Online Supplementary Material for Ford et al., "Use of Compartmental Modeling and Retinol Isotope Dilution to Determine Vitamin A Stores in Young People with Sickle Cell Disease Before and After Vitamin A Supplementation"

Supplemental Methods

Adjusting plasma retinol fraction of dose

To obtain the most representative central tendency for the group composite data on FD_p for modeling, we adjusted (normalized) each individual's values for FDp in samples collected later than 3 d postdosing based on their position relative to the geometric mean at 3 d. Specifically, for each subject, we calculated a 3 d ratio using the equation:

$$3\text{ d ratio}_{(i)} = \text{geometric mean } FD_p \text{ at 3 d} / FD_{p(i)} \text{ at 3 d}$$

where *i* is the i^{th} subject. Then, we multiplied each subject's FD_p at post-3 d times by the 3 d ratio using the equation:

$$\text{Adjusted } FD_{p(i)} = 3\text{ d ratio}_{(i)} \times \text{post-3 d } FD_{p(i)}$$

The composite super-subject dataset was defined as the geometric mean FD_p at each time, including adjusted FD_p values at all sampling times after 3 d.

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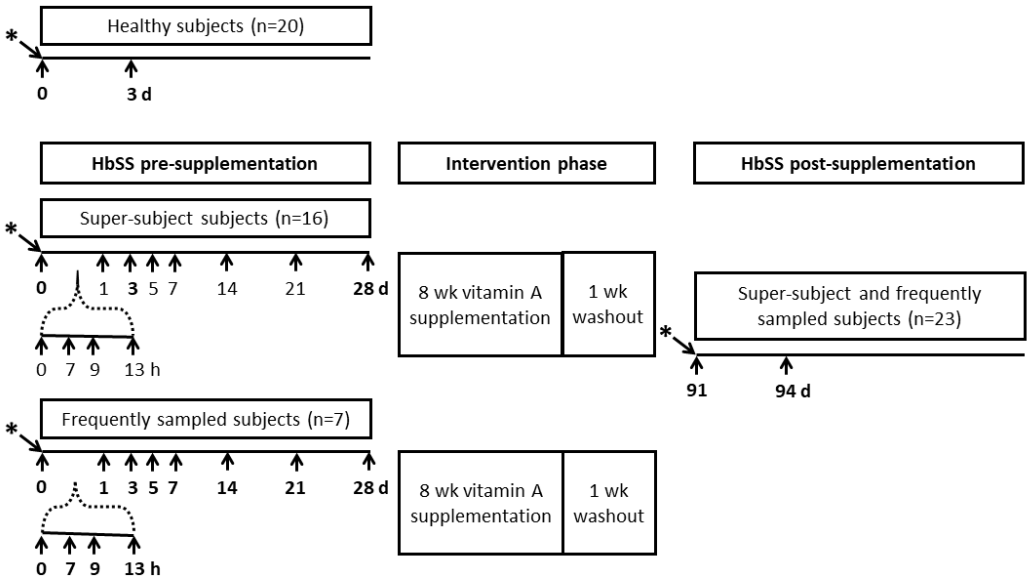

Supplemental Figure 1 Study design and blood sampling schedule. Healthy subjects were sampled at baseline and 3 d after dosing; SCD-HbSS super-subject participants were sampled before supplementation at baseline and at 3 d after dosing and at one additional time; after the intervention phase, they were sampled at baseline and 3 d post-dose; frequently sampled subjects were sampled at all times indicated from 0 to 28 d post-dose. The asterisk (*) represents the time that the oral [$^{13}C_{10}$]retinyl acetate dose was administered; times indicated in bold show when blood samples were collected from all subjects in the specified group. SCD-HbSS, sickle cell disease hemoglobin SS type.

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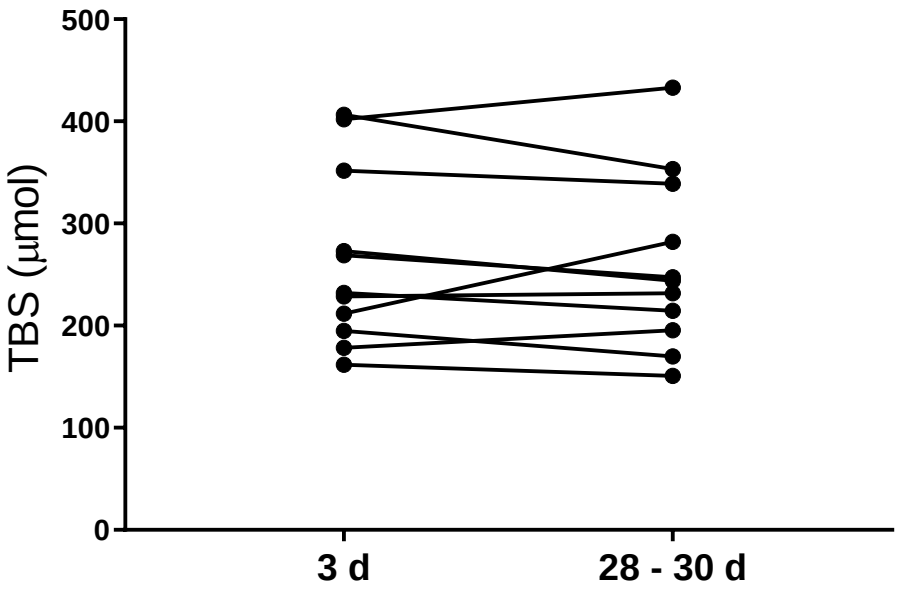

Supplemental Figure 2 Paired predictions for TBS calculated by RID at 3 d and at later times for a subgroup (n=11) of young people with SCD-HbSS before supplementation. Symbols show TBS predicted for individual subjects and lines indicate their paired predictions at the 2 times. Later times were 28 d for 8 subjects and 29 or 30 d for 2 others. Values were calculated using Equation 1 (see Methods) with group values for the equation's composite coefficient *FaS* calculