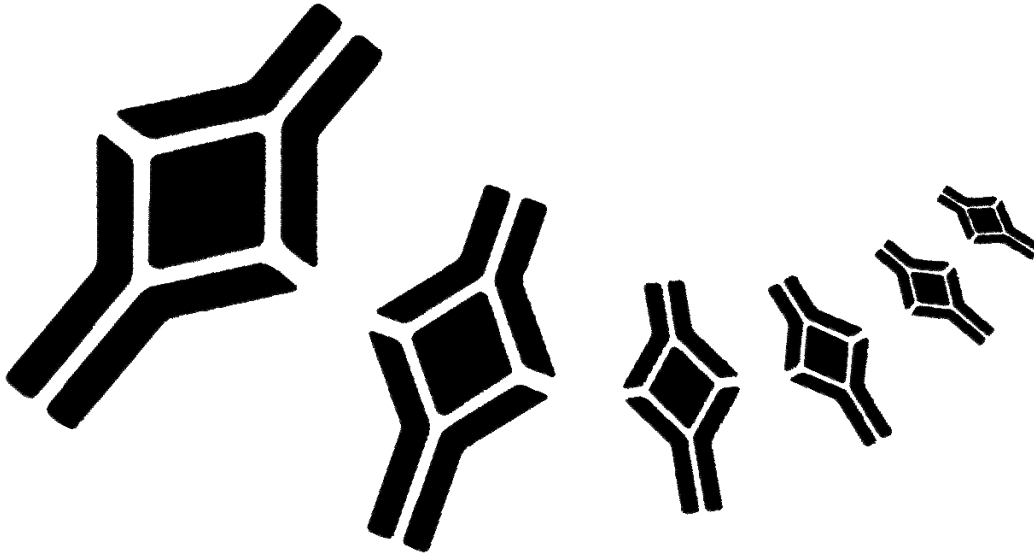


BioVendor

Research
and Diagnostic Products



HUMAN CARTILAGE OLIGOMERIC MATRIX PROTEIN ELISA

Product Data Sheet

Cat. No.: RD194080200



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BioVendor – Laboratorní medicína, a.s.

»» Use only the current version of Product Data Sheet enclosed with the kit!

1. INTENDED USE

The RD194080200 Human Cartilage Oligomeric Matrix Protein ELISA is a sandwich enzyme immunoassay for the quantitative measurement of human cartilage oligomeric matrix protein (COMP).

»» Features

- It is intended for *in vitro* diagnostic use.
- The total assay time is less than 3.5 hours.
- The kit measures COMP in serum and plasma (EDTA, citrate, heparin).
- Assay format is 96 wells.
- Quality Controls are human serum based. No animal sera are used.
- Standard is recombinant protein based.
- Components of the kit are provided ready to use, concentrated or lyophilized.

2. STORAGE, EXPIRATION

Store the complete kit at 2-8°C. Under these conditions, the kit is stable until the expiration date (see label on the box).

For stability of opened reagents see Chapter 9.

3. INTRODUCTION

Cartilage oligomeric matrix protein (COMP), also designated thrombospondin 5 (TSP 5), is non-collagenous glycoprotein and is a member of the thrombospondin family of extracellular proteins. COMP is a calcium-binding protein of high molecular weight (>500kDa) present in the extracellular matrix of articular, nasal and tracheal cartilage. COMP is not only cartilage-derived but was found widely in other tissues, including synovium and tendon.

Intact COMP is pentameric, with five identical subunits and the carboxy-terminal globular domain of native COMP binds to collagens I, II, and IX. It has been proposed that COMP molecules are important for maintaining the properties and integrity of collagen network. In addition COMP may have a storage and delivery function for hydrophobic cell-signaling molecules such as vitamin D. The significance of COMP for normal development and function

of cartilage has been underscored by the discovery that mutations of the COMP gene result in pseudoachondroplasia and some forms of multiple epiphyseal dysplasia.

Most published studies have shown that serum levels of COMP provide important information about metabolic changes occurring in the cartilage matrix in joint disease. These studies describe that serum COMP level correlated with cartilage degradation and is a potential prognostic marker in inflammatory joint diseases such as osteoarthritis (OA) and rheumatoid arthritis (RA). Results have demonstrated an association of increasing serum COMP levels with progressive destruction of articular cartilage monitored radiographically. OA and RA are a common disease causing pain and disability in a significant proportion of the adult population and early diagnostics of these diseases is very important for future therapy.

Areas of investigation:

Joint diseases

Osteoarthritis

Rheumatoid arthritis

4. TEST PRINCIPLE

In the BioVendor Human Cartilage Oligomeric Matrix Protein ELISA, Standards, Quality Controls and diluted samples are incubated in microplate wells pre-coated with monoclonal anti-human COMP antibody. After 60 minutes incubation and washing, biotin-labelled second monoclonal anti-human COMP antibody is added and incubated with captured COMP for 60 minutes. After another washing, streptavidin-HRP conjugate is added. After 30 minutes incubation and the last washing step, the remaining conjugate is allowed to react with the substrate solution (TMB). The reaction is stopped by addition of acidic solution and absorbance of the resulting yellow product is measured spectrophotometrically at 450 nm. The absorbance is proportional to the concentration of COMP. A standard curve is constructed by plotting absorbance values against concentrations of Standards, and concentrations of unknown samples are determined using this standard curve.

