ZIMS Global Medical Resources- Expected Test Results

Local Reference Intervals in ZIMS

Reference Intervals:

"Reference intervals are health-associated benchmarks essential for the interpretation of quantitative laboratory test results by medical practitioners. An interval is formally defined as a statistically derived range of values determined from a reference interval study encompassing the central 95% of values from a healthy reference population. Biomarker test results lying outside of the reference interval suggest an abnormal result and as such, establishing accurate reference intervals is crucial to informed clinical decision-making."

Karbasy K, Ariadne P, Gaglione S, Nieuwesteeg M, Adeli K. Advances in Pediatric Reference Intervals for Biochemical Markers: Establishment of the Caliper Database in Healthy Children and Adolescents. Journal of Medical Biochemistry. 2015;34(1):23-30

ZIMS Global Reference Intervals:

ZIMS uses test result records entered by users around the world to calculate a global reference interval (or expected test results) for a specific combination of a test, sample type and species. When there is a larger amount of data, more specific reference intervals may be created, that also account for the subspecies, sex and/or the restraint method used during sampling. Millions of test results are processed and the end result of all these calculations is the ZIMS Expected Test Results resource, which has over 350,000 global reference intervals covering most of the common hematology and chemistry tests for over 1000 species. These global reference intervals provide essential diagnostic assistance to clinicians when they evaluate test results on their animals. The ZIMS data set currently grows by 5000-7000 test results *every day* and the global reference intervals are updated monthly to reflect the changing data set.

ZIMS Local Reference Intervals:

Local reference intervals are calculated in ZIMS by the same algorithm as global reference intervals, but using only test result data from your institution. This means that your local reference intervals reflect your data quality, data quantity and the laboratory results for the population of animals at your institution.

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Data quantity: the primary requirement for calculating a reference interval is a minimum of *40 local test results from animals with a normal health status at the time of sample collection*. Sample quality problems or outlier values can exclude some test result values from the calculations, increasing the number of local test results needed to obtain a reference interval.

Once the quantity goal is met, data quality becomes the most important factor in determining the usefulness of your local reference intervals. In theory, reference intervals calculated on a single population (animals at your institution), managed with the same husbandry methods, with more consistent sample collection and handling techniques and largely analyzed by the same laboratory will have a narrower width than the equivalent global reference interval and thus have improved diagnostic value. However, this outcome does assume equivalent data quality for the global and local data sets and that may not always be true. The large data set available at the global level allows statistical analysis to identify and remove outlier values ("bad data"); this process is less efficient with smaller local data sets for a single institution. Under these conditions, a single unusual data point that is discarded as an outlier value in the global calculations may be retained for the local calculations, producing a local reference interval that is actually wider than the global reference interval. If the test result causing this problem is a result of a data entry error, then correcting that error will improve the local reference interval at the next calculations. *There are multiple types of error that can occur:*

- *Incorrect health status*: If the animal was marked as healthy at the time of sample collection, but in fact was not healthy, then abnormal test results are being included in the calculations. Correct the health status for the date of sample collection to fix this data problem.
- *Incorrect sample type*: Sample type can impact some test results and if the wrong sample type was specified, the reference interval may not be valid. The quickest and easiest method to fix this error is to edit the sample record and check the box labeled "Exclude from reference intervals"
- *Incorrect test result entry*: Despite best efforts, typographical and other data entry errors will occur. If the original laboratory report is available, such errors can be corrected. If not, then this would be a time when it is acceptable to exclude that single test result from reference interval calculations.

Display of Local Reference Intervals in ZIMS:

Whenever a local reference interval is available, it always has a higher priority than any global reference interval in ZIMS. This means that when you review your test results, and a local reference interval is available for that sample type, species and test combination, then the local reference interval is displayed in the expected test results column and the high/low evaluations are based on that local reference interval. When no local reference interval is available for a test, you will continue to see the global reference interval that best matches species/subspecies, sample type, sex and restraint method for the patient in context. The result may be a mixture of local and global reference intervals within a single set of test result records.

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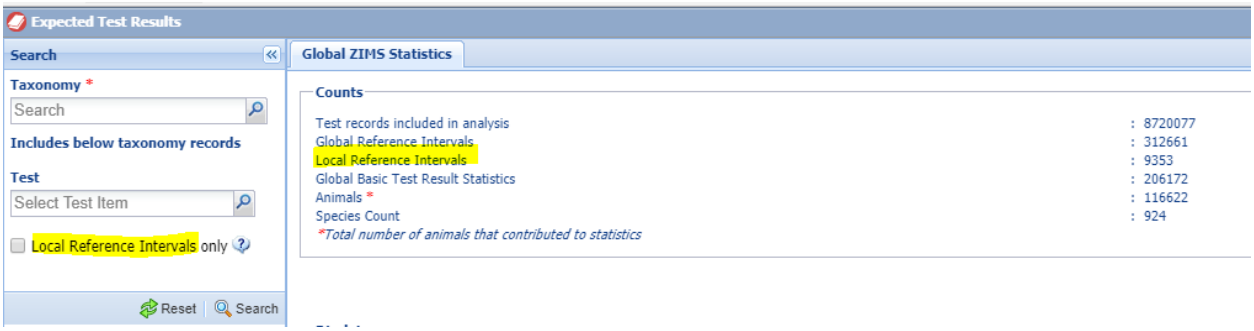
Test Requests & Test Results

