ANIARA DIAGNOSTICA LLC

Please note that the uses described in the following page(s) have not been approved or cleared by FDA, with respect to the described assay or test.

In the US, the product is intended **For Research Use Only. Not for Use in Diagnostic Procedures.**

Aniara Diagnostica LLC • 7768 Service Center Drive • West Chester, OH 45069 • Phone (513) 770-1991
Fax (513) 573-9241 • Email info@aniara com • www.aniara.com

ANIARA
Manufactured By: HYPHEN BioMed

BIOPHEN Arixtra® Calibrators and Controls technical file (#A222501/A224001)

Intended use and applications

Stastus: IVD: CE mark.

Intended use: Calibration and quality control plasmas for the measurement of Arixtra® (Fondaparinux) using a chromogenic anti-Xa assay. Obtained values are determined using Biophen Heparin assay from HYPHEN.

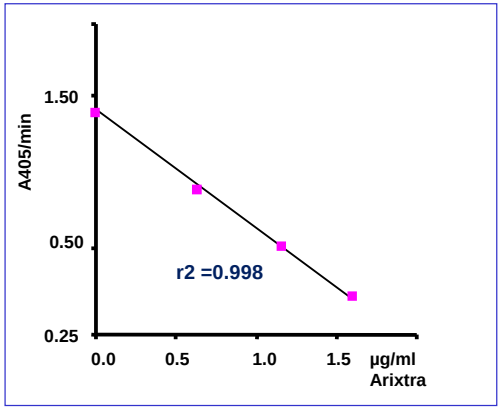
Characteristics and advantages

- Standardized calibrators and controls, validated against an Internal Reference Standard, accurately determined against a reference preparation of pharmaceutical Arixtra® spiked into a reference normal plasma pool. Inter lots correlation r2 = 0.99.
- Easy to use with automated method or basic equipment,
- Linearity and dynamic range : 0 – 1.5 µg/ml in human citrated plasma (using Biophen Heparin kit)
- Highly stable (7 days at 2-8°C , 48 hours at RT (18-25°C)).
- Safe: high quality human plasma tested with registered methods.
- Caution: avoid any contamination or evaporation during use.

Reagents

Calibrators: 3 sets of 4 calibrators covering the range from 0 to about 1.5µg/ml Arixtra® (1ml vials, lyophilized).
Controls: 6 sets of 2 levels at about 0.40 and 1.20µg/ml Arixtra® (1ml vials, lyophilized).

Calibration curve (STAR)



Stability studies (reconstituted at 2-8°C or RT(18-25°C); "Heath stress" (accelerated ageing) at 30°C and expiration date for lyophilized product) :

Reagents are reconstituted and stored for 48h at RT or 7 days at 2-8°C, or heated (lyophilized) at 30°C for 3 weeks then freshly reconstituted. They are then compared with the same reagents stored at 2-8°C and freshly reconstituted, for their Arixtra® concentration measured against a reference calibration curve.

After:	Fresh	48h at RT	7 days at 2-8°C
Measured µg/ml Arixtra®			
Cal 1	0.01	0.01	0
Cal 2	0.49	0.48	0.50
Cal 3	0.95	0.96	0.96
Cal 4	1.42	1.40	1.40
C1	0.43	0.40	0.43
C2	1.19	1.20	1.14

Storage:	Fresh	3 weeks at 30°C
Measured µg/ml Arixtra®		
C1	0.43	0.44
C2	1.19	1.13

Storage:	Fresh	30months (Expiration)
Measured µg/ml Arixtra®		
Cal 1	0	0
Cal 2	0.48	0.46
Cal 3	0.99	0.98
Cal 4	1.40	1.48 – 1.48

Conclusion: The performances are not affected in the various storage conditions. Excellent recovery for controls. Reagents are stable for 48h at RT or 7 days at 2-8°C. Performances are well preserved during the storage at 30°C, which allows shipping the reagents at RT.

