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Changes: § 1, 4, 7, 8, 10, 11, 13, 14, 15
Deletions: § 8, 10, 12

LIAISON® IGF-I (REF 313231)

1. INTENDED USE

In vitro assay for the quantitative determination of IGF-I (Insulin-like Growth Factor I) in human serum. The test has to be performed on the LIAISON® Analyzer family*.

2. SUMMARY AND EXPLANATION OF THE TEST

Insulin-like growth factor-I (IGF-I, also referred to as somatomedin-C or Sm-C) is a single-chain polypeptide of 70 amino acids. It is a trophic factor that circulates at high levels in the blood stream and mediates many, if not most, of the effects of growth hormone. Although the main source of IGF-I in the blood is the liver, which is rich in GH receptors, many other tissues synthesize it and are sensitive to its trophic action. IGF-I and insulin have similar 3-dimensional structures.
IGF-I is one of a class of peptides whose serum concentrations are stimulated principally by human growth hormone (GH) and retarded by malnutrition. In humans, 2 peptides have been identified: IGF-I and IGF-II. Much of the GH-dependent, growth-promoting activity in serum is due to IGF-I. The anabolic and growth promoting effects mediated by the IGFs include cell proliferation and protein synthesis.
Almost every cell in the human body is affected by IGF-I, especially cells in muscle, bone, liver, kidney, nerves, skin, and lungs. In addition to the insulin-like effects, IGF-I can also regulate cells growth and development, especially in nerve cells, as well as cellular DNA synthesis. IGF-I is produced throughout life. The highest rates of IGF-I production occur during the pubertal growth spurt. The lowest levels occur in infancy and old age.
IGF-I appears to influence neuronal structure and functions throughout the life span. It has been shown to have the ability to preserve nerve cell function and promote nerve growth in experimental studies. Because of these properties, recombinant human IGF-I is used in clinical trials for the treatment of amyotrophic lateral sclerosis (ALS).
Recently, recombinant human IGF-I has entered the dietary supplement market place, as have recombinant human growth hormone and several so-called growth hormone secretagogues or releasers.
Supplemental IGF-I has putative anabolic and lipolytic activities with an unknown action.
In blood, IGFs are bound to carrier. The binding proteins are undoubtedly responsible for the relatively high concentrations of IGF-I in blood and for lack of rapid levels fluctuations. This relative stability of IGF-I blood concentrations makes IGF-determination a reliable indicator of GH output, whereas GH levels themselves vary considerably and often requires provocative testing to be interpreted.
Use as a diagnostic test
IGF-I levels can be measured in the blood from 10-1000 ng/mL amounts.
As levels do not fluctuate greatly throughout the day, physicians use IGF-I as a screening test for growth hormone deficiency and excess.
IGF-I as a therapeutic agent
IGF-I has been implicated as a possible neuroprotective agent in fighting the adverse effects of amyotrophic lateral sclerosis (ALS).
Claims for supplemental IGF-I include anti-aging, promotion of lean muscle mass, enhanced athletic and sexual performance, joint protection, anti-diabetic and anti-atherosclerotic effects, sleep aid, immune enhancer, neuroprotector and much more. There is no credible evidence to support these claims for oral IGF-I. High levels of IGF-I have been associated with elevated risk of several cancers, especially prostate cancer.
Low levels:
IGF-I values are consistently low in children with **GH deficiency (hypopituitarism)** and rise with GH injections. In general, normal concentration in a short child is strong evidence against the diagnosis of GH deficiency, particularly when the patient is 5-6 years old; at this time abnormally low values can be discriminated from normal.
Serum levels may be low in **GH-deficient children** who have a craniopharyngioma. Although a normal value suggests that GH deficiency is not present, a low value in a growth-retarded child is not diagnostic of hypopituitarism.
Increased levels:
Serum IGF-I concentrations are reliably and predictably elevated in patients with **acromegaly** and in **children with gigantism** due to excess of pituitary GH.
Care should be taken in interpretation of elevated IGF-I serum values in pubertal patients, however, because levels are normally increased at this time and may be as much as 4-5 times adult concentration.
Pregnancy is also associated with high serum levels.
Rare diseases characterized by inability to make, or respond to, IGF-I produce a distinctive type of growth failure termed Laron dwarfism which does not respond well to growth hormone treatment.

