**Standard Markers of Bone Mineral Metabolism from Blood**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Test | Result | Unit for Result | Date | Time | Fasting Status |
| Calcium | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Albumin | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Alkaline Phosphatase | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Phosphorus | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Creatinine | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Intact Parathyroid Hormone | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| 25-hydroxy vitamin D | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |

**Standard Markers of Bone Mineral Metabolism from Urine1**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Test | Result | Unit for Result | Date | Time | Fasting Status | Spot or Timed sample? |
| Urine Calcium2 | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Urine Creatinine | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Urine Phosphorus3 | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Urine Osmolality2 | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |

1 In most cases, a spot urine sample is sufficient. If a more detailed assessment of mineral excretion is desired, a 24 hour sample is indicated. In case of a 24 hour sample collection start time, stop time, and volume should be recorded.

2 Urinary calcium excretion can be assessed by random spot urine calcium to creatinine ratio. If the participant has low muscle mass, a spot urine to osmolality ratio (x10) should be used instead.

3 Urinary phosphorus excretion can be assessed by tubular reabsorption of phosphorus (TRP), [1-(Urine Phosphorus x Serum Creatinine) / (Serum phosphorus x urine creatinine)] x100 , best done in fasting state. A more thorough assessment of urinary phosphorus is assessed by calculating the tubular maximum reabsorption of phosphorus to glomerular filtration rate (TmP/GFR) (Walton RJ & Bijvoet OL, 1975).

**Bone Turnover Markers**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Test | Result | Unit for Result | Date | Time | Fasting Status |
| Procollagen type 1 N-propeptide (P1NP)- Bone formation marker | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Bone alkaline phosphatase (BALP)- Bone formation marker | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Osteocalcin (OC)- Bone formation marker | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Carboxyterminal telopeptide α1 chain of type 1 collagen (CTX)- Bone resorption marker | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Tartrate resistant acid phosphatase 5b (Trap-5b)- Bone resorption marker | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |
| Other, specify: | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site | Data to be filled in by site |

Recorder Signature:

General Instructions

This form contains data elements that correspond to laboratory studies commonly performed to evaluate bone health of participants.

Important note: None of the data elements included on this CRF Module are classified as Core (i.e., strongly recommended for all mitochondrial disease clinical studies to collect). All of the data elements are classified as Supplemental and should only be collected if the research team considers them appropriate for their study.

Please see the Data Dictionary for element classifications.

Specific Instructions

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

Date/time should be recorded to the level of granularity known (e.g., year, year and month, complete date plus hours and minutes, etc.) and in an unambiguous format acceptable to the study database like DD-MMM-YYYY. When date/time data are prepared for aggregation or sharing, they should be converted to the format specified by [ISO 8601](https://www.iso.org/iso-8601-date-and-time-format.html);  YYYY-MM-DD T:hh:mm:ss.

**Bone Turnover Markers**

Bone turnover markers are systemic markers indicative of the overall activity of the osteoblast and osteoclast system. When interpreting these markers, it is crucial to consider the age of the participant, particularly during growth and puberty stages, necessitating a control group. In childhood chronic conditions, bone turnover markers have demonstrated a strong correlation with growth, making it essential to account for this relationship when interpreting results during periods of growth (Tuchman et. al., 2008).

Furthermore, the assessment of bone turnover markers requires careful consideration of various influencing factors, such as fasting, diet, and recent fractures among others. If bone turnover markers are the primary focus of a research study, these factors should be meticulously taken into account to ensure accurate and reliable results.

As of the current time, there exists a clinical review on bone turnover markers in children, which summarizes the published normative data (Ladang et. al., 2023). Additionally, a comprehensive review covering the fundamental biology and clinical application of bone turnover markers in both adults and children offers insights into critical factors contributing to the variability in these markers (Schini et. al., 2023).

By acknowledging and incorporating these considerations, we can enhance the interpretation and application of bone turnover markers in clinical and research settings, contributing to a better understanding of bone health in participant of different age groups.

References

Ladang A, Rauch F, Delvin E, Cavalier E. Bone Turnover Markers in Children: From Laboratory Challenges to Clinical Interpretation. Calcif Tissue Int. 2023 Feb;112(2):218-232.

Schini M, Vilaca T, Gossiel F, Salam S, Eastell R. Bone Turnover Markers: Basic Biology to Clinical Applications. Endocr Rev. 2023 May 8;44(3):417-473.

Tuchman S, Thayu M, Shults J, Zemel BS, Burnham JM, Leonard MB. Interpretation of biomarkers of bone metabolism in children: impact of growth velocity and body size in healthy children and chronic disease. J Pediatr. 2008 Oct;153(4):484-90.

Walton RJ, Bijvoet OL. Nomogram for derivation of renal threshold phosphate concentration. Lancet. 1975 Aug 16;2(7929):309-10.