AA 53. Recommendations for biochemical monitoring of enteral nutritional adequacy for vitamin D, zinc, full blood count, ferritin, sodium, potassium, phosphate, blood glucose, blood urea nitrogen, prealbumin and albumin, conjugated bilirubin, bone mineral status (alkaline phosphatase, calcium, phosphate, vitamin D, parathyroid hormone). Who should be monitored and when (gestational age, birthweight, steroids, short gut syndrome)

Source recommendation	Back to question list
Source guideline title and developer	ESPGHAN 2022 Enteral Nutrition in Preterm Infants (2022) A Position Paper from the ESPGHAN Committee on Nutrition and Invited Experts https://pubmed.ncbi.nlm.nih.gov/36705703/
Existing guidelines recommendation	**Zinc** Measurement of serum zinc should be considered in preterm infants with growth and low alkaline phosphatase level, especially if they have excessive GI fluid losses. **Ferritin** Since individual iron status in VLBW infants is highly variable, depending on the number of received blood transfusions and blood losses from phlebotomy, it is recommended to follow these infants with repeated measurements of serum ferritin. **Blood urea nitrogen** We conditionally recommend monitoring plasma urea concentrations at regular intervals in case standard fortification is insufficient to support desired growth and more protein is added. There are no data that allow conclusive determination of optimal levels, and every baby is unique and clinicians have to individualise and exercise judgment. **Bone mineral status: Phosphorus and calcium** Regular monitoring of phosphorus and calcium status is recommended.
Year published	2022
Strength of recommendation	Low certainty
GRADE certainty of evidence *Conclusions and recommendations were assessed using both the Level of Evidence (LOE) and the Grade of Recommendation (GOR) frameworks, with all achieving greater than 90% expert consensus.*	**Ferritin and zinc:** LOE 4, GOR GPP. Level of evidence is very limited/low level. Grade of recommendation and Good Practice Point indicated no formal evidence, but board expert consensus indicated the recommendation reflects common sense, safe and effective clinical practice. **Blood urea and bone mineral status phosphorus and calcium**: GOR C, Grade of recommendation is weak/conditional.
Were EtD and SoF available?	No
Is the recommendation recent and credible (e.g. AGREE II >60%)?	Yes AGREE II: 65%
Source recommendation	
Source guideline title and developer	**French 2022** Vitamin D and calcium intakes in general paediatric populations: A French expert consensus paper

	https://pubmed.ncbi.nlm.nih.gov/35305879/
Recommendation	**Vitamin D** We recommend measurement of 25(OH)D in children born before 32 weeks of gestation or weighing less than 1,500 g at 1 month of age.
Year published	2022
Strength of recommendation	Moderate recommendation.
GRADE certainty of evidence	Grading system applied: American Academy of Paediatrics Graded C – Single or few observation studies or multiple studies with inconsistent findings or major limitations.
Were EtD and SoF available?	No
Is the recommendation recent and credible (e.g. AGREE II >60%)?	Yes 90%
Assessment of suitability for adolopment	
Is the recommendation relevant to local setting (population/ intervention/comparator)?	Yes
Are the judgements in the source EtD acceptable without modification?	Yes
Are any local contextual factors different (e.g. cost, equity, feasibility)?	Yes ability to undertake biochemical monitoring may be restricted in some centres by limited resources.

EtD Criterion	Summary of local evidence or context	Judgement	Notes
Problem	Infants receiving enteral nutrition are vulnerable to nutritional inadequacy which could impair long-term outcomes. Biochemical monitoring guides clinical decisions to improve outcomes.	Yes	Supports high risk populations, that would benefit from improved enteral nutrition.
Desirable effects	Enables management of enteral nutrition adapted to specific infants' requirements.	Favourable	Supports individual infants to thrive based on their unique needs.
Undesirable effects	Repeated blood sampling increases infant discomfort and anaemia risk. Additionally, the workload of staff and expenses increase.	Manageable	Manageable with minimal sampling strategies and coordination in clinical tests.
Certainty of evidence	ESPGHAN 2022: All recommendations achieved greater than 90% expert consensus. Low level certainty. French 2022 Moderate certainty.	Low to Moderate.	
Values and preferences	Clinicians and families value early detection of nutritional issues.	Potential variability	
Balance of effects	Benefits of early detection and prevention outweigh risks of over testing when guided	Favourable	Aligns with international standards.

	by standardise protocols and awareness of the risks.		
Resources required	Requires access to biochemical testing and adequality trained staff.	Moderate	The testing frequency may vary between infants, so ensuring staff that can adapt to these changes.
Certainty of resource evidence	Cost data is available.	Yes	
Cost-effectiveness	Early monitoring may prevent future health complications which lead to longer NICU stays and re-admissions.	Likely	Supported by modelling of improved growth and reduced complication cost.
Equity	Standardised monitoring protocols would contribute to equitable care across gestation ages and ethnic groups, including pēpi Māori and Pacific infants.	Favourable	Reduction in outcome disparities due to inconsistent nutritional surveillance across hospitals.
Acceptability	Clinically and ethically acceptable, families are likely to support as part of routine care.	High	If appropriate staff are available, then it will be no disturbance to infant's usual care.
Feasibility	For the biochemical markers identified and recommended for monitoring.	Yes	It is not feasible to monitor the other biochemical markers that do not have sufficient evidence behind them. Low resource settings need to be considered for how feasible biochemical monitoring is to implement in these centres.

Judgement criteria for EtD	
Decision Type	☐ Adopted as is ☑ Adapted ☐ De novo recommendation required
Explanation of adaptation	The ESPGHAN 2022 and French 2022 recommendation wording has been modified to align with the rest of our guidelines and with Aotearoa New Zealand current practice for preterm infants.
Final Recommendation	
Recommendation statement (adapted)	**Biochemical monitoring of enteral nutrition:** **Zinc:** Consider measuring serum zinc in infants with faltering growth and low serum alkaline phosphatase, especially if they have excessive gastrointestinal fluid losses. **Urea:** Plasma urea concentration can be used to indicate whether standard breastmilk fortification is sufficient to support appropriate growth. More protein may be needed if serum urea is <2.0 mmol/L **Bone mineral status:** Phosphorus, calcium, ALP and parathyroid hormone status should be monitored regularly **Vitamin D:** Serum Vitamin D (25-hydroxyvitamin D) should be measured at one month of age in infants born before 32 weeks' gestation or birthweight <1,500 g. If low, adjust dose and monitor every 10 – 14 days until well into the reference range.
Strength	Conditional
Certainty of evidence	Low to moderate
Basis for decision	Monitoring enables early intervention and enhances the safety of enteral nutrition. Although primarily supported by expert consensus, this recommendation aligns with established neonatal practice.
Subgroup Considerations	Extremely preterm or severely unwell infants may require case specific changes to the testing they receive, such as reduced frequency of testing.
Implementation Considerations	Protocols should define recommended monitoring intervals and the available investigations, with established referral or courier pathways to ensure regional access to specialised assays.

Monitoring and Evaluation	Review compliance with testing protocols, turnaround times, complication rates, and the incidence of critical abnormal results to support quality improvement initiatives.
Research Priorities	Establish evidence-based monitoring levels, identify and validate biochemical markers of nutrient sufficiency and toxicity, and explore less invasive testing methodologies.

EtD = Evidence to Decision framework, SoF = Summary of Findings table, NEC = necrotising enterocolitis, LC-PUFA = Long chain polyunsaturated fatty acids, *LOE = Level of Evidence, GOR = Grade of Recommendation, GPP = Good Practice Point*.