3. PRINCIPLE OF THE PROCEDURE

The method for the quantitative determination of IGF-I is a one-step sandwich chemiluminescence immunoassay (CLIA), after prior separation of IGF-I from binding proteins. A monoclonal antibody is used for coating magnetic particles (solid-phase) and another monoclonal antibody is linked to an isoluminol derivative (isoluminol-antibody conjugate).
During the incubation, IGF-I present in calibrators, samples or controls binds to the solid phase as well as to the conjugate.
After the incubation, the unbound material is removed with a wash cycle.
Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced.
The light signal, and hence the amount of isoluminol conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of IGF-I concentration present in calibrators, samples or controls.

*(LIAISON®, LIAISON® XL and LIAISON® XS)

4. MATERIALS PROVIDED

The order of reagents reflects the layout of containers in the reagent integral.

Reagent Integral for 100 determinations			
2.3	mL	SORB	Magnetic particles suspension: containing magnetic particles coated with anti-IGF-I (6B), monoclonal (mouse), BSA, 0.09% sodium azide
12.0	mL	CONJ	Conjugate: containing anti-IGF-I (2D 557112), labelled with isoluminol derivative, monoclonal (mouse), BSA, 0.09% sodium azide
18.0	mL	BUF N	Neutralisation buffer: containing IGF-II (human, recombinant), BSA, 0.09% sodium azide
28.0	mL	BUF Ac	Acidification solution: containing 0.01 Mol HCl

All components are provided ready-to-use.

Included with Integral

3	x 1.0	mL	CAL 1	Calibrator low: containing IGF-I (human, recombinant) in BSA, 0.1% ProClin® 300
3	x 1.0	mL	CAL 2	Calibrator high: containing IGF-I (human, recombinant) in BSA, 0.1% ProClin® 300
8	x white		CAL 1 Barcode label, small	For labeling the aliquoted calibrator tubes
8	x white		CAL 2 Barcode label, small	For labeling the aliquoted calibrator tubes

Calibrators are provided lyophilized.

Materials required but not provided (system related)

LIAISON® XL Analyzer	LIAISON® Analyzer
LIAISON® Wash/System Liquid (REF 319100)	LIAISON® Wash/System Liquid (REF 319100)
LIAISON® XL Waste Bags (REF X0025)	LIAISON® Waste Bags (REF 450003)
LIAISON® XL Cuvettes (REF X0016)	LIAISON® Module (REF 319130)
LIAISON® XL Starter Kit (REF 319200) or	LIAISON® Starter Kit (REF 319102) or
LIAISON® EASY Starter Kit (REF 319300)	LIAISON® XL Starter Kit (REF 319200) or
LIAISON® XL Disposable Tips (REF X0015) or	LIAISON® EASY Starter Kit (REF 319300)
LIAISON® Disposable Tips (REF X0055)	LIAISON® Cleaning Kit (REF 310990)
	LIAISON® Light Check 12 (REF 319150)

LIAISON® XS Analyzer
LIAISON® EASY Wash Buffer (REF 319301)
LIAISON® EASY System Liquid (REF 319302)
LIAISON® EASY Waste (REF X0054)
LIAISON® Cuvettes on Tray (REF X0053)
LIAISON® EASY Starter Kit (REF 319300)
LIAISON® Disposable Tips (REF X0055)
LIAISON® EASY Cleaning Tool (REF 310996)

Additionally required materials

LIAISON® IGF-I Control (REF 319134)

5. WARNINGS AND PRECAUTIONS

For *in vitro* diagnostic use only.
As, however, no absolute assurance can be given that pathogens are absent, all components of human and animal origin should be considered potentially infectious and handled with care.

6. SAFETY PRECAUTIONS

Do not eat, drink, smoke or apply cosmetics during the assay.
Do not pipette by mouth.
Avoid direct contact with all potentially infectious materials by wearing laboratory clothing, protective goggles and disposable gloves.
Wash hands thoroughly at the end of each assay.
Avoid splashing or forming an aerosol. Any drops of biological reagent must be removed with a sodium hypochlorite solution with 0.5% active chlorine, and the means used must be treated as infected waste.
All samples and reagents containing biological materials used for the assay must be considered potentially able to transmit infectious agents; the waste must be handled with care and disposed of in compliance with the laboratory guidelines and the statutory provisions in force in each country.
Any materials for reuse must be appropriately sterilized in compliance with the local laws and guidelines.
Check the effectiveness of the sterilization/decontamination cycle.
Do not use kits or components beyond the expiration date given on the label.

