laboratory professional staff a more objective review, saving time and increasing their effectiveness in detecting doubtful patients' measured values, as has been previously demonstrated for some specialized and computerized plausibility control systems (e.g. VALAB system) [12, 13, 14]. Even though partially computerized plausibility control systems have existed for more than 20 years and they are available in the most of laboratory information systems, published data on the use of them are limited. Some surveys report that about 64% of clinical laboratories use computerized plausibility control systems [15]. Most of them are clinical laboratories with high workload in which plausibility control are applied mainly to biochemical quantities, with a lack of standardization in the algorithms used and criteria applied.

To perform the plausibility control applying the alert and change limits is necessary to develop a procedure for establishing these limits [4-7, 16-18]. In the proposed model, the percentiles of the population distribution of the differences were chosen for estimating change limits, rather than the change limits based on biological variability. The main reason has been that change limits based on biological variability only include physiological variability whereas change limits based on percentiles also include pathological and iatrogenic variability. These change limits are particularly relevant in the plausibility control of measured values from hospital population. In this way, an unmanageable number of doubtful clinical laboratory reports that finally they will be issued after a detailed inspection (false positive) are avoided [4, 6].

The proposed model provide different fractions (in %) of the number of doubtful patients' measured values of some haematological quantities, excluded by the alert or change limits, depending on the percentiles applied; these clinical laboratory reports which contain doubtful patients' measured values would not be automatically validated. Since a wide range of combinations are provided, each laboratory may choose the appropriate alert or change limits, that is the appropriate percentiles to obtain a fraction (in %) of doubtful patients' measured values which the clinical laboratory professionals would decide whether each clinical laboratory report could be issued (*validated*) or it should be retained for a more detailed inspection. The selection of the appropriate combination is established according to clinical laboratory needs, mainly the time or the clinical laboratory staff available to be dedicated to plausibility control, bearing in mind that the frequency of clinical laboratory errors reported in the literature range from 0.05% to 2% [19-22].

Despite all above, it should be remarked that, as stated in the introduction section, the aim of this study is to propose a model for establishing alert and change limits, but the clinical relevance of the doubtful patients' measured values is not under the scope of this article.

The fractions (in %) of patients' measured values excluded by the alert or change limits of some quantities were far from the expected theoretical. Some reasons could explain this fact: those quantities with different percentiles with coincident values do not behave as expected, as in the case of leukocytes number concentration (Table 1, *WBC*) in which percentiles 0.005 and 0.05 of estimated alert limits were coincident with the corresponding detection limit of the measuring system; or in the case of estimated alert limits of eosinophils (Table 1, *Eos*) and basophils (Table 1, *Baso*) number fractions, in which there were low percentiles with coincident values probably due to the narrow range of the measured values; in the case of entitic volume of erythrocytes, only the percentile 90.0 of the relative differences of pairs of measured values was far from the expected theoretical (Table 4, *DMCV*). The rest of the percentiles were according to the expected.

Despite of estimating all the alert limits for each quantity, there are some cases that the lower limit should not to be included in the plausibility control, as in the case of percentiles 0.005, 0.05, 0.5 and 5.0 of blood monocytes, eosinophils and basophils number fractions due to the low prevalence of these types of leukocytes (lower limits of reference ranges very close to 0 %).

This study shows how to set alert and change limits to apply the plausibility control of a large number of haematological quantities in an objective and standardized way. Despite the estimation of these limits has been focused on a particular sort of clinical laboratory (emergency laboratory from a university hospital), the proposed way to set these limits can be applied to any kind of clinical laboratory without any limitation.

This model has some advantages against other systems. Since these limits are configurable in a simple middleware or an information system that allows the configuration of logic rules, the plausibility control can be carried out without the need of using specialized systems [12, 13, 14]. Thus, the objective and standardized plausibility control remains available to all sorts of clinical laboratories, regardless of their size. Furthermore, the estimation of change limits based on percentiles, which include physiological, pathological and iatrogenic biological variability, is suitable to be used in clinical laboratories working with samples from hospital patients as well as in clinical laboratories working with samples from non-hospital source. Since these limits are estimated in a relatively simple way and taking into account that and the results of the different percentiles may vary depending on the origin of the population (e.g. laboratories serving population from primary health care centres or laboratories of a tertiary hospital with Haematology and Oncology departments among others), the plausibility control can be adapted to workflow and needs from each clinical laboratory by calculating its own limits and selecting the most appropriate combination for each quantity. If interested, these limits can also be estimated by dividing the measured values in some subpopulations according to the origin (inpatients versus outpatients, emergency laboratory versus routine laboratory), requesting department, diagnosis and so on.

The selection of the appropriate combinations, together with an appropriate software, should allow computerizing the plausibility control to help, improve and standardize the process of detection of doubtful measured values which have gone unnoticed in the previous phases (sample inspection, internal quality control and microscopic examination of blood film) and leaving time for other tasks.

As said before, this study is focused on two tools used in the plausibility control: alert and change limits. Nevertheless, the use of another tool applicable to the plausibility control —detection of patients' measured values which are not in agreement with patients' measured values of other patho-physiologically related quantities obtained in same sample has been published for biochemical quantities by some of the present authors [3]. These series of studies will be finished (as a doctoral thesis) applying together all these tools to the computerization of the plausibility control.

5. References

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