Example of Arixtra® recovery results

Various Arixtra® concentrations (from 3 different lots) were spiked into a normal plasma pool and allowed verifying good and homogeneous recovery results (95-115%), as an example:

		STAR		*ACL7000*	
Arixtra lot :	*Target µg/ml*	*Measured µg/ml*	*% recovery*	*Measured µg/ml*	*% recovery*
AL0099	*0*	0	na	0	na
	0.5	0.51	102%	0.52	104%
	1.0	1.08	108%	1.01	101%
	1.5	1.56	104%	1.52	101%
300976	*0*	0	na	0	na
	0.5	0.52	104%	0.53	106%
	1.0	1.06	106%	1.05	105%
	1.5	1.63	109%	1.50	100%
13	*0*	0.01	na	0	na
	0.5	0.57	114%	0.53	106%
	1.0	1.17	117%	1.07	107%
	1.5	1.68	112%	1.48	99%

Intra and inter-assay variability using Biophen Heparin kit

INTRA-ASSAY: The 2 controls are tested 20 fold in the same series.
INTER-ASSAY : The 2 controls are tested 9 fold, in 9 independent series, each one being newly calibrated .
Mean measured value (µgml), SD and CV% are reported:

	Intra assay (N=20) (ACL7000)			Inter assay (N= 9) ((1water bath/1 ACL7000/7 STAR)		
Sample	Mean µg/ml	SD	CV%	Mean µg/ml	SD	CV%
C1	0.44	0.015	3.5	0.44	0.02	4.4
C2	1.15	0.024	2.1	1.18	0.04	3.0

Conclusion:
Intra assay CV (on measured concentrations): 2.1 – 3.5 %.
Inter assay CV (on measured concentrations): 3.0 – 4.4%.
For the low concentrations, close to the hedge part of the calibration curve, SD is more significant than CV, and remains <0.02µg/ml.

ANIARA
7768 Service Center Drive • West Chester OH 45069
Phone: 513.770.1991 Toll Free: 866.783.3797 Fax: 513.573.9241 Email: info@aniara.com
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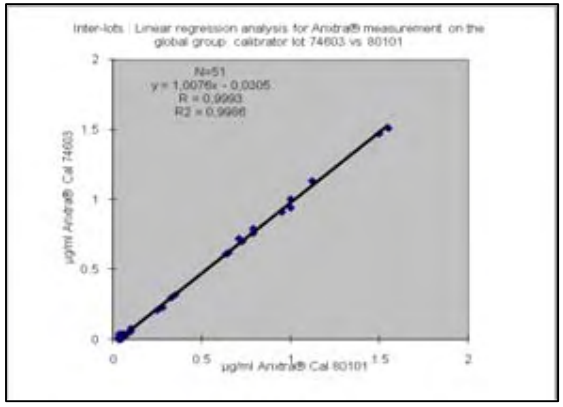
BIOPHEN Arixtra® Calibrators and Controls technical file (#A222501/A224001)

Arixtra® Calibrators inter-lots homogeneity

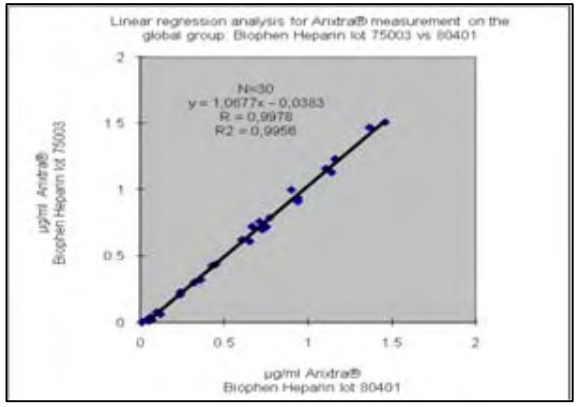
Internal inter-lots comparison for Arixtra® measurement (µg/ml) using Biophen Heparin device (lot 75003, STAR), calibrated using Biophen Arixtra® calibrators lot 74603 or 80101, on N=4 lyophilized Arixtra® controls (HYPHEN), and N=51 samples (N=30 citrated normal plasmas (untreated, French blood bank), N=21 plasmas from Arixtra® treated patients (left from analysis).