Reagents containing sodium azide (< 0.1%) [EC no: 247-852-1]:

DIRECTIVE	**EC No. 1272/2008**
HAZARD / RISK STATEMENTS	**EUH 210 -** Safety data sheet available on request

Reagents containing ProClin®:

DIRECTIVE	**EC No. 1272/2008**
REAGENTS	CAL 1 CAL 2
CLASSIFICATION OF SUBSTANCE	Skin sensitizer, Category 1
SIGNAL WORD	Warning!
SYMBOLS / PICTOGRAMS	 GHS07 - Exclamation mark
HAZARD / RISK STATEMENTS	H317 - May cause an allergic skin reaction.
PRECAUTIONARY / SAFETY STATEMENTS	P261 - Avoid breathing mist or spray. P280 - Wear protective gloves and clothing and eye protection. P363 - Wash contaminated clothing before reuse
CONTAINS: (only substances prescribed pursuant to Article 18 of EC Regulation 1272/2008).	reaction mass of: 5-chloro-2-methyl-4-isothiazolin-3-one [EC no. 247-500-7] and 2-methyl-2H -isothiazol-3-one [EC no. 220-239-6] (3:1) (ProClin® 300).

7. REAGENT PREPARATION

7.1. Reagent Integral

Please note the following important reagent handling precautions:

To ensure proper assay performance carefully rotate or turn upside-down the integral before placing on the analyzer. Please ensure that any eventually present flocculation in the integral reagents is vanished prior to placing the integral on board the analyzer. Avoid formation of foam.

Resuspension of magnetic particles

Magnetic particles must be completely resuspended before the integral is placed on the instrument. Follow the steps below to ensure complete suspension:

Before the seal is removed, rotate the small wheel at the magnetic particle compartment until the colour of the suspension has changed to brown. Gentle and careful side-to-side mixing may assist in the suspension of the magnetic particles (avoid foam formation). Visually check the bottom of the magnetic particle vial to confirm that all settled magnetic particles have resuspended. Repeat as necessary until the magnetic particles are completely resuspended. After removal of the seal carefully wipe the surface of each septum to remove residual liquid if necessary.

Foaming of reagents

In order to ensure optimal performance of the integral, foaming of reagents should be avoided. Adhere to the recommendation below to prevent this occurrence:

Visually inspect the reagents, calibrators in particular to ensure there is no foaming present before using the integral. If foam is present after resuspension of the magnetic particles, place the integral on the instrument and allow the foam to dissipate. The integral is ready to use once the foam has dissipated and the integral has remained onboard and mixing.

Loading of integral into the reagent area

LIAISON® Analyzer

Place the integral into the reagent area of the analyzer with the bar code label facing left and let it stand for 30 minutes before using. The analyzer automatically stirs and completely resuspends the magnetic particles.

Follow the analyzer operator's manual to load the specimens and start the run.

LIAISON® XL Analyzer and LIAISON® XS Analyzer

LIAISON® XL Analyzer and LIAISON® XS Analyzer are equipped with a built-in solid-state magnetic device which aids in the dispersal of microparticles prior to placement of a reagent integral into the reagent area of the analyzer. Refer to the analyzer operator's manual for details.

Insert the reagent integral into the dedicated slot.

Allow the reagent integral to remain in the solid-state magnetic device for at least 30 seconds (up to several minutes). Repeat as necessary.

Place the integral into the reagent area of the analyzer with the label facing left and let it stand for 15 minutes before using. The analyzer automatically stirs and completely resuspends the magnetic particles.

Follow the analyzer operator's manual to load the specimens and start the run.

7.2. Calibrators

LIAISON® IGF-I calibrators are supplied lyophilized.

Reconstitute with 1.0 mL deionized or distilled water.

Allow the vials to stand for 10 minutes at approximately 18-25 °C.

Mix thoroughly by gentle inversion, avoid foaming.

If necessary, aliquot the calibrators as directed in paragraph 8 and label the tubes with the provided small white labels.

For details on the use of the calibrators, refer to the analyzer operator's manual.

Refer to paragraph 8 to store the calibrators.

7.3. Controls

Refer to the LIAISON® IGF-I Control Set instructions for use section for proper preparation and handling instructions.

8. REAGENT STORAGE AND STABILITY

8.1. Reagent integral

Sealed: Stable at 2-8 °C until the expiry date.
Opened: onboard or at 2-8 °C: Stability four (4) weeks.
After this period, it is still possible to keep on using the reagent integral provided that the controls are found within the expected ranges.
Use always the same LIAISON® Analyzer for a reagent integral already opened.
Do not freeze.
Keep upright for storage to facilitate later proper resuspension of magnetic particles.
Use storage rack provided with the LIAISON® Analyzer family for upright storage of reagent integral.
Keep away from direct light.

