**Supplemental Table 1**

**Centers**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Code** | **Center (all in Germany)** | **Description and patient population** | **Analytical device** | **Patients** | **Samples** |
| A | University Hospital Erlangen, Erlangen (main center) | Pediatric tertiary care center, all pediatric specialties | SYSMEX XE-2100 | 51,176 | 2,626,712 |
| B | University Hospital of Würzburg, Würzburg | Pediatric tertiary care center, all pediatric specialties | SYSMEX XE-2100, XE-5000 | 30,421 | 1,182,878 |
| C | University Medical Centre Ulm, Ulm | Pediatric tertiary care center, all pediatric specialties | SYSMEX XE-2100, XE-5000 | 24,379 | 1,068,251 |
| D | Klinikum Augsburg, Augsburg | Pediatric tertiary care center, all pediatric specialties | SYSMEX XN-9000, XP-800i | 41,385 | 1,262,616 |
| E | MVZ Labor PD Dr. Volkmann und Kollegen, Karlsruhe | Private laboratory service provider, mainly primary care samples | SYSMEX XE-2100, XE-2100D | 54,457 | 648,318 |
| F | University Hospital of Cologne, Cologne | Pediatric tertiary care center, all pediatric specialties | SYSMEX XE-5000 | 46,841 | 849,782 |
| G | Institute of Clinical Chemistry, MHH, Hannover | Pediatric tertiary care center, all pediatric specialties | SYSMEX XE-5000, XS-800i | 10,467 | 452,861 |
| H | MVZ wagnerstibbe, amedes Gruppe, Hannover | Private laboratory service provider, mainly primary care samples | SYSMEX XN-1000, XN-2000, XT-1800i | 35,462 | 48,156 |
| I | University Hospital Schleswig-Holstein, Kiel | Pediatric tertiary care center, all pediatric specialties | SYSMEX XN, XS-800i, XE-2100, XT-1800i, XN-350 | 46,372 | 66,643 |
| J | Klinikum Bremen-Nord, Bremen | Pediatric tertiary care center, all pediatric specialties w/o pediatric hematology/oncology | Beckmann Coulter DxH800 | 17,332 | 337,502 |

Participating centers, analytical devices, and number of patients/samples. The time period examined covered January 2008 to December 2016, depending on the center, in order to provide a maximum number of samples measured with identical analytical methods which could be retrieved from the hospital laboratory information systems (see Supplemental Table 2 for details). Supplemental Table 4 shows the proportion of test results outside the created reference intervals to enable appreciation of the differences in centers’ patient populations.

**Supplemental Table 2**

Due to its size, we included supplemental table 2 in a separate file “Supplemental Table 2”.

