| **Insulin-Like Growth Factor-1 (IGF-1)** |
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| **Purpose** | This procedure provides instructions for performing the INSULIN-LIKE GROWTH FACTOR-1 (Somatomedin C) assay on the IDS iSYS. |
| **Policy Statements** | This procedure applies to all personnel responsible for performing testing on the IDS iSYS. |
| **Principle** | The assay is based on chemiluminescence technology. 10 μL of patient sample are incubated with an acidic solution to dissociate IGF-I from the binding proteins. A portion of this, along with neutralization buffer is incubated with a biotinylated anti-IGF-I monoclonal antibody, and an acridinium labeled anti-IGF-I monoclonal antibody. Streptavidin labeled magnetic particles are then added. The magnetic particles are captured using a magnet and a wash step performed to remove any unbound analyte. Trigger reagents are added; the resulting light emitted by the acridinium label is directly proportional to the concentration of IGF-I in the original sample. |
| **Clinical Significance** | Insulin-like growth factor-I (IGF-I) is a polypeptide of 70 amino acids (7650 Daltons), and is one of a number of related insulin like growth factors present in the circulation. The molecule shows approximately 50% sequence homology with proinsulin and has a number of biological activities similar to insulin. The peptide is growth hormone (GH) dependent to a high degree, but there is growing evidence of GH-independent secretion. IGF-I has numerous growth-promoting effects, including mitogenic effects and the promotion of cartilage sulphation. It also mediates growth promoting actions of growth hormone on skeletal and other body tissues. Almost all (>95%) of serum IGF-I circulates bound to specific IGF binding proteins, of which six classes (IGFBPs 1-6) are now recognized. IGFBP-3 is thought to be the major binding protein of IGF-I, forming a ternary complex of 140 000 Daltons with IGF-I and an acid labile subunit. The measurement of serum IGF-I is of recognized value in children with growth disorders and in the diagnosis and monitoring of acromegaly. IGF-I concentrations change with age, nutritional status, body composition and GH secretion. A single basal IGF-I determination is useful in the assessment of short stature in children and in nutritional support studies of acutely ill patients. For the diagnosis of acromegaly, a single IGF-I determination is considered more reliable than a random GH determination. |
| **Instrument** | **PRIMARY METHOD: IDS iSYS****BACKUP METHOD: Mayo Medical Laboratories (IGFP)** |
| **Sunquest Test Code** | INGF1 |
| **Specimen** | **Sample type: Preferred: Red No Gel**Also acceptable: Green No Gel**Preferred Draw Volume**: 1.8 mL (minimum 0.6 mL)**Preferred Sample Volume:** 0.6 mL (minimum 0.2 mL) Note: minimum volume does not allow for repeat testing.**Stability When Separated Within 1 Hour of Draw:** Stable 24 hours at Room Temperature, 48 hours at 2-8°C, 4 weeks frozen at -20°C**Shipping Temperature:** Draw sites other than Minneapolis should ship samples frozen.**Rejection criteria:** Unlabeled specimens, incorrect sample type, samples from patients currently receiving biotin supplementation.**Preparation:** 1. Serum specimens should be centrifuged following complete clot formation, according to Specimen Processing procedures prior to analysis. Plasma samples may be centrifuged immediately.
2. Serum or plasma should be physically separated from cells as soon as possible with a maximum limit of one hour from the time of collection.
3. Lipemic samples should be ultrafuged.
4. Specimens must be be free of particulate matter.
5. Thawed samples must be completely thawed and fully mixed by end to end inversion several times to ensure homogeneity prior to testing.
6. Transfer serum or plasma to a properly labeled sendout tube. Minimum labeling includes sample accession ID, and/ or patient name, medical record number, collection date and time.
7. Sample volume less than 500 uL should be transferred to an iSYS sample cup by the tech performing the testing. Sample cups must be properly labeled at all times, as described in step 5.
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| **Reagents** |