8.2. Calibrators

Lyophilized: Stable at 2-8 °C until the expiry date.
Reconstituted: Stable for 1 day on the analyzer.
Frozen: Aliquots can be stored at -20 °C for up to one month.
Immediately after complete reconstitution it is possible to aliquot the calibrators and deep-freeze them. After thawing the calibrators must be used up in the same day. The minimum volume of the aliquot is 210 µL (60 µL calibrator + 150 µL dead volume).
Only one freeze and thaw cycle is allowed for each aliquot.
During handling, use appropriate precautions to avoid bacterial contamination of calibrators.

9. SPECIMEN COLLECTION AND PREPARATION

The only sample material validated is human serum.
Collect serum according to established methods. Avoid haemolysis. Carefully thaw before testing, mix the thawed samples and check for and remove air bubbles before assaying. Thawed samples kept at 2-8 °C must be used within 6 hours.
If the test is not performed on the day of sample collection, the serum should be separated from the sediment and be stored in a separate tube at -20 °C.
Grossly haemolyzed or lipaemic samples as well as samples containing particulate matter or exhibiting obvious microbial contamination should not be tested.
Do not use clotted samples.
Avoid repeated freeze and thaw cycles. Dispose of any left aliquot volume.
The minimum volume required for a single determination is 170 µL specimen (20 µL specimen + 150 µL dead volume).
The acidification solution provided in the integral is validated for predilution only. No diluent is provided for specimens with concentrations above the assay range.

10. CALIBRATION

Test of assay specific calibrators allows the detected relative light units (RLU) values to adjust the assigned master curve. Up to 11 calibrations can be performed (in total).

Calibrators must be used only with the reagent integral lot they are matched with. Do not use calibrators matched with a different reagent integral lot in the same assay. For correct lot matching, calibrator lot number is printed also on the reagent integral label.

Recalibration in triplicate is mandatory whenever at least one of the following conditions occurs:

- A new lot of reagent integral or of Starter Kit is used.
- The previous calibration was performed more than fourteen (14) days before.
- The analyzer has been serviced.
- Control values lie outside the expected ranges.

LIAISON® Analyzer: Calibrator values are stored in the barcodes on the integral label.
LIAISON® XL Analyzer: Calibrator values are stored in the reagent integral Radio Frequency IDentification transponder (RFID Tag).
LIAISON® XS Analyzer: Calibrator values are stored in the reagent integral Radio Frequency IDentification transponder (RFID Tag).

11. ASSAY PROCEDURE

Strict adherence to the analyzer operator's manual ensures proper assay performance.
LIAISON® Analyzer: Each test parameter is identified via barcodes on the reagent integral label. In the event that the barcode label cannot be read by the analyzer, the integral cannot be used. Do not discard the reagent integral; contact your local DiaSorin technical support for instruction.
LIAISON® XL Analyzer and LIAISON® XS Analyzer: Each test parameter is identified via information encoded in the reagent integral Radio Frequency Identification Transponder (RFID Tag). In the event the RFID Tag cannot be read by the analyzer, the integral cannot be used. Do not discard the reagent integral; contact your local DiaSorin technical support for instruction.

The LIAISON® Analyzer operations are as follows:

Automatic pre-treatment (1:20)
1. Dispense sample or controls into the Reaction Module
2. Dispense acidification solution
3. Dispense diluted sample, diluted controls or calibrator into the Reaction Module
4. Dispense coated magnetic particles (Solid Phase), neutralisation buffer and conjugate
5. Incubate
6. Wash with LIAISON® Wash/System Liquid
7. Add the Starter reagent and measure the light emitted

The LIAISON® XL Analyzer operations are as follows:

Automatic pre-treatment (1:20)
1. Dispense sample or controls into the Reaction Cuvette
2. Dispense acidification solution
3. Dispense neutralisation buffer, coated magnetic particles (Solid Phase) and conjugate
4. Dispense diluted sample, diluted controls or calibrator into the Reaction Cuvette
5. Incubate
6. Wash with LIAISON® Wash/System Liquid
7. Add the Starter reagent and measure the light emitted

The LIAISON® XS Analyzer operations are as follows:

Automatic pre-treatment (1:20)
1. Dispense sample or controls into the Reaction Cuvette
2. Dispense acidification solution
3. Dispense neutralisation buffer, coated magnetic particles (Solid Phase) and conjugate
4. Dispense diluted sample, diluted controls or calibrator into the Reaction Cuvette
5. Incubate
6. Wash with LIAISON® EASY Wash Buffer
7. Add the Starter reagent and measure the light emitted

12. QUALITY CONTROL

LIAISON® controls should be run in singlicate to monitor the assay performance. Quality control could be performed by running the LIAISON® control sera or dedicated commercial controls:
- at least once per day of use,
- whenever a new reagent integral is used,
- whenever the kit is calibrated,
- whenever a new lot of Starter Reagents is used,
- or in agreement with guidelines or requirements of local regulations or accredited organizations.

Control values must lie within the expected ranges: whenever one of the controls lies outside the expected ranges, calibration should be repeated and controls retested. If control values obtained after successful calibration lie repeatedly outside the predefined ranges, the test should be repeated using an unopened control vial. If control values lie outside the expected ranges, patient results must not be reported.
The performance of other controls should be evaluated for compatibility with this assay before they are used. Appropriate value ranges should then be established for quality control materials used.

13. INTERPRETATION OF RESULTS

The analyzer automatically calculates IGF-I concentrations for the unknown samples in ng/mL. For details, refer to the LIAISON® operator's manual.
Calibrators and controls may give different RLU or dose results on LIAISON® and LIAISON® XL and LIAISON® XS, but patient results are equivalent.

13.1. Assay range:

The analyzer directly calculates IGF-I concentration up to 1,500 ng/mL.

Conversion factor:

1	ng/mL	x	0.13	=	0.13	nmol/L
1	nmol/L	x	7.69	=	7.69	ng/mL

13.2. Reference standard

The assay is referenced to the 1st WHO International Standard for Insulin-like Growth Factor-I NIBSC code: 02/254. The results are expressed in ng/mL.

13.3. Reference range

To determine basal reference ranges by age and gender, a study was performed with LIAISON IGF-I on 4419 specimens (2813 paediatric and 1606 adult patients) from an apparently healthy population.
The central 95% range values were established following CLSI guideline C28-A3 and applying centile smoothing Royston-Wright method. The results are expressed as ng/mL and fully reported in paragraph 15.11. tables and graphs.
It is recommended that each laboratory establishs its own range of expected values for the population taken into consideration.

14. LIMITATIONS OF THE PROCEDURE

The reagents should be used only in the LIAISON® Analyzer family.
Single components of the reagent integral should not be removed from the integral.
This kit must not be used after the expiry date printed on the package label.
A skilful technique and strict adherence to the instructions are necessary to obtain reliable results.
Bacterial contamination or heat inactivation of the specimens may affect the test results.
A non-pathological result does not always rule out the presence of growth dysfunction and should be interpreted together with other diagnostic procedures.
Test results are reported quantitatively. However, diagnosis of a growth disease should not be based on the result of a single test, but should be determined in conjunction with clinical findings in association with medical judgement. Any therapeutically decision must also be taken on a case-by-case basis.
Although HAMA-neutralizing agents are added, extremely high HAMA (human anti-mouse antibodies) concentrations may occasionally influence results.
Integrals may not be exchanged between analyzer types (LIAISON® and LIAISON® XL and LIAISON® XS). Once an integral has been introduced to a particular analyzer type, it must always be used on that analyzer until it has been exhausted. Due to traceability issues resulting from the above statement, patient follow-ups may not be concluded between analyzer types. These must be accomplished on one particular analyzer type (either LIAISON® or LIAISON® XL or LIAISON® XS).

15. SPECIFIC PERFORMANCE CHARACTERISTICS

15.1. Analytical specificity

Analytical specificity may be defined as the ability of the assay to accurately detect specific analyte in the presence of potentially interfering factors in the sample matrix

15.2. Interference

Controlled studies of potentially interfering substances or conditions showed that the assay performance was not affected by concentrations of bilirubin < 0.2 mg/mL, haemoglobin < 1000 mg/dL or triglycerides < 30 mg/mL.

15.3. Cross-reactions

Controlled studies of potentially interfering substances showed no interference at the concentration for each substance listed below in the LIAISON® IGF-I assay.

Substances	Tested concentration
Triglycerides	3,000 mg/dL
Hemoglobin	1,000 mg/dL
Unconjugated bilirubin	30 mg/dL
Conjugated bilirubin	20 mg/dL
HSA	4 g/dL
Proinsulin	140,000 ng/mL
Insulin	12,000 µIU/mL
TSH	450 mIU/L
IGF-II	100,000 ng/dL
LH	500 mIU/mL
IGFBP1	5,000 ng/mL
IGFBP2	5,000 ng/mL
IGFBP3	20,000 ng/mL
IGFBP4	5,000 ng/mL
IGFBP5	5,000 ng/mL
IGFBP6	5,000 ng/mL
HGH	1,000 ng/mL

15.4. Precision with LIAISON® Analyzer

Different samples, containing different concentrations of IGF-I, were assayed to estimate repeatability and reproducibility of the assay (i.e., within- and between-assay variability).
Repeatability. 40 replicates were performed in the same run to evaluate repeatability.
Reproducibility. 20 replicates were performed in different days with 2 different lots of integral to evaluate reproducibility.

Intra-assay variation			Inter-assay variation		
Mean value (ng/mL)	CV (%)	n*	Mean value (ng/mL)	CV (%)	n*
71.2	4.40	40	77.5	8.5	20
189.3	4.59	40	202.6	4.3	20
412.7	2.37	40	367.9	3.8	20

* number of determinations

15.5. Precision with LIAISON® XL Analyzer

Different samples, containing different concentrations of IGF-I, were assayed to estimate repeatability and reproducibility of the assay (i.e., within- and between-assay variability).
Repeatability. 20 replicates were performed in the same run to evaluate repeatability.
Reproducibility. 20 replicates were performed in different days with 2 different lots of integral to evaluate reproducibility.

The results refer to the groups of samples investigated and are not guaranteed specifications, as differences may exist between laboratories and locations.

Intra-assay variation			Inter-assay variation		
Mean value (ng/mL)	CV (%)	n*	Mean value (ng/mL)	CV (%)	n*
69.9	5.1	20	79.7	9.6	20
182.9	3.5	20	186.9	7.1	20
589.5	3.0	20	316.9	5.6	20

* number of determinations

15.6. Precision with LIAISON® XS Analyzer

Different samples, containing different concentrations of IGF-I, were assayed to estimate repeatability and reproducibility of the assay (i.e., intra- and inter- (total within) variability).
Repeatability and Reproducibility. 90 replicates were performed in 5 different days with 3 different XS instruments to evaluate repeatability and reproducibility concurrently.
The results refer to the groups of samples investigated and are not guaranteed specifications, as differences may exist between laboratories and locations.

Intra-assay variation			Inter-assay variation		
Mean value (ng/mL)	CV (%)	n*	Mean value (ng/mL)	CV (%)	n*
57.03	2.24	90	57.03	3.95	90
100.7	2.34	90	100.7	4.93	90
255.4	2.37	90	255.4	5.86	90
419.4	2.21	90	419.4	6.21	90
701.3	1.87	90	701.3	5.41	90
1029	2.42	90	1029	5.34	90
67.22	3.19	90	67.22	3.95	90
270.7	3.72	90	270.7	4.02	90

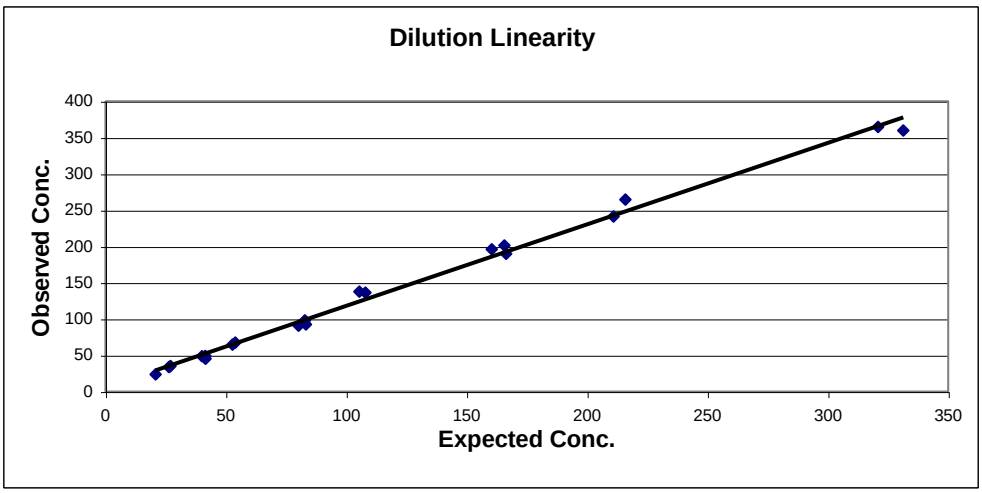
* number of determinations

15.7. Trueness

The assay trueness has been checked by the dilution and recovery tests.