**Supplemental Table 3**

|  |  | **Hemoglobin** | **Hematocrit** | **Red cell count** | **White cell count** | **Platelet count** | **MCH** | **MCHC** | **MCV** | **RDW** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **0-28 days** | before filtering  after filtering | 152,822/47,390  21,249/21,249 | 106,322/35,671  15,628/15,628 | 109,224/37,186  16,552/16,552 | 109,217/37,203  12,631/12,631 | 109,000/37,178  16,553/16,553 | 150,766/47,386  21,278/21,278 | 138,075/44,972  19,568/19,568 | 109,212/37,181  16,547/16,547 | 54,364/18,301  8,262/8,262 |
| **29 days-1 year** | before filtering  after filtering | 153,220/36,547  21,249/21,249 | 114,378/29,819  15,628/15,628 | 118,889/31,621  16,552/16,552 | 118,964/31,632  12,631/12,631 | 118,725/31,613  16,553/16,553 | 151,641/36,547  21,278/21,278 | 141,106/36,011  19,568/19,568 | 118,876/31,620  16,547/16,547 | 56,089/11,344  8,262/8,262 |
| **1 year** | before filtering  after filtering | 77,825/27,617  11,687/11,687 | 65,547/23,437  10,017/10,017 | 68,790/24,935  10,894/10,894 | 68,841/24,949  8,322/8,322 | 68,761/24,930  10,892/10,892 | 77,459/27,614  11,692/11,692 | 75,573/27,217  10,976/10,976 | 68,770/24,932  10,895/10,895 | 28,211/8,844  3,045/3,045 |
| **2 years** | before filtering  after filtering | 65,464/21,043  8,792/8,792 | 54,210/18,223  7,753/7,753 | 57,300/19,159  8,227/8,227 | 57,362/19,170  6,652/6,652 | 57,298/19,150  8,222/8,222 | 64,989/21,042  8,796/8,796 | 63,017/20,712  8,087/8,087 | 57,238/19,157  8,225/8,225 | 22,687/6,477  2,083/2,083 |
| **3 years** | before filtering  after filtering | 62,375/20,278  8,674/8,674 | 53,305/17,718  7,709/7,709 | 55,825/18,542  8,097/8,097 | 55,856/18,548  6,626/6,626 | 55,835/18,541  8,097/8,097 | 62,066/20,278  8,678/8,678 | 60,679/19,913  7,796/7,796 | 55,815/18,542  8,096/8,096 | 21,163/5,966  1,924/1,924 |
| **4 years** | before filtering  after filtering | 54,371/19,311  8,390/8,390 | 45,912/16,896  7,516/7,516 | 48,272/17,784  7,920/7,920 | 48,268/17,792  6,618/6,618 | 48,266/17,781  7,918/7,918 | 54,119/19,311  8,392/8,392 | 52,738/18,913  7,440/7,440 | 48,252/17,777  7,913/7,913 | 18,001/5,866  1,955/1,955 |
| **5 years** | before filtering  after filtering | 50,946/18,759  8,367/8,367 | 42,292/16,376  7,458/7,458 | 45,319/17,304  7,883/7,883 | 45,359/17,311  6,648/6,648 | 45,314/17,304  7,882/7,882 | 50,757/18,758  8,369/8,369 | 49,239/18,276  7,366/7,366 | 45,292/17,301  7,881/7,881 | 18,075/5,639  1,894/1,894 |
| **6 years** | before filtering  after filtering | 47,755/17,303  7,332/7,332 | 40,627/14,999  6,554/6,554 | 42,968/15,897  6,911/6,911 | 42,994/15,905  5,828/5,828 | 42,887/15,892  6,908/6,908 | 47,618/17,303  7,335/7,335 | 45,930/16,829  6,546/6,546 | 42,880/15,895  6,912/6,912 | 17,537/5,219  1,643/1,643 |
| **7 years** | before filtering  after filtering | 43,530/17,163  7,316/7,316 | 37,141/14,880  6,557/6,557 | 39,451/15,800  6,911/6,911 | 39,464/15,811  5,865/5,865 | 39,442/15,794  6,909/6,909 | 43,420/17,163  7,316/7,316 | 41,889/16,643  6,439/6,439 | 39,431/15,793  6,909/6,909 | 14,291/4,966  1,544/1,544 |
| **8 years** | before filtering  after filtering | 42,142/18,187  7,772/7,772 | 35,424/15,810  6,990/6,990 | 37,671/16,791  7,337/7,337 | 37,709/16,801  6,252/6,252 | 37,652/16,790  7,337/7,337 | 42,030/18,187  7,773/7,773 | 40,402/17,580  6,813/6,813 | 37,652/16,791  7,338/7,338 | 13,677/5,119  1,609/1,609 |
| **9 years** | before filtering  after filtering | 42,874/19,103  8,102/8,102 | 36,124/16,534  7,244/7,244 | 38,329/17,612  7,643/7,643 | 38,348/17,627  6,420/6,420 | 38,310/17,609  7,642/7,642 | 42,736/19,102  8,104/8,104 | 40,837/18,408  7,115/7,115 | 38,313/17,607  7,640/7,640 | 12,999/5,320  1,673/1,673 |
| **10 years** | before filtering  after filtering | 44,671/19,954  8,340/8,340 | 37,096/17,353  7,476/7,476 | 39,445/18,452  7,873/7,873 | 39,515/18,461  6,624/6,624 | 39,469/18,445  7,867/7,867 | 44,491/19,951  8,342/8,342 | 42,332/19,224  7,238/7,238 | 39,433/18,447  7,873/7,873 | 14,400/5,483  1,760/1,760 |
| **11 years** | before filtering  after filtering | 48,070/20,714  8,569/8,569 | 40,186/18,049  7,731/7,731 | 42,858/19,210  8,147/8,147 | 42,895/19,227  6,860/6,860 | 42,834/19,205  8,145/8,145 | 47,920/20,714  8,569/8,569 | 45,600/19,970  7,459/7,459 | 42,840/19,204  8,145/8,145 | 14,422/5,595  1,761/1,761 |
| **12 years** | before filtering  after filtering | 48,950/22,700  9,724/9,724 | 40,586/19,876  8,846/8,846 | 43,610/21,130  9,298/9,298 | 43,662/21,153  7,924/7,924 | 43,615/21,125  9,296/9,296 | 48,682/22,699  9,725/9,725 | 46,250/21,851  8,324/8,324 | 43,591/21,126  9,295/9,295 | 14,696/5,776  1,913/1,913 |
| **13 years** | before filtering  after filtering | 58,550/26,839  12,041/12,041 | 48,685/23,583  10,956/10,956 | 51,735/25,061  11,494/11,494 | 51,772/25,082  10,110/10,110 | 51,723/25,055  11,490/11,490 | 58,293/26,837  12,040/12,040 | 55,371/25,880  10,091/10,091 | 51,713/25,054  11,490/11,490 | 16,357/6,025  1,868/1,868 |
| **14 years** | before filtering  after filtering | 63,530/28,036  12,422/12,422 | 53,789/24,652  11,293/11,293 | 56,927/26,052  11,807/11,807 | 56,981/26,082  10,222/10,222 | 56,889/26,049  11,806/11,806 | 63,338/28,035  12,425/12,425 | 60,057/27,001  10,343/10,343 | 56,891/26,050  11,806/11,806 | 18,070/6,332  2,055/2,055 |
| **15 years** | before filtering  after filtering | 69,681/29,852  13,165/13,165 | 57,352/26,172  11,869/11,869 | 60,665/27,586  12,442/12,442 | 60,753/27,638  10,751/10,751 | 60,647/27,573  12,435/12,435 | 69,402/29,850  13,168/13,168 | 65,517/28,742  10,714/10,714 | 60,636/27,575  12,435/12,435 | 19,642/6,608  2,135/2,135 |
| **16 years** | before filtering  after filtering | 75,801/32,736  15,019/15,019 | 63,593/28,934  13,619/13,619 | 67,069/30,428  14,265/14,265 | 67,139/30,461  12,356/12,356 | 66,987/30,403  14,253/14,253 | 75,568/32,726  15,019/15,019 | 71,567/31,512  11,845/11,845 | 67,018/30,407  14,257/14,257 | 20,230/6,386  2,104/2,104 |
| **17 years** | before filtering  after filtering | 76,410/34,550  17,096/17,096 | 64,557/30,903  15,666/15,666 | 67,830/32,233  16,234/16,234 | 67,901/32,276  14,117/14,117 | 67,795/32,220  16,228/16,228 | 76,140/34,523  17,088/17,088 | 71,998/33,252  12,607/12,607 | 67,801/32,220  16,227/16,227 | 17,994/5,991  2,070/2,070 |
| **Total** | before filtering  after filtering | 1,278,987/351,839  210,224/209,922 | 1,037,126/304,144  184,338/184,082 | 1,092,177/320,204  194,502/194,239 | 1,093,000/320,487  161,994/161,806 | 1,091,449/320,095  194,440/194,177 | 1,271,435/351,794  210,284/209,981 | 1,208,177/342,334  182,120/181,817 | 1,091,654/320,120  194,449/194,186 | 412,905/87,385  45,595/45,476 |

**Number of samples and individuals for each analyte in different age ranges before and after filtering.** Sample counts are shown before (upper column) and after (lower column) removal of samples from patients with multiple measurements and exclusion of white cell counts from centers D and J, and MCHC measurements from center H. Abbreviations: MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; RDW, red cell distribution width.

**Supplemental Table 4**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **A** | | **B** | | **C** | | **D** | | **E** | | **F** | | **G** | | **H** | | **I** | | **J** | |
|  | **< 2.5th** | **> 97.5th** | **< 2.5th** | **> 97.5th** | **< 2.5th** | **> 97.5th** | **< 2.5th** | **> 97.5th** | **< 2.5th** | **> 97.5th** | **< 2.5th** | **> 97.5th** | **< 2.5th** | **> 97.5th** | **< 2.5th** | **> 97.5th** | **< 2.5th** | **> 97.5th** | **< 2.5th** | **> 97.5th** |
| **Hemoglobin** | 28.2/2.8 | 5.5/3.6 | 31.8/3.3 | 1.7/2.2 | 43.1/4.1 | 2.1/2.7 | 27.1/3.7 | 3.5/3.7 | 4.3/3.2 | 2.3/2.3 | 30.4/6.3 | 4.5/2.9 | 35.0/7.8 | 4.2/1.7 | 8.5/4.6 | 1.9/2.0 | 26.0/8.6 | 5.8/4.0 | 11.7/4.6 | 1.8/1.9 |
| **Hematocrit** | 23.8/1.7 | 9.1/6.9 | 27.7/2.9 | 3.8/3.9 | 39.7/3.5 | 2.3/2.4 | 25.0/3.3 | 5.6/6.1 | 4.3/3.4 | 1.5/1.6 | N/A | N/A | 35.7/8.9 | 2.8/0.9 | 4.8/2.3 | 5.2/5.7 | 26.9/8.8 | 4.6/2.7 | 10.4/3.8 | 2.6/2.8 |
| **Red cell count** | 31.1/2.7 | 4.7/4.1 | 33.7/2.8 | 1.9/2.9 | 45.1/2.9 | 2.6/4.5 | 33.7/5.3 | 2.5/3.3 | 3.1/2.3 | 2.8/2.9 | 35.4/4.1 | 3.9/4.3 | 34.8/6.4 | 3.4/2.8 | 5.7/2.5 | 4.5/4.4 | 24.9/6.3 | 5.8/5.2 | 13.2/6.0 | 2.3/2.5 |
| **MCH** | 9.2/4.8 | 14.2/3.0 | 7.3/5.0 | 15.4/2.6 | 10.7/6.5 | 15.6/1.5 | 5.2/3.7 | 19.8/5.4 | 6.4/5.5 | 2.6/2.0 | 14.2/8.2 | 9.2/3.8 | 13.0/7.5 | 11.9/3.2 | 10.2/8.9 | 1.4/1.1 | 11.1/9.1 | 9.7/3.3 | 7.4/5.6 | 7.8/4.8 |
| **MCHC** | 18.2/9.2 | 1.1/0.7 | 17.0/6.8 | 2.0/1.2 | 9.3/2.1 | 0.9/0.6 | 8.5/4.6 | 0.9/0.5 | 3.9/3.6 | 1.2/1.2 | 15.9/8.8 | 3.2/3.3 | 4.1/2.1 | 3.1/3.1 | N/A | N/A | 3.8/3.2 | 3.7/2.0 | 2.5/2.0 | 0.1/0.1 |
| **MCV** | 2.9/1.7 | 23.1/6.4 | 3.2/2.7 | 22.4/5.1 | 5.2/3.9 | 18.4/1.4 | 2.6/2.0 | 23.2/6.7 | 5.1/4.4 | 2.2/1.9 | 6.7/5.0 | 9.0/2.5 | 9.4/5.5 | 6.7/0.9 | 3.8/3.2 | 6.3/5.9 | 8.1/6.4 | 6.0/1.7 | 3.8/2.5 | 5.3/3.9 |
| **RDW** | 0.8/0.7 | 32.5/9.9 | N/A | N/A | N/A | N/A | 4.7/8.2 | 49.7/12.1 | 1.3/1.7 | 22.3/23.0 | 1.1/0.9 | 32.9/8.1 | 0.6/1.1 | 33.2/8.0 | N/A | N/A | N/A | N/A | 0.5/0.4 | 17.1/11.2 |
| **Platelet count** | 26.2/4.4 | 4.5/2.1 | 20.8/2.5 | 8.6/5.4 | 38.0/4.4 | 4.8/2.6 | 23.6/4.5 | 5.8/3.3 | 3.5/2.8 | 3.5/3.0 | 20.5/4.2 | 5.8/2.9 | 29.4/5.0 | 5.2/2.7 | 3.6/2.7 | 4.0/3.6 | 19.6/5.3 | 6.5/5.1 | 9.8/5.7 | 4.3/2.8 |
| **White cell count** | 19.0/2.2 | 10.9/11.1 | 22.7/1.8 | 9.6/12.5 | 35.2/2.4 | 9.2/10.9 | N/A | N/A | 2.9/2.4 | 3.1/2.8 | 17.7/2.7 | 8.6/7.6 | 14.1/2.5 | 13.4/13.8 | 2.4/2.1 | 4.5/3.2 | 14.0/3.1 | 14.6/12.9 | N/A | N/A |

**Proportion of test results outside the generated reference intervals before and after filtering.** Center- and analyte-specific proportion of test results in the input dataset of test results below (columns < 2.5th) and above (columns > 97.5th) the respective percentiles from the generated reference intervals. Proportions are shown before and after removal of samples from patients with multiple measurements as described in the methods section.