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| ***Product Description*** | ***Product*** | ***Stability*** |
| IDS iSYS IGF-1 Reagent  |  IS-3900 | **Store at:** 2 – 8 °C**Unopened:** Manufacturer expiration date.**Open:** 28 Days**On-board:** 10 Days |
| IDS iSYS IGF-1 Calibrator (Included in Reagent kit) | IS-3900 | **Store at:**  -20°C once reconstituted**Unopened**: Manufacturer expiration date.**Reconstituted:** 7 weeks frozen**On Board:** 3 hours**Instructions:** Reconstitute with 1.0 mL of DI water. Replace. Let sit for 10 minutes, swirling occasionally by hand. If frozen in aliquots, calibrator must be put in the freezer within 15 minutes of reconstitution. Freeze only once. When thawed, must be at room temperature prior to testing and must be tested within 30 minutes of thaw. |
| IDS iSYS IGF-1 Quality Control Materials  | IS-3930  | **Store at:** 2 – 8 °C**Instructions:**  Add 1.0 mL of distilled or deionized water to each vial. Replace the stopper. Leave for 10 minutes to reconstitute with occasional gentle mixing by hand. Avoid formation of foam.Aliquot and store at -20°C or lower within 15 minutes of reconstitution. When re-using frozen controls, thaw at room temperature and mix well. Ensure that controls are at room temperature before they are placed on the machine. Controls should be placed on the machine within 30 minutes of thawing. Aliquots should not be re-frozen.**Open Stability:** After reconstitution, 7 weeks at -20°C**Onboard**: 3 hours |
| IDS-iSYS Cuvettes  | IS-CC100 |  |
| System Liquid  | IS-CS100 | **Store at:** 15-25°C **Open Stability:** Managed by System Software |
| Wash Solution  | IS-CW100 | **Store at:** 15-25°C **Open Stability:** Managed by System Software |
| IDS-iSYS Triggers Set (A and B)  | IS-CT100 | **Store at:** 15-25°C **Open Stability:** Managed by System Software |
| Cartridge Check System  | IS-6010 | **Store at:** 2-8°C**Unopened Stability:** Until Manufacturer Expiration Date**Open Stability:** 9 weeks**Open and loaded on the Analyzer:** 8 weeks |
| D-SORB solution  | IS-DS200 | **Store at:** 15-25°C**Open Stability:** Managed by System Software |
| IDS iSYS IGF-1 Calibration Verifiers | IS-3935 | **Store at**: 2-8°C**Stability**: Manufacturer Expiration Date**Onboard the Analyzer**: 2.5 Hours |

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| **Risk and Safety:** | Contains sodium azide. Avoid contact with skin and eye. Causes serious eye irritation. Wear gloves. Contact with acids liberates very toxic gas. Dispose of in appropriate Hazardous Waste Containers:* **IGF-1 Control Set A, B, C**: if remaining product, dispose of in dual waste (hemocue waste).
* **IGF-1 Calibrators A and B**: If remaining product, dispose of in dual waste (hemocue waste.)
* **Trigger A**: Recap and dispose of in Hazardous Acid waste container (acid flex waste.)
* **Trigger B**: Recap and dispose of in Hazardous Basic/Caustic waste container (base flex waste.)
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| Calibration Verification/AMR |

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| Analytical Measuring Range: | 10-1200 ng/mL |
| Reference Material: | IDS iSYS IGF-1 Calibrators: included in the Reagent Kit (IS-3900) |
| Approximate Calibration Levels | A – 22.7 ng/mLB – 576.0 ng/mL |
| Calibration Scheme: | n=2 |
| Calibration Frequency: | * Calibration of assay is performed every 10 days
* For each new lot of reagent
* After major maintenance or service, if indicated by quality control results
* As indicated in laboratory quality control procedures
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| AMR | Verification of AMR is accomplished with the IGF-1 Calibration Verifier materials and entering the results into EP Evaluator. Results are reviewed by the Technical Specialist for acceptability.* Cal Verification and AMR verification are performed at least once every six (6) months.
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| **Quality Control** | **IDS iSYS IGF-1 Control Set, Levels 1, 2, 3****Frequency:** 3 Levels, once per shift of use (day and evening shift)**Stability:** 7 weeks frozen in aliquots at -20°C**,** 3 hours onboard.**Preparation**: Add 1.0 mL of distilled or deionized water to each vial. Replace the stopper. Leave for 10 minutes to reconstitute with occasional gentle mixing by hand. Avoid formation of foam.Aliquot and store at -20°C or lower within 15 minutes of reconstitution. When re-using frozen controls, thaw at room temperature and mix well. Ensure that controls are at room temperature before they are placed on the machine. Controls should be placed on the machine within 30 minutes of thawing. Aliquots should not be re-frozen. **Sunquest Control names:** Level 1 = C-IGF11, Level 2 = C-IGF12, Level 3= C-IGF13Instrument Method Code: ISYS**Acceptable ranges:** * Ranges are current in Sunquest and the instrument. Refer to the Quality Control in Chemistry procedure for QC exception codes.
* If a control value is outside the confidence interval, the determination must be repeated. If the repeat determination confirms the deviation, a new reference curve should be established.
* Do not release patient results until the cause of deviation has been identified and corrected
* When a new lot of assayed control is received, validate the manufacturer’s insert range by running the new lot in parallel with the current lot, and confirming that the results obtained are within the stated range
* When a new lot of unassayed control is received, verify new ranges by running the new lot in parallel with the current lot 20 times, and calculate a new range using the method mean ± 2 SD. Ranges are current in Sunquest and the instrument. Refer to the Quality Control Procedure for QC exception codes.
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| **Interferences** | * Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed.
* Biotin interferes with this assay and is not appropriate for patients receiving biotin supplementation. Allow at least 24 hours post-supplementation of biotin-containing medication before testing.
* The IDS iSYS analyzer does not contain a level-sensing mechanism. Therefore, every sample must be checked for bubbles or fibrin prior to loading the sample on the analyzer. Any questionable results must be checked by repeat after rechecking the sample for the presence of these testing interferences.