15.8. Dilution test

Serum samples containing high IGF-I concentrations were tested as such and after serially diluting with a diluent. IGF-I concentrations measured versus expected were analyzed by linear regression. Results reported in ng/mL:



Y = 1.1223x + 5.86 r = 0.997

15.9. Recovery test

Serum samples spiked with IGF-I were tested to evaluate the recovery of the LIAISON® IGF-I assay.
The table gives an example of the recovery of IGF-I concentrations in a low-titred serum spiked with a high-titred serum.

	Dilution	Measured Value (ng/mL)	Expected Value (ng/mL)	Recovery (%)		Dilution	Measured Value (ng/mL)	Expected Value (ng/mL)	Recovery (%)
Serum 1: high	1.0	434.8	-	-	Serum 3: high	1.0	421.2	-	-
	0.8	387.5	379.2	102		0.8	372.4	374.6	99
	0.6	335.5	323.6	104		0.6	349.5	328.1	107
	0.4	278.7	268.0	104		0.4	296.5	281.6	105
	0.2	219.6	212.3	103		0.2	230.8	235.1	98
	0.1	183.3	184.5	99		0.1	209.9	211.8	99
Serum 2: low	0.0	156.7	-	-	Serum 4: low	0.0	188.6	-	-

15.10. High-dose hook effect

The high-dose hook (HDH) was determined by addition of IGF-I to human serum pools to a maximum of 11,000 ng/mL.
Whenever samples containing extremely high analyte concentrations are tested, the HDH can mimic concentrations lower than real analysis of HDH was evaluated by testing 5 high-concentration IGF-I -spiked samples. All samples resulted in calculated concentration values above the measuring range, indicating no sample misclassification.

15.11. Analytical and functional sensitivity

Analytical sensitivity:

Analytical sensitivity is defined as the minimum detectable dose distinguishable from zero by 2 standard deviations.

Functional sensitivity:

The functional sensitivity is (defined as the lowest analyte concentration that can be determined with an inter-assay CV < 20%)

	Limit of Detection (Analytical sensitivity)	Limit of Quantitation (Functional sensitivity)
LIAISON® Analyzer family	3 ng/mL	10 ng/mL

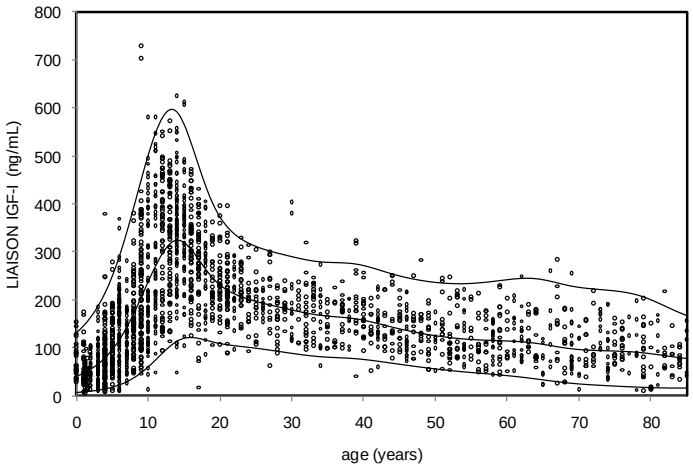
15.12 Reference range tables and graphs

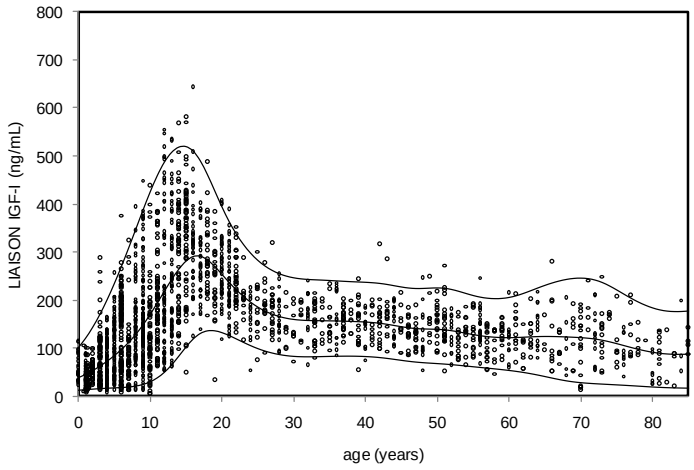
FEMALES				
Age	N	IGF-I percentiles (ng/mL)		
(years)		Median	2.5th	97.5th
0	26	42	8	131
1	28	49	9	146
2	84	57	11	165
3	78	68	13	187
4	82	81	15	216
5	84	98	19	251
6	112	119	24	293
7	58	145	30	342
8	71	174	39	396
9	106	206	49	451
10	69	240	62	504
11	59	271	76	549
12	62	298	90	581
13	70	317	104	596
14	85	324	115	591
15	55	319	121	564
16	61	304	122	524
17	49	284	120	479
18	33	263	117	436
19	28	245	113	399
20	36	231	109	372
21	45	221	107	351
22	21	213	105	337
23	24	207	103	326
24	18	202	102	317
25	16	197	100	311
26	13	193	98	305
27	15	190	96	301
28	17	186	93	297
29	14	183	91	293
30	14	179	89	290
31	9	176	87	286
32	19	173	85	283
33	18	170	83	280
34	14	168	82	279
35	11	167	81	278
36	8	165	80	277
37	16	164	80	277
38	9	163	79	276
39	15	161	78	274
40	18	158	76	271
41	12	155	75	267
42	19	151	73	263
43	11	147	71	258
44	13	144	69	253
45	15	140	66	249
46	24	137	64	246
47	11	134	62	243
48	12	131	60	240
49	16	128	59	238
50	8	126	57	236
51	13	124	55	235
52	19	122	53	234
53	16	121	52	233
54	17	119	51	233
55	8	118	49	234
56	15	117	48	235
57	12	117	47	236