5. PRECAUTIONS

- Wear gloves and laboratory coats when handling immunodiagnostic materials.
- Do not drink, eat or smoke in the areas where immunodiagnostic materials are being handled.
- This kit contains components of human origin. These materials were found non-reactive for HBsAg, HCV antibody and for HIV 1/2 antigen and antibody. However, these materials should be handled as potentially infectious, as no test can guarantee the complete absence of infectious agents.
- Avoid contact with the acidic Stop Solution and Substrate Solution, which contains hydrogen peroxide and tetramethylbenzidine (TMB). Wear gloves and eye and clothing protection when handling these reagents. Stop and/or Substrate Solutions may cause skin/eyes irritation. In case of contact with the Stop Solution and the Substrate Solution wash skin/eyes thoroughly with water and seek medical attention, when necessary.
- The materials must not be pipetted by mouth.

6. TECHNICAL HINTS

- Reagents with different lot numbers should not be mixed.
- Use thoroughly clean glassware.
- Use deionized (distilled) water, stored in clean containers.
- Avoid any contamination among samples and reagents. For this purpose, disposable tips should be used for each sample and reagent.
- Substrate Solution should remain colourless until added to the plate. Keep Substrate Solution protected from light.
- Stop Solution should remain colourless until added to the plate. The colour developed in the wells will turn from blue to yellow immediately after the addition of the Stop Solution. Wells that are green in colour indicate that the Stop Solution has not mixed thoroughly with the Substrate Solution.
- Dispose of consumable materials and unused contents in accordance with applicable national regulatory requirements.

7. REAGENT SUPPLIED

| <i>Kit Components</i> | <i>State</i> | <i>Quantity</i> |
|--|--------------|-----------------|
| Antibody Coated Microtiter Strips | ready to use | 96 wells |
| Biotin Labeled Antibody | ready to use | 13 ml |
| Streptavidin-HRP Conjugate | ready to use | 13 ml |
| Master Standard | lyophilized | 2 vial |
| Quality Control High | lyophilized | 2 vial |
| Quality Control Low | lyophilized | 2 vial |
| Dilution Buffer | ready to use | 2 x 13 ml |
| Wash Solution Concentrate (10x) | concentrated | 100 ml |
| Substrate Solution | ready to use | 13 ml |
| Stop Solution | ready to use | 13 ml |
| Product Data Sheet + Certificate of Analysis | | 1 pc |

8. MATERIAL REQUIRED BUT NOT SUPPLIED

- Deionized (distilled) water
- Test tubes for diluting samples
- Glassware (graduated cylinder and bottle) for Wash Solution (Dilution Buffer)
- Precision pipettes to deliver 5-1000 μ l with disposable tips
- Multichannel pipette to deliver 50-200 μ l with disposable tips
- Absorbent material (e.g. paper towels) for blotting the microtiter plate after washing
- Vortex mixer
- Orbital microplate shaker capable of approximately 300 rpm
- Microplate washer (optional). [Manual washing is possible but not preferable.]
- Microplate reader with 450 \pm 10 nm filter
- Software package facilitating data generation and analysis (optional)

9. PREPARATION OF REAGENTS

- All reagents need to be brought to room temperature prior to use.
- Always prepare only the appropriate quantity of reagents for your test.
- Do not use components after the expiration date marked on their label.

- Assay reagents supplied ready to use:

Antibody Coated Microtiter Strips

Stability and storage:

Return the unused strips to the provided aluminium zip-sealed bag with desiccant and seal carefully. Remaining Microtiter Strips are stable 3 months stored at 2-8°C and protected from the moisture.

Biotin Labelled Antibody

Streptavidin-HRP Conjugate

Dilution Buffer

Substrate Solution

Stop Solution

Stability and storage:

Opened reagents are stable 3 months when stored at 2-8°C.

- Assay reagents supplied concentrated or lyophilized:

Human COMP Master Standard

Refer to the Certificate of Analysis for current volume of Dilution Buffer needed for reconstitution of standard!!!

Reconstitute the lyophilized Master Standard with Dilution Buffer just prior to the assay. Let it dissolve at least 15 minutes with occasionally gently shaking (not to foam). The resulting concentration of the COMP in the stock solution is **128 ng/ml**.

Prepare set of standards using Dilution Buffer as follows:

| Volume of Standard | Dilution Buffer | Concentration |
|--------------------|-----------------|---------------|
| Stock | - | 128 ng/ml |
| 300 µl of stock | 300 µl | 64 ng/ml |
| 300 µl of 64 ng/ml | 300 µl | 32 ng/ml |
| 300 µl of 32 ng/ml | 300 µl | 16 ng/ml |
| 300 µl of 16 ng/ml | 300 µl | 8 ng/ml |
| 300 µl of 8 ng/ml | 300 µl | 4 ng/ml |

Prepared Standards are ready to use, do not dilute them.

Stability and storage:

Do not store standard stock solution and other standard.

Quality Controls High, Low

Refer to the Certificate of Analysis for current volume of Dilution Buffer needed for reconstitution and for current Quality Controls concentrations!!!

