Immunological work-up and vaccination recommendations for children with 22q11 microdeletion

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Background:

Current practices regarding the immunological work-up and vaccine recommendations for children affected with 22q11 microdeletion varies (1,2). The below recommendations are based on expert opinion (2).

For newborn diagnosis of 22q11 microdeletion, please refer to figure 1 for recommendations related to immunological work-up and vaccine recommendations.

- Prior to administration of Rotavirus vaccines please ensure criteria 1, 2 and 4 are fulfilled in table one.
- Prior to administration of measles, mumps and rubella (MMR) or measles, mumps, rubella and varicella (MMRV) vaccination please ensure criteria 1-4 are fulfilled in table one.

For children diagnosed beyond the neonatal period, please ensure the following:

1. Immunisations are up to date as per the National Immunisation Program (NIP), including medical at-risk doses of Prevenar 13 (13vPCV) and Pneumovax-23 (23vPPV). Annual Influenza vaccination is also recommended. If a child is not up to date, see the National Immunisation Catch Up for further information.
2. If MMR and MMRV have not been received, please ensure criteria 1-4 are fulfilled in table 1 before proceeding. Children aged ≥ 14 years unvaccinated against varicella disease require 2 doses (1 month apart). See the National Immunisation Catch Up for further information.
3. See table 2 for suggested baseline immunological workup. If the child has received a primary course of diphtheria, tetanus and pertussis (dTpa) vaccination (ie. 3 doses), please also perform tetanus serology. Ongoing recommended periodic laboratory evaluation in patients with no T cell lymphopenia or mild lymphopenia can also be seen in table 2.

Additional vaccination requirements in children with 22q11 microdeletion:

- For all children with 22q11 microdeletion, we recommend additional medical at-risk doses of the pneumococcal vaccine (dose 4 Prevenar 13 and Pneumovax 23 from 4 years of age or ≥8 weeks following Prevenar 13, whichever is later).
    - Please also note, that patients with 22q11 microdeletion would also be eligible for a once in a lifetime booster dose of Pneumovax-23 five years following dose 1.
- Annual influenza vaccination should also be recommended.

- COVID-19 vaccination should also be considered, see ATAGI recommendations for further information.

Immunological assessment in children with 22q11 microdeletion:

An immunologic assessment in all children with 22q11 microdeletion is necessary to characterise immune status (see table 2 for suggested investigations) and use the information to help assess infection susceptibility. There is also the risk of immunoglobulin or humoral defects developing with time. Due to this, periodic immunologic evaluation in 22q11 microdeletion patients is also recommended (see table 3). For children with an abnormal immunological work-up, please contact immunology and consider referral to Specialist Immunisation Service for facilitation of medical at-risk immunisations.

Approach to children with limited tetanus immunity:

Where feasible tetanus serology should be completed 4-6 week post a tetanus containing vaccine. In children with limited tetanus immunity who **have not** received a tetanus containing vaccine within the last 3-5 years, we recommend an age-appropriate tetanus containing vaccine. In children with limited tetanus immunity who **have** received a tetanus containing vaccine within the last 3 years, then we would suggest counselling that in the event of a tetanus prone wound, they would require an age-appropriate tetanus containing vaccine +/- consideration of tetanus immunoglobulin (see National Immunisation Handbook Table: Guide to tetanus prophylaxis in wound management).

Figure 1: Immunological investigation for newborn diagnosis of 22q11 microdeletion in relation to live vaccines as per the National Immunisation Program (NIP)