Conclusion:
Excellent correlation between the results obtained using the 2 different lots of Biophen Arixtra® Calibrators for Arixtra® measurement.

Biophen Heparin kit inter-lots homogeneity for Arixtra® measurement

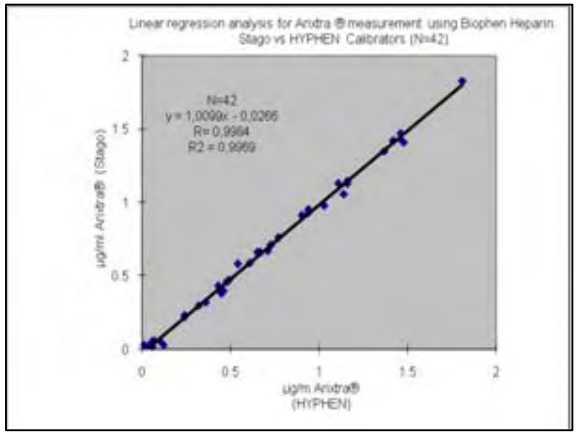
Internal inter-lots comparison for Arixtra® measurement (µg/ml) using Biophen Heparin device (lot 75003 and 80401, STAR, 2 different days), calibrated using Biophen Arixtra® calibrator lot 74603, on N=30 samples (N=4 lyophilized Arixtra® controls (HYPHEN), N=5 citrated normal plasmas (untreated, French blood bank), N=21 plasmas from Arixtra® treated patients (left from analysis).



Conclusion:
Excellent correlation between the results obtained using the 2 different lots of Biophen Heparin device for Arixtra® measurement.

HYPHEN vs Diagnostica Stago Calibrators for Arixtra® measurement (using Biophen Heparin kit, STAR)

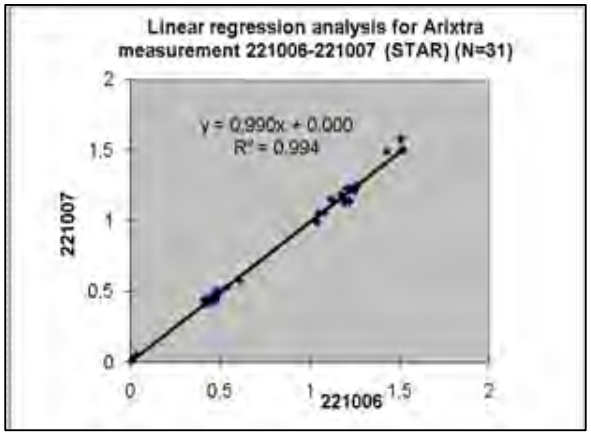
Internal comparison for Arixtra® measurement (µg/ml), using Biophen Heparin device (lot 80401, STAR), calibrated using HYPHEN (lot 74603) or Diagnostica Stago (lot 101794) Arixtra® calibrators, on N=42 samples (N=15 lyophilized Arixtra® plasmas and controls (HYPHEN), N=2 Arixtra® Controls (Stago), N=5 citrated normal plasmas (untreated, French blood bank), N=20 plasmas from Arixtra® treated patients (left from analysis).



Conclusion:
Excellent correlation between the results obtained using the 2 calibration systems, using Biophen Heparin on STA-R, for Arixtra® measurement.

Calibration system checked with or w/o AT supplementation

Arixtra® anti-Xa activity being mediated by Antithrombin (AT), HYPHEN calibrators and controls lots were tested for Arixtra® content without (Biophen Heparin #A221006) or with (Biophen Heparin AT+, #A221007) AT supplementation in the assay, on STAR instrument.



Conclusion:
Tested Arixtra® calibrators and controls are verified well and homogeneously determined without or with AT supplementation in the assay.

Important note:
a low AT level for a sample, assayed by anti-Xa method without AT supplementation, may lead to underestimation of Arixtra® concentration.

Related products :

Biophen Heparin (#A221003/A221006) (CE) ; Biophen Heparin LRT (#A221011) (CE) ; Biophen Heparin (AT+) (#A221007)

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