MALES				
Age	N	IGF-I percentiles (ng/mL)		
(years)		Median	2.5th	97.5th
0	26	37	11	100
1	48	44	12	120
2	90	52	13	143
3	96	61	14	169
4	90	72	15	200
5	102	83	16	233
6	117	96	17	269
7	57	111	18	307
8	83	128	20	347
9	105	147	23	386
10	68	169	29	424
11	73	193	37	459
12	74	218	49	487
13	67	242	64	508
14	55	264	83	519
15	63	281	102	520
16	39	291	119	511
17	37	291	131	490
18	31	284	137	461
19	28	270	137	428
20	43	254	133	395
21	40	237	127	364
22	36	222	120	338
23	12	208	112	316
24	15	196	105	298
25	13	185	99	283
26	15	177	94	271
27	20	170	90	262
28	19	165	87	255
29	8	162	84	250
30	8	159	83	246
31	8	158	82	244
32	14	157	82	243
33	23	157	82	242
34	7	157	82	242
35	13	156	83	241
36	15	156	83	240
37	22	156	83	239
38	7	155	83	238
39	19	155	83	238
40	13	154	82	237
41	10	153	81	236
42	18	151	80	235
43	13	149	78	233
44	19	147	76	230
45	10	144	74	227
46	16	142	72	225
47	16	140	71	224
48	13	139	69	224
49	9	139	68	225
50	18	139	67	225
51	23	138	66	225
52	12	136	65	222
53	14	133	64	218
54	12	130	62	214
55	16	128	61	210
56	25	125	59	206
57	16	123	58	204

FEMALES				
Age	N	IGF-I percentiles (ng/mL)		
(years)		Median	2.5th	97.5th
58	18	116	46	238
59	17	116	44	240
60	9	115	43	241
61	11	114	41	243
62	18	113	40	244
63	9	112	38	244
64	14	110	36	244
65	8	108	34	241
66	7	106	32	238
67	10	103	30	235
68	11	101	28	231
69	22	99	27	228
70	7	97	26	226
71	10	96	24	224
72	8	96	24	222
73	10	95	23	221
74	18	95	22	220
75	11	94	21	218
76	14	94	20	216
77	4	93	20	214
78	8	92	19	210
79	16	90	18	206
80	7	89	18	200
81	6	87	18	193
82	8	85	17	186
83	7	82	17	179
84	11	81	17	173
85	5	79	17	167

MALES				
Age	N	IGF-I percentiles (ng/mL)		
(years)		Median	2.5th	97.5th
58	9	122	56	203
59	15	121	55	203
60	11	121	53	206
61	13	122	51	209
62	8	122	49	214
63	10	123	46	219
64	13	123	43	225
65	4	124	40	231
66	10	124	37	236
67	7	123	34	240
68	6	123	31	243
69	7	122	29	245
70	17	121	27	246
71	4	120	26	245
72	12	118	25	242
73	13	116	24	236
74	4	112	23	229
75	7	109	22	221
76	9	105	22	212
77	7	101	21	204
78	5	97	20	196
79	1	94	19	189
80	7	91	18	184
81	10	89	17	180
82	2	87	16	177
83	4	86	16	176
84	3	86	16	176
85	5	87	15	177





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