Reconstitute each Quality Control (High and Low) with Dilution Buffer just prior to the assay. Let it dissolve at least 15 minutes with occasional gentle shaking (not to foam).

Reconstituted Quality Controls are ready to use, do not dilute them.

Stability and storage:

The reconstituted Quality Controls must be used immediately or stored frozen at -20°C for 1 month. Avoid repeated freeze/thaw cycles.

Wash Solution Concentrate (10x)

Dilute Wash Solution Concentrate (10x) ten-fold in distilled water to prepare a 1x working solution. Example: 100 ml of Wash Solution Concentrate (10x)+ 900 ml of distilled water for use of all 96-wells.

Stability and storage:

The diluted Wash Solution is stable 1 month when stored at 2-8°C. Opened Wash Solution Concentrate (10x) is stable 3 months when stored at 2-8°C.

10. PREPARATION OF SAMPLES

The kit measures human COMP in serum or plasma.

Samples should be assayed immediately after collection or should be stored at -20°C. Mix thoroughly thawed samples just prior to the assay and avoid repeated freeze/thaw cycles, which may cause erroneous results. Avoid using hemolyzed or lipemic samples.

Dilute samples 50x with Dilution Buffer just prior to the assay (e.g. 5 µl of sample + 245µl of Dilution Buffer for singlets or duplicates). **Mix well** (not to foam). Vortex is recommended.

Stability and storage:

Do not store the diluted samples.

Samples should be stored at -20°C, or preferably at -70°C for long-term storage.

See Chapter 13 for stability of serum and plasma samples if stored at 2-8°C, effect of freezing/thawing and effect of sample matrix (serum/plasma) on the concentration of human COMP.

Note: It is recommended to use a precision pipette and a careful technique to perform the dilution in order to get precise results.

11. ASSAY PROCEDURE

1. Pipet **100 µl** of Standards, Quality Controls, Dilution Buffer (=Blank) and samples, preferably in duplicates, into the appropriate wells.
2. Incubate the plate at room temperature (ca. 25°C) for **1 hour**, shaking at ca. 300 rpm on an orbital microplate shaker.
3. Wash the wells **3-times** with Wash Solution (0.35 ml per well). After final wash, invert and tap the plate strongly against paper towel.
4. Add **100 µl** of Biotin Labelled Antibody Solution into each well.
5. Incubate the plate at room temperature (ca. 25°C) for **1 hour**, shaking at ca. 300 rpm on an orbital microplate shaker.
6. Wash the wells **3-times** with Wash Solution (0.35 ml per well). After final wash, invert and tap the plate strongly against paper towel.
7. Add **100 µl** of Streptavidin-HRP Conjugate into each well.
8. Incubate the plate at room temperature (ca. 25°C) for **30 min**, shaking at ca. 300 rpm on an orbital microplate shaker.
9. Wash the wells **3-times** with Wash Solution (0.35 ml per well). After final wash, invert and tap the plate strongly against paper towel.
10. Add **100 µl** of Substrate Solution into each well. Avoid exposing the microtiter plate to direct sunlight. Covering the plate with e.g. aluminium foil is recommended.
11. Incubate the plate for **10 minutes** at room temperature. The incubation time may be extended [up to 20 minutes] if the reaction temperature is below than 20°C. Do not shake the plate during the incubation.
12. Stop the colour development by adding **100 µl** of Stop Solution.
13. Determine the absorbance by reading the plate at 450 nm. The absorbance should be read within 5 minutes following step 12.

Note 1: If the microplate reader is not capable of reading absorbance greater than the absorbance of the highest standard, perform a second reading at 405 nm. A new standard curve, constructed using the values measured at 405 nm, is used to determine COMP concentration of off-scale samples. The readings at 405 nm should not replace the on-scale readings at 450 nm.

Note 2: Manual washing: Aspirate wells and pipet 0.35 ml Wash Solution into each well. Aspirate wells and repeat twice. After final wash, invert and tap the plate strongly against paper towel. Make certain that Wash Solution has been removed entirely.

| | strip 1+2 | strip 3+4 | strip 5+6 | strip 7+8 | strip 9+10 | strip 11+12 |
|----------|--------------|-----------|-----------|-----------|------------|-------------|
| A | Standard 128 | Blank | Sample 8 | Sample 16 | Sample 24 | Sample 32 |
| B | Standard 64 | Sample 1 | Sample 9 | Sample 17 | Sample 25 | Sample 33 |
| C | Standard 32 | Sample 2 | Sample 10 | Sample 18 | Sample 26 | Sample 34 |
| D | Standard 16 | Sample 3 | Sample 11 | Sample 19 | Sample 27 | Sample 35 |
| E | Standard 8 | Sample 4 | Sample 12 | Sample 20 | Sample 28 | Sample 36 |
| F | Standard 4 | Sample 5 | Sample 13 | Sample 21 | Sample 29 | Sample 37 |
| G | QC High | Sample 6 | Sample 14 | Sample 22 | Sample 30 | Sample 38 |
| H | QC Low | Sample 7 | Sample 15 | Sample 23 | Sample 31 | Sample 39 |

Figure 1: Example of a work sheet.