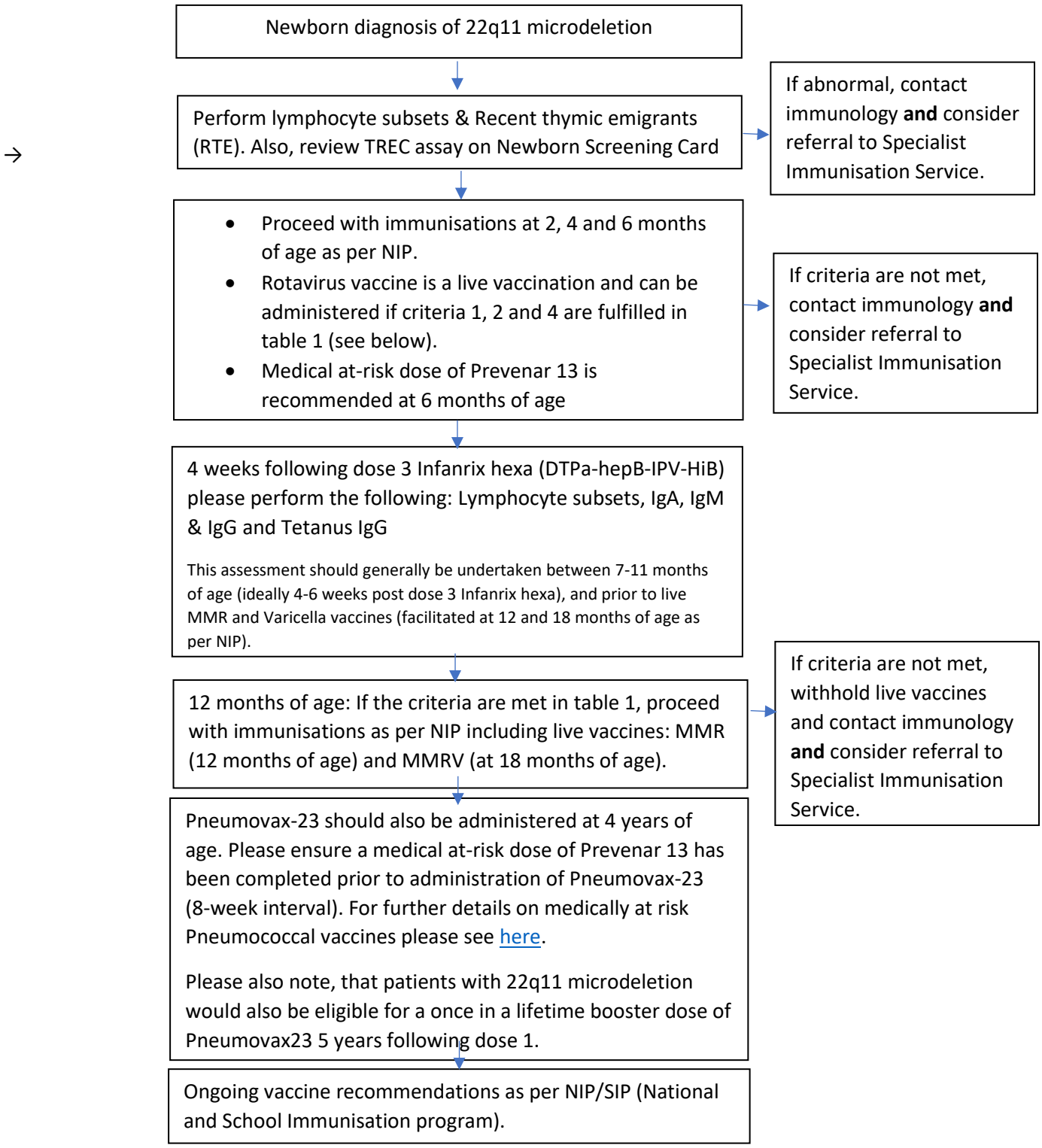

Table 1: Guideline recommendations for live vaccine administration in children with 22q11 microdeletion.

Criteria	Laboratory results (blood)
1.	CD4 ≥ $0.4x10^9$
2.	CD8 ≥ $0.2x10^9$
3.	Tetanus IgG ≥ 0.11 IU/ml (4+ weeks after dose 3 Infanrix hexa (DTPa-hepB-IPV-HiB))
4.	Recent thymic emigrant (RTE) ≥50% Please utilise data from earliest assessment.
If available and T cell numbers abnormal, consider either confirmation of normal TREC assay result on NBS.	

Table 2: Recommended periodic laboratory evaluation in 22q11 deletion in patients with no T cell lymphopenia or mild lymphopenia.

	At diagnosis	8-11 months	Age 4-5 years	Age 12 years or year 7*	Every 5-10 Years
Lymphocyte subsets	X	X	±		
RTE	X				
IgA, IgG, IgM		X	X	X	X
Tetanus IgG		X	X	X	±
Pneumococcal serology			±#	±#	±#
*Boostrix (dTpa) is administered as part of the School Based Immunisation Program at 12 years or grade 7. Please facilitate tetanus serology 4-6 weeks post Boostrix administration. # Decision to do pneumococcal serology is discretionary, with the need determined by other lab results, infection history, access, cost, cardiac surgery with partial thymectomy and shared decision making with immunology. Recent thymic emigrant (RTE)					

References:

1. Berkhout A, Preece K, Varghese V, et al. Optimising immunisation in children with 22q11 microdeletion. Ther Adv Vaccines Immunother. 2020 Oct 16;8:2515135520957139. doi: 10.1177/2515135520957139.
2. Mustillo PJ, Sullivan KE, Chinn IK, et al. Clinical Practice Guidelines for the Immunological Management of Chromosome 22q11.2 Deletion Syndrome and Other Defects in Thymic Development. J Clin Immunol. 2023 Feb;43(2):247-270. doi: 10.1007/s10875-022-01418-y.