

Risk Levels of Pediatric Procedures and Chart of Maximum Allowable Total Blood Draw Volumes in Children

The IRB convened a group of pediatricians and other specialists to discuss minimal risk pediatric procedures. The objective was for the IRB to identify what procedures are considered minimal risk in pediatric populations and what procedures are not considered minimal risk.

Pediatric Procedures that are Minimal Risk

1. One heel stick, particularly in healthy neonates
2. Nail/hair clippings
3. Lower nasal cavity swabs
 - a. This can be reviewed and approved under expedited category 3, provided that the mucosal swab does not extend beyond the nares, since category 3 is noninvasive collection and 21 CFR 812 defines invasive as beyond the nares.
4. Blood draws with certain constraints
 - a. For children older than 2 years of age, one research phlebotomy only for children under 6 years of age, with a limit of 3 attempts; remainder of planned blood draws should be coordinated to occur at the time of clinical care draws; use of local anesthetic left to judgement of phlebotomist.
 - b. For children older than 6 years of age but less than 12 years of age, 2 research phlebotomies at least 28 days apart, with a limit of 3 attempts at each procedure; remainder of planned blood draws should be coordinated to occur at the time of clinical care draws; use of local anesthetic left to judgement of phlebotomist.
 - c. For children older than 12 years of age, 3 research phlebotomies at least 28 days apart between each procedure, with a limit of 3 attempts at each procedure; remainder of planned blood draws should be coordinated to occur at the time of clinical care draws; use of local anesthetic left to judgement of phlebotomist.
 - d. Maximum allowable volumes (Clinical & Research combined): 2.5% of total blood volume, with 7.0 Hgb minimum; refer to blood volume allowable draw by weight below
 - e. Keep in mind that regardless of allowable volumes, phlebotomy on children under 2 years of age is not considered minimal risk and must be reviewed by full committee.
5. Collection of cerebrospinal fluid with certain constraints
 - a. For children older than one year of age, up to 10ccs of CSF combined clinical care and research volume may be taken, in the absence of general anesthesia
 - b. If the child will be under anesthesia, full committee review will be required.
6. MRI
 - a. 3T MRI without contrast or sedation qualifies for expedited review.
 - b. 7T MRI requires full committee review
 - c. Any use of contrast or sedation requires full committee review.

Pediatric Procedures that are Not Minimal Risk

1. Extra biopsies performed during standard of care procedures (such as colonoscopy and cardiac catheterizations) to collect additional specimen – these are not minimal risk given prolongation of anesthesia and risk of perforation associated with any biopsy.
2. Radiation, even in small amount (such as chest-x-rays) and even without sedation, is not minimal risk.
3. Use/administration of drugs for research purposes, through various routes of administration, is not minimal risk.
4. Skin biopsies for both healthy and affected children are not minimal risk because they are associated with pain, scarring, risk of infection, risk of bleeding, and the magnitude of harm and discomfort is greater “than ordinarily encountered in daily life.” There is little difference between a 2 mm, 3 mm, and 4 mm biopsy—with use of lidocaine, small risk of bleeding, risk of scar, infection rate less than half of 1% for all patients — except that usually no stitch is required at 2 mm and 3 mm. A skin biopsy larger than 4 mm will require stitches, and have greater potential for pain, bleeding and infection.
 - Pediatricians should be advised to document in the study application why a biopsy is necessary, what the risks are for the population (affected or control), and what the benefits are to the child or whether results may yield generalizable knowledge. Unless a strong argument can be made for direct benefit for a 405/52, skin biopsies in children will likely be a 406/53 requiring 2 parent/guardian consent.
5. Except for one heel stick, blood draws for children two years of age and younger are not minimal risk. Blood draws for children in the NICU are also not minimal risk.
 - Review Process: There should be restrictions on timing and attempts, *i.e.*, there should be one research phlebotomy only and the remainder should be at time of clinical draws, and there should be no more than three attempts for research venipuncture consistent with Pediatric Clinical Research Center policy.
6. Collection of cerebrospinal fluid in children less than one year of age is not considered minimal risk.
7. Any studies including randomization of participants cannot be considered minimal risk and must be referred to full committee, based on the need to protect children against being randomized to an inferior group.

Pediatric Procedures that May or May Not Be Minimal Risk

1. Questionnaires, online learning, focus groups, educational testing related to mental/emotion health, substance use, sexual/reproductive health

MAXIMUM ALLOWABLE TOTAL BLOOD DRAW VOLUMES IN CHILDREN

The below blood volume limits include blood drawn for **both clinical and research purposes**, e.g., if a 4 kg infant has 5 cc drawn for clinical use, then only 3 cc may be drawn at the same time for research. If the same infant has 10 cc drawn for clinical care over the course of a 28-day period, the study team is only allowed to draw 6cc in total over that same period for research purposes.

Body Weight (Kg)	Maximum volume (mL) drawn in a 28-day period	Maximum volume (mL) drawn for any single draw*
1	5	2.5
2	10	5
3	12	6
4	16	8
5	20	10
6	24	12
7	28	14
8	32	16
9	36	18
10	40	20
11-15	44-60	22-30
16-20	64-80	32-40
21-25	84-100	42-50
26-30	104-120	52-60
31-35	124-140	62-70
36-40	144-160	72-80
41-45	164-180	82-90
46-50	184-200	92-100
51-55	204-220	102-110
56-60	224-240	112-120
61-65	244-260	122-130
66-70	264-275	132-138
Greater than 70	275	138

*Maximum allowable volume in one blood draw is limited to 2.5% of total blood volume, or one-half of the 28-day maximum allowable volume.

Based on blood volume of:		
kg	mL/kg	
1-2	100	Pre-term infant
> 2	80	Term infant - adult