12. CALCULATIONS

Most microplate readers perform automatic calculations of analyte concentration. The standard curve is constructed by plotting the mean absorbance at 450 nm (Y) of Standards against log of the known concentration (X) of Standards, using the four-parameter algorithm. Results are reported as concentration of COMP ng/ml in samples.

Alternatively, the logit log function can be used to linearize the standard curve (i.e. logit of the mean absorbance (Y) is plotted against log of the known concentration (X) of Standards).

The measured concentration of samples calculated from the standard curve must be multiplied by their respective dilution factor, because samples have been diluted prior to the assay.

e.g. 20 ng/ml (from standard curve) x 50 (dilution factor) = 1 000 ng/ml.

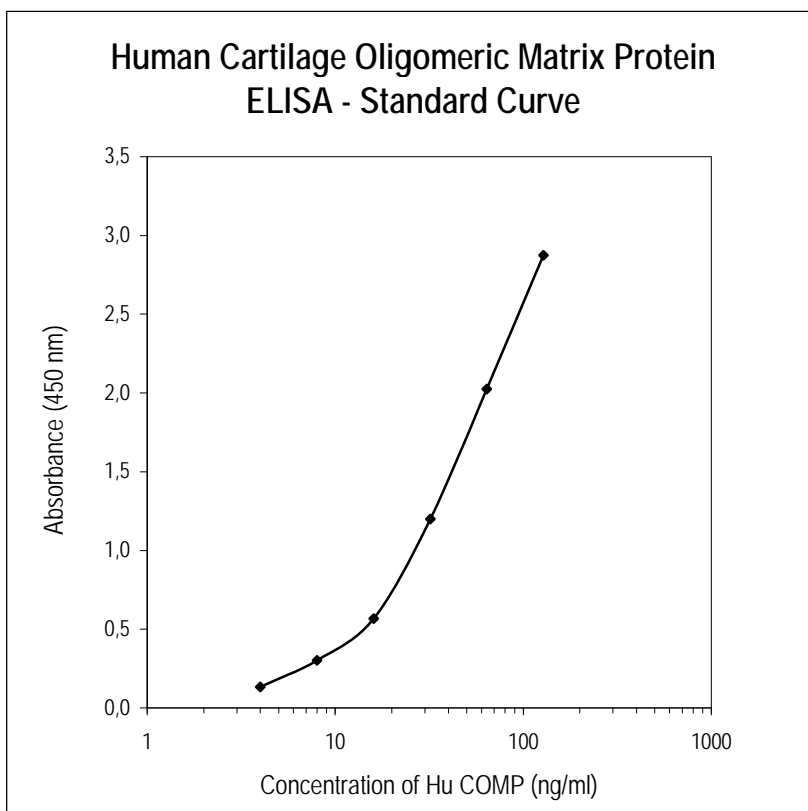


Figure 2: Typical Standard Curve for Human Cartilage Oligomeric Matrix Protein ELISA.

13. PERFORMANCE CHARACTERISTICS

➤➤ Typical analytical data of BioVendor Human Cartilage Oligomeric Matrix Protein ELISA are presented in this chapter.

- **Sensitivity**

Limit of Detection (LOD) (defined as concentration of analyte giving absorbance higher than mean absorbance of blank* plus three standard deviations of the absorbance of blank: $A_{\text{blank}} + 3 \times \text{SD}_{\text{blank}}$) is calculated from the real human COMP values in wells and is 0.5 ng/ml.

*Dilution Buffer is pipetted into blank wells.

- **Limit of assay**

Results exceeding COMP level of 128 ng/ml should be repeated with more diluted samples. Dilution factor needs to be taken into consideration in calculating the COMP concentration.

- **Specificity**

The antibodies used in this ELISA are highly specific for human COMP.

Sera of several mammalian species were measured in the assay. See results below.

For details please contact us at info@biovendor.com.

| <i>Mammalian serum sample</i> | <i>Observed crossreactivity</i> |
|-------------------------------|---------------------------------|
| Bovine | no |
| Goat | no |
| Hamster | no |
| Horse | no |
| Monkey | no |
| Mouse | no |
| Pig | no |
| Rabbit | no |
| Sheep | no |
| Rat | no |
| Cat | no |
| Dog | no |

- **Precision**

Intra-assay (Within-Run) (n=8)

| <i>Sample</i> | <i>Mean (ng/ml)</i> | <i>SD (ng/ml)</i> | <i>CV (%)</i> |
|---------------|---------------------|-------------------|---------------|
| 1 | 645 | 29.0 | 4.5 |
| 2 | 1330 | 96.0 | 7.2 |

Inter assay (Run-to-Run) (n=8)

| <i>Sample</i> | <i>Mean (ng/ml)</i> | <i>SD (ng/ml)</i> | <i>CV (%)</i> |
|---------------|-------------------------|-----------------------|-------------------|
| 1 | 695 | 49.0 | 7.1 |
| 2 | 1475 | 66.0 | 4.5 |

- Spiking Recovery**

Serum samples were spiked with different amounts of human COMP and assayed.