**Supplemental Table 5**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Influence of filtering** | | | | | | | | **Influence of samples with other test results outside the reference limits** | | | | | | | | **Comparison to KiGGS** | | | |
|  | **age ≤ 100 days** | | | | **age > 100 days** | | | | **age ≤ 100 days** | | | | **age > 100 days** | | | |
|  | **2.5th** | | **97.5th** | | **2.5th** | | **97.5th** | | **2.5th** | | **97.5th** | | **2.5th** | | **97.5th** | | **2.5th** | | **97.5th** | |
|  | **abs.** | **rel.** | **abs.** | **rel.** | **abs.** | **rel.** | **abs.** | **rel.** | **abs.** | **rel.** | **abs.** | **rel.** | **abs.** | **rel.** | **abs.** | **rel.** | **abs.** | **rel.** | **abs.** | **rel.** |
| **Hemoglobin (g/dl)** | 1,3 | 14,9% | 0,2 | 1,8% | 0,5 | 3,2% | 0,1 | 0,7% | 0,2 | 1,7% | 0,1 | 0,9% | 0,1 | 0,8% | 0,1 | 0,7% | 0,2 | 1,4% | 0,5 | 3,1% |
| **Hematocrit (%)** | 2 | 8,0% | 0 | 0,0% | 1 | 2,6% | 0 | 0,0% | 0 | 0,0% | 0 | 0,0% | 1 | 2,6% | 0 | 0,0% | 0,7 | 0,7% | 1,2 | 2,7% |
| **Red cell count (10³/nl)** | 0,46 | 15,8% | 0,07 | 1,7% | 0,1 | 2,2% | 0,02 | 0,4% | 0,04 | 1,4% | 0,02 | 0,5% | 0,04 | 0,9% | 0,07 | 1,2% | 0,07 | 1,6% | 0,18 | 3,3% |
| **MCH (pg)** | 1,4 | 4,6% | 0,1 | 0,4% | 0,55 | 1,6% | 0,2 | 0,7% | 0,15 | 0,5% | 0,1 | 0,4% | 0,1 | 0,3% | 0,1 | 0,3% | 0,5 | 1,9% | 0,2 | 0,6% |
| **MCHC (g/dl)** | 1,9 | 6,1% | 0,5 | 1,6% | 0,9 | 2,4% | 0,1 | 0,3% | 0,1 | 0,3% | 0,1 | 0,3% | 0,1 | 0,3% | 0 | 0,0% | 0,1 | 0,4% | 1,2 | 3,4% |
| **MCV (fl)** | 0 | 0,0% | 0 | 0,0% | 5 | 4,9% | 1 | 1,1% | 0 | 0,0% | 0 | 0,0% | 0 | 0,0% | 0 | 0,0% | 2 | 2,1% | 0 | 0,4% |
| **RDW (%)** | 0,3 | 2,4% | 0 | 0,0% | 0,4 | 2,2% | 0,1 | 0,7% | 0,1 | 0,8% | 0 | 0,0% | 0,1 | 0,6% | 0,1 | 0,7% | N/A | N/A | N/A | N/A |
| **Platelet count (/nl)** | 25 | 11,3% | 10 | 5,7% | 22 | 3,5% | 6 | 1,4% | 3 | 1,5% | 3 | 1,9% | 9,5 | 1,6% | 5 | 1,2% | N/A | N/A | N/A | N/A |
| **White cell count (/nl)** | 0,2 | 3,6% | 0,1 | 2,4% | 1,2 | 7,1% | 0,3 | 2,7% | 0,2 | 3,1% | 0,1 | 2,1% | 0,3 | 1,8% | 0,2 | 1,7% | N/A | N/A | N/A | N/A |

**Analysis of influencing factors and comparison to the KiGGS study.** Median absolute and relative differences of 2.5th and 97.5th percentiles and reference intervals established without filtering, when samples from children with abnormal test results in other examined hematology are excluded, and comparison to the KiGGS study.