Test	Results	Expected Results (Based on Best Available Match) Type: Min- Max | Mean [Median] N (Animals)
Anion Gap	16 mEq/L	Local RI: 14.0 - 25.0 | 18.0 [17.0] N=47 (22 animals)
GGT [a]	<3 U/L	Global sp RI: 0 - 9 | 3 [3] N=60 (34 animals)
Ca/Phos ratio [c]	2.70 ratio	Local RI: 1.8 - 6.0 | 2.9 [2.8] N=48 (23 animals)
BUN/Creat ratio [c]	33.70 ratio (US)	Local RI: 15.7 - 46.0 | 30.1 [28.6] N=50 (24 animals)
Na/K ratio [c]	37.30 ratio	Local RI: 30.3 - 39.4 | 35.4 [35.6] N=49 (23 animals)
Total Protein	6.4 g/dL	Local RI: 5.2 - 7.4 | 6.3 [6.3] N=52 (24 animals)
Glucose	111 mg/dL	Local RI: 95 - 168 | 118 [115] N=51 (25 animals)
BUN	27 mg/dL	Local RI: 14.0 - 48.5 | 24.4 [23.0] N=53 (25 animals)

Your local references intervals can also be viewed within the Expected Test results resource. They can be displayed along with the global reference intervals or the view can be filtered to show only the local data.



Calculating Local Reference Intervals in ZIMS:

To avoid over-loading the servers and slowing ZIMS for all users, Species360 staff must setup and schedule the job to calculate local reference intervals for an institution; this is **not** a process that users can initiate from within ZIMS. *The first calculation of local reference intervals will be done at no cost*, so that you can evaluate the reference intervals produced from your data. If you find the local reference intervals to be a significant improvement over global values, future recalculations can be performed allowing your local reference interval data set to grow as the number of test result records expand over time. These *additional local reference interval calculations will incur a service fee of $150 for each calculation event.* This allows each institution to choose a recalculation schedule that fits their budget and data needs. Complete and submit the Local Reference Interval Request Form to initiate the process. An email will be sent once your local reference interval calculations have been completed.

Improving Data Quality and Quantity:

As mentioned above, both data quantity and data quality are critical to producing good local reference intervals and both can be impacted by a number of factors. Quantity and quality are not completely independent factors, and improvements aimed at either factor can impact the other. Data entry time, local animal population size and laboratory resources can all impact the quantity of data in the system. We

recognize that when there are no resources available to enter test results, or your institution only holds a pair of leopards, it will be difficult to accumulate 40 results from healthy animals for any test. Under these conditions, the global reference intervals will continue to be the best resource available to you. For the vast majority of species held at member institutions, the global reference intervals will be the best information available; few published reference intervals for wildlife species will be based on larger data sets or will use better calculation techniques.

Once the data quantity requirement has been met, data quality becomes the factor that has the greatest impact on local reference intervals. Since the primary filter for the calculations is health status, having the correct health status has the single largest impact on local reference intervals. Leaving the health status of a healthy animal either undefined or set to anything other than Normal will exclude test results that otherwise should improve your local reference intervals. Conversely, marking an injured, sick or otherwise unhealthy animal as healthy will include those test results in the initial data set for the calculations, increasing the width of your local reference intervals. Sample quality (e.g., hemolysis and/or lipemia) is probably the next most important factor that will impact data quality; make sure that poor quality samples are correctly identified in the sample quality section of the sample record. Finally, review all your test panels to ensure that the tests run by your laboratory correctly match the test name and method used for data entry in ZIMS. If your laboratory is running automated white blood cell counts, then your results should be entered using the ZIMS test: *White Blood Cell count (automated)*. Entering your automated WBC count results using any of the manual methods for WBC count - *White Blood Cell count (Natt-Herrick.manual)*, *White Blood Cell count (indirect.manual)* or *White Blood Cell count (direct.manual)* – is detrimental to your data quality and negatively impacts the global data set. Similarly, if you are performing estimated WBC counts, there is a different test - *Estimated White Blood Cell count (manual)* – for entry of those results. We recognize that many laboratories do not clearly state the method they use when testing samples, but the method can make a huge difference and mixing results obtained using different methods is equivalent to the proverbial "comparing apples to oranges". If you have any questions about which ZIMS test name and method is appropriate for entering your laboratory results and the laboratory staff are not able to answer your questions, please contact support@species360.org and we will do our best to assist you with determining the correct ZIMS test to use for data entry.