| <i>Sample</i> | <i>Observed (ng/ml)</i> | <i>Expected (ng/ml)</i> | <i>Recovery O/E (%)</i> |
|---------------|-----------------------------|-----------------------------|-----------------------------|
| 1 | 525 | - | - |
| | 2300 | 2525 | 91.1 |
| | 1580 | 1525 | 103.6 |
| | 930 | 1025 | 90.7 |
| 2 | 740 | - | - |
| | 2410 | 2740 | 88.0 |
| | 1510 | 1740 | 86.8 |
| | 1085 | 1240 | 87.5 |

- Linearity**

Serum samples were serially diluted with Dilution Buffer and assayed.

| <i>Sample</i> | <i>Dilution</i> | <i>Observed (ng/ml)</i> | <i>Expected (ng/ml)</i> | <i>Recovery O/E (%)</i> |
|---------------|-----------------|-----------------------------|-----------------------------|-----------------------------|
| 1 | - | 2675 | - | - |
| | 2x | 1390 | 1338 | 103.9 |
| | 4x | 705 | 669 | 105.4 |
| | 8x | 280 | 334 | 83.7 |
| 2 | - | 3970 | - | - |
| | 2x | 1940 | 1985 | 97.7 |
| | 4x | 990 | 992 | 99.7 |
| | 8x | 420 | 496 | 84.6 |

- **Effect of sample matrix**

Heparin, citrate and EDTA plasmas were compared to respective serum samples from the same 10 individuals.

Results are shown below:

| Volunteer No. | Serum (ng/ml) | Plasma (ng/ml) | | |
|--|---------------|----------------|-------------|-------------|
| | | EDTA | Citrate | Heparin |
| 1 | 480 | 303 | 410 | 498 |
| 2 | 1265 | 530 | 880 | 1090 |
| 3 | 1593 | 810 | 1010 | 1460 |
| 4 | 1070 | 510 | 630 | 995 |
| 5 | 1105 | 640 | 860 | 1060 |
| 6 | 2115 | 1240 | 1655 | 2205 |
| 7 | 1040 | 639 | 710 | 1065 |
| 8 | 705 | 340 | 475 | 700 |
| 9 | 980 | 395 | 725 | 1005 |
| 10 | 380 | 280 | 295 | 360 |
| Mean (ng/ml) | 1073 | 569 | 765 | 1044 |
| Mean Plasma/Serum (%) | - | 53 | 71 | 97 |
| Correlation. coeff. R² | - | 0.90 | 0.95 | 0.98 |

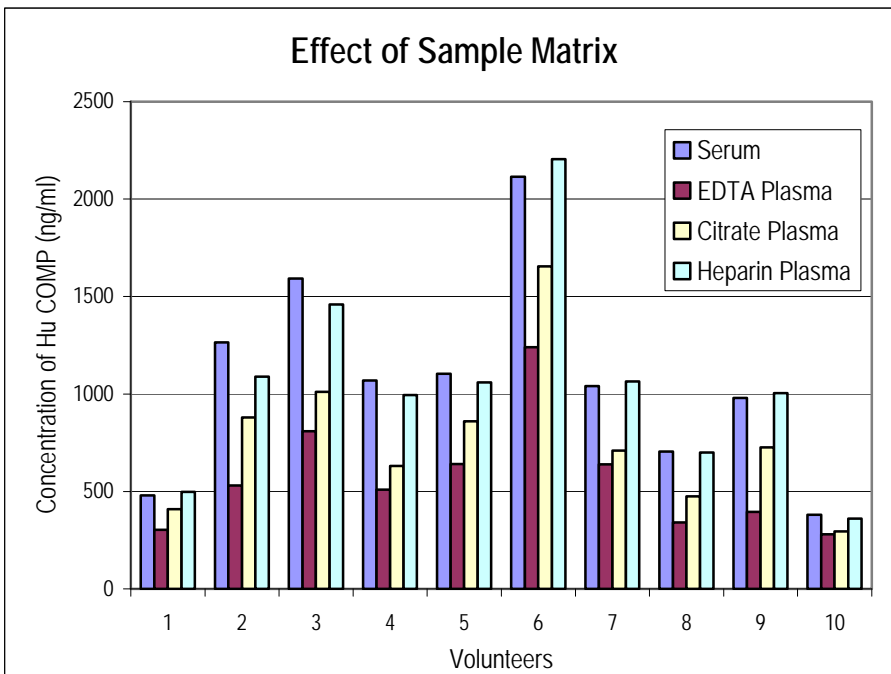


Figure 3: COMP levels measured using Human Cartilage Oligomeric Matrix Protein ELISA from 10 individuals using serum, heparin, citrate and EDTA plasma, respectively.