**Interfering Substances:** The following substances do not interfere with the assay when the concentrations are below the stated threshold:Lipid 3000 mg/dLBilirubin 20 mg/dLHemoglobin 500 mg/dLBiotin 300 nmol/LIGFBP1 5000 ng/mLIGFBP2 5000 ng/mLIGFBP3 20000 ng/mLIGFBP4 5000 ng/mLIGFBP5 5000 ng/mLIGFBP6 5000 ng/mL |
| **Reference Intervals** |

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| IGF-1 Reference Intervals, ng/mL |
| Age | Male | Female |
| 0-11 mo | 27-166 | 18-130 |
| 1y | 30-175 | 20-138 |
| 2y | 34-194 | 22-154 |
| 3y | 39-215 | 26-175 |
| 4y | 44-235 | 31-201 |
| 5y | 50-256 | 36-227 |
| 6y | 56-279 | 42-254 |
| 7y | 63-306 | 49-286 |
| 8y | 72-341 | 57-326 |
| 9y | 84-384 | 67-374 |
| 10y | 97-431 | 80-427 |
| 11y | 112-477 | 93-477 |
| 12y | 126-517 | 105-518 |
| 13y | 139-544 | 116-545 |
| 14y | 148-554 | 123-555 |
| 15y | 152-554 | 127-554 |
| 16y | 152-542 | 127-542 |
| 17y | 149-521 | 123-517 |
| 18y | 143-494 | 118-486 |
| 19y | 137-463 | 111-451 |
| 20y | 129-430 | 105-416 |
| 21-25y | 106-414 | 86-383 |
| 25-35y | 86-309 | 70-296 |
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| Tanner Stages | Male | Female |
| I | 81-255 | 86-323 |
| II | 106-432 | 118-451 |
| III | 245-511 | 258-529 |
| IV | 223-578 | 224-586 |
| V | 227-518 | 188-512 |

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| **Critical Values** | None specified. |
| **Limitations** | * The instrument reporting system contains error messages to warn the operator of specific malfunctions. Refer to Operator’s Manual for troubleshooting specific error messages.
* This assay is affected by biotin interference. See interfering substances for more information.
* As in the case of any diagnostic procedure, results must be interpreted in conjunction with the patient’s clinical presentation and other information available to the physician.
* The hook effect was tested using concentrations of IGF-I up to 20000 ng/mL. No hook effect was observed.
* Partially thawed or improperly mixed samples will give erroneous results.

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| **Dilutions** | Do Not Dilute. |
| **Result Reporting** | 1. In OEM, enter method code ISYS to review all results.
2. Results will show reference interval flags based on the physical age of the child. Tanner Stage Reference Intervals will append to each result based on the patient sex.
3. Results <10 ng/mL are reported as <10 ng/mL, rather than the numerical value.
4. Results >1200 ng/mL are reported as >1200 ng/mL, rather than the numerical value.
5. Any result below 30 ng/mL must be repeated after physically checking the sample
6. The sample of any questionable result must be checked and the test repeated prior to resulting.
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| **Specimen Storage** | After testing completion, samples are moved within 8 hours to the Special Chemistry freezer where they are stored for 2 weeks.  |
| **References** | 1. IDS iSYS IGF-1 Reagent Package Insert, Immunodiagnostic Systems Limited, Gaithersburg, MD. IS-3900 v7 updated August 17, 2017.
2. Bidlingmaier M, Friedrich N, Emeny RT, et al. Reference Intervals for Insulin-like Growth Factor-1 (IGF-1) From Birth to Senescence: Results From a Multicenter Study Using a New Automated Chemiluminescence IGF-1 Immunoassay Conforming to Recent International Recommendations. J Clin Endocrinol Metab. 2014; 99(5): 1712-21.
3. IDS-iSYS User Manual - Revision M1 IA, Software version V 14.
4. IDS iSYS IGF-1 Calibration Verifiers Package Insert, Immunodiagnostic Systems Limited, Gaithersburg, MD. IFU Version: 04 27 August 2014
5. IDS-iSYS Insulin like Growth Factor–I (IGF-I) Control Set Package Insert, Immunodiagnostic Systems Limited, Gaithersburg, MD IFU Version: (USA) 23 March 2011 V01
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| **Historical Record** |

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| **Version** | **Written/Revised By** | **Effective Date** | **Summary of Revisions** |
| 1 | Erin Bartos | 6/19/2018 | New Procedure |
| 2 | Erin Bartos | 6/25/2018 | Updated Backup Method to MML |
| 3 | Erin Bartos | 7/9/2018 | Added language regarding thawed samples, fully mixing, checking samples for questionable results, and repeating test results below 30 ng/mL. |

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