- **Stability of samples stored at 2-8°C**

Samples should be stored at -20°C. However, no decline in concentration of COMP was observed in serum and plasma samples after 7 days when stored at 2-8°C. To avoid microbial contamination, samples were treated with ε-aminocaproic acid and sodium azide, resulting in the final concentration of 0.03% and 0.1%, respectively.

| Sample | Incubation Temp, Period | Serum (ng/ml) | Plasma (ng/ml) | | |
|--------|-------------------------|---------------|----------------|---------|------|
| | | | Heparin | Citrate | EDTA |
| 1 | -20°C | 443 | 488 | 352 | 328 |
| | 2-8°C, 1 day | 481 | 499 | 355 | 302 |
| | 2-8°C, 7 days | 482 | 374 | 345 | 264 |
| 2 | -20°C | 985 | 910 | 711 | 674 |
| | 2-8°C, 1 day | 993 | 837 | 728 | 631 |
| | 2-8°C, 7 days | 1024 | 1036 | 771 | 601 |
| 3 | -20°C | 847 | 713 | 629 | 491 |
| | 2-8°C, 1 day | 866 | 793 | 654 | 515 |
| | 2-8°C, 7 days | 905 | 853 | 605 | 493 |

- **Effect of Freezing/Thawing**

No decline was observed in concentration of human COMP in serum and plasma samples after repeated (5x) freeze/thaw cycles. However it is recommended to avoid unnecessary repeated freezing/thawing of the samples.

| Sample | Number of f/t cycles | Serum (ng/ml) | Plasma (ng/ml) | | |
|--------|----------------------|---------------|----------------|---------|------|
| | | | Heparin | Citrate | EDTA |
| 1 | 1x | 1105 | 1121 | 820 | 632 |
| | 3x | 1040 | 914 | 783 | 610 |
| | 5x | 1010 | 867 | 727 | 559 |
| 2 | 1x | 942 | 921 | 733 | 702 |
| | 3x | 893 | 764 | 707 | 665 |
| | 5x | 894 | 728 | 614 | 716 |
| 3 | 1x | 1224 | 1100 | 1133 | 884 |
| | 3x | 1275 | 1182 | 975 | 843 |
| | 5x | 1220 | 1080 | 873 | 856 |

14. DEFINITION OF THE STANDARD

The recombinant Human COMP is used as the Standard. The recombinant Human COMP (Gln 21 – Ala 757) is produced in mouse myeloma cell line NS0.

15. METHOD COMPARISON

The BioVendor Human Cartilage Oligomeric Matrix Protein ELISA was compared to the other commercial immunoassay, by measuring 35 serum samples. The following correlation graph was obtained.

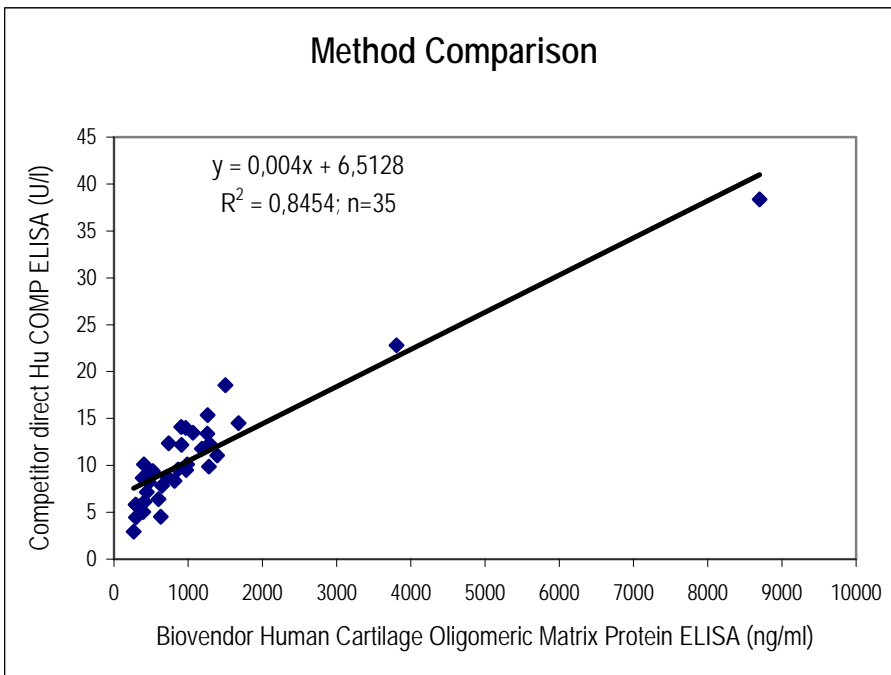
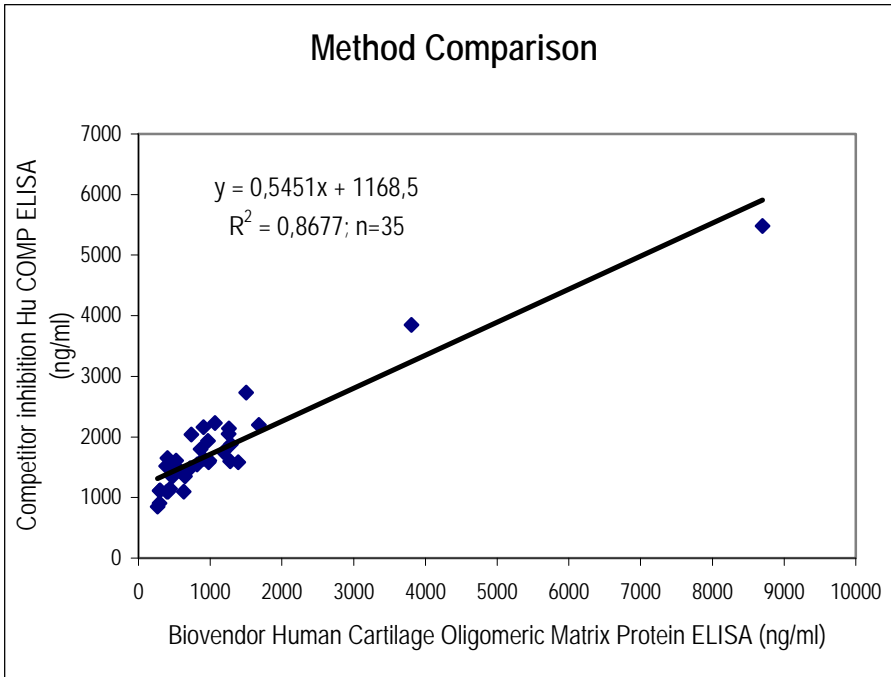


Figure 4: Method comparison

16. PRELIMINARY POPULATION AND CLINICAL DATA

The following results were obtained when serum samples from 246 unselected donors (165 female + 81 male) 7-92 years old were assayed with the Biovendor Human Cartilage Oligomeric Matrix Protein ELISA in our laboratory.

The presented data should be regarded as a guideline only.

- Age dependent distribution of COMP

| Sex | Age (years) | n | Mean | SD | Min | Max |
|-------|-------------|----|------------|-----|-----|------|
| | | | COMP ng/ml | | | |
| Women | 7-19 | 7 | 257 | 98 | 93 | 414 |
| | 20-29 | 25 | 488 | 268 | 255 | 1329 |
| | 30-39 | 20 | 487 | 206 | 204 | 888 |
| | 40-49 | 24 | 621 | 269 | 270 | 1299 |
| | 50-59 | 22 | 867 | 407 | 408 | 1884 |
| | 60-69 | 29 | 1018 | 429 | 423 | 2111 |
| | 70-92 | 38 | 1091 | 527 | 432 | 3250 |
| Men | 7-19 | 5 | 453 | 314 | 180 | 987 |
| | 20-29 | 9 | 523 | 221 | 234 | 939 |
| | 30-39 | 8 | 530 | 212 | 249 | 963 |
| | 40-49 | 15 | 763 | 268 | 260 | 1242 |
| | 50-59 | 13 | 915 | 320 | 516 | 1911 |
| | 60-69 | 20 | 925 | 272 | 519 | 1551 |
| | 70-92 | 11 | 1136 | 244 | 729 | 1620 |

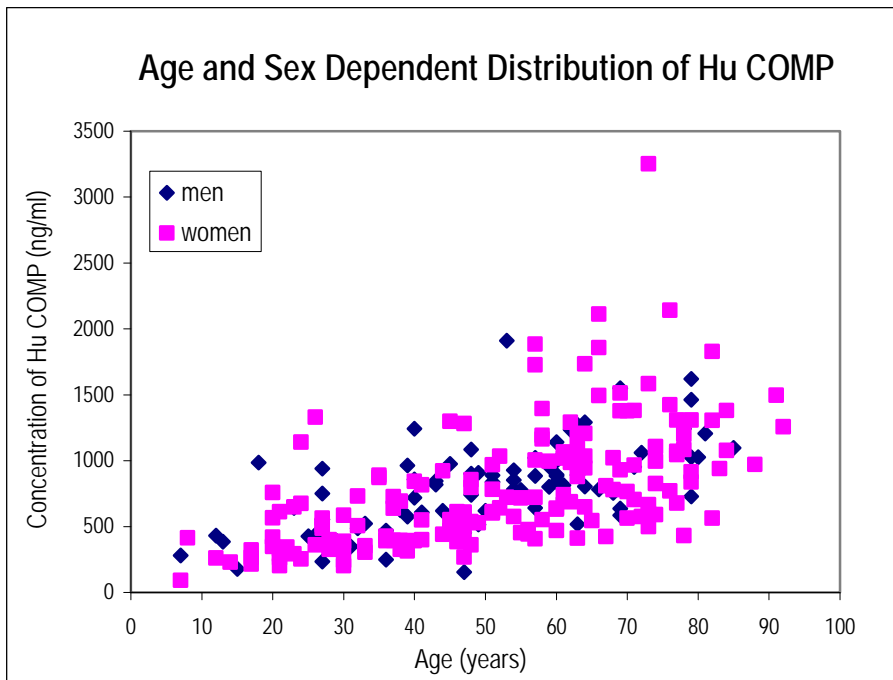


Figure 5: COMP concentration plotted against donor age.

17. TROUBLESHOOTING AND FAQs

»» Weak signal in all wells

Possible explanations:

- Omission of a reagent or a step
- Improper preparation or storage of a reagent
- Assay performed before reagents were allowed to come to room temperature
- Improper wavelength when reading absorbance

»» High signal and background in all wells

Possible explanations:

- Improper or inadequate washing
- Overdeveloping; incubation time with Substrate Solution should be decreased before addition of Stop Solution
- Incubation temperature over 30°C

»» High coefficient of variation (CV)

Possible explanation:

- Improper or inadequate washing
- Improper mixing Standards, Quality Controls or samples







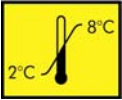


18. REFERENCES

»» References to human COMP:

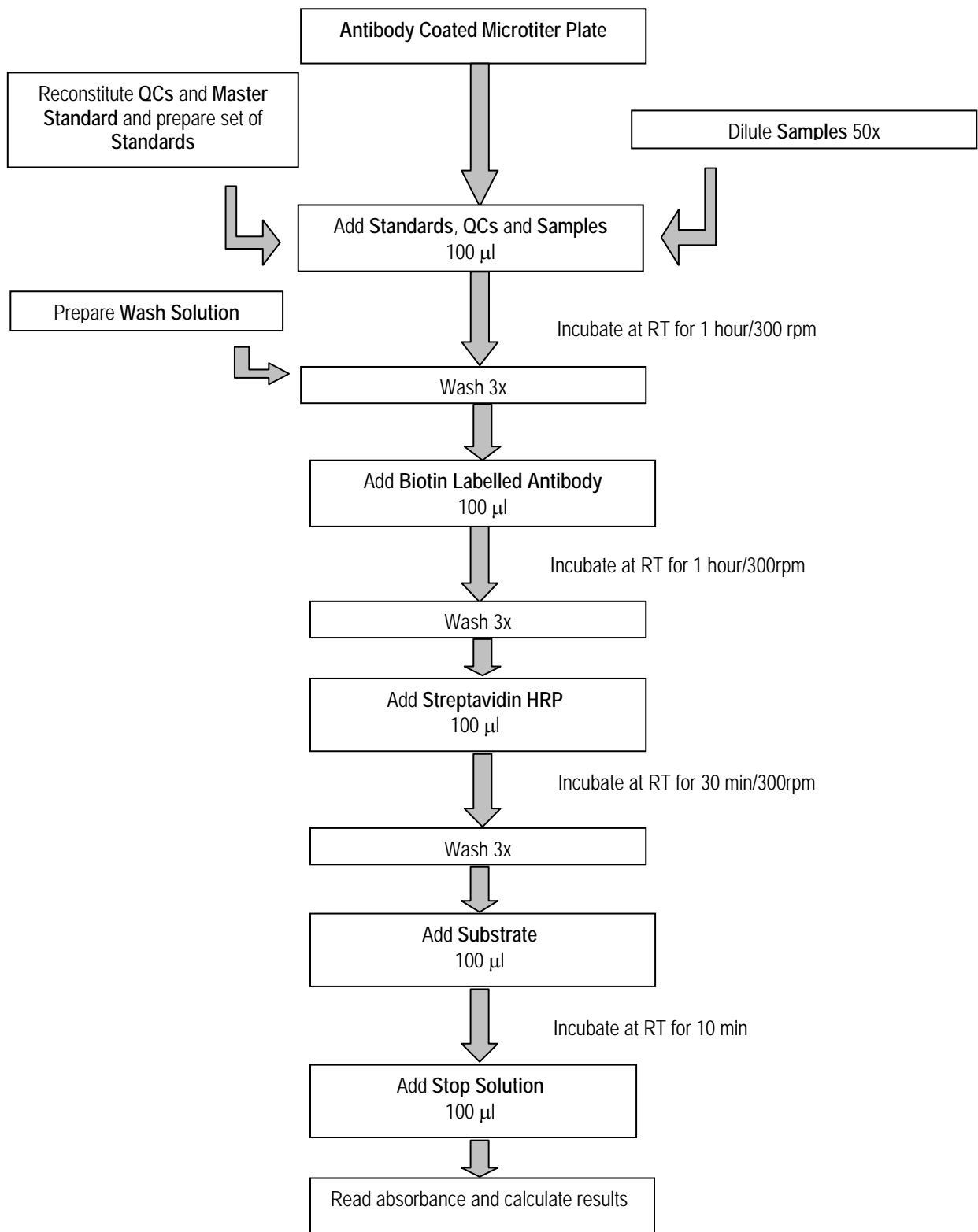
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»» For more references on this product see our WebPages at www.biovendor.com

19. EXPLANATION OF SYMBOLS

| | |
|---|---------------------------------------|
|  | Catalogue number |
|  | Content |
|  | Lot number |
|  | See instructions for use |
|  | Biological hazard |
|  | Expiry date |
|  | Storage conditions |
|  | Identification of packaging materials |
|  | In vitro diagnostic medical device |

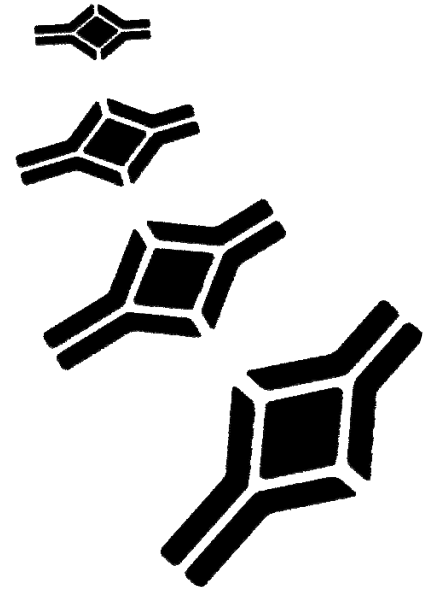
Assay Procedure Summary



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| | A | B | C | D | E | F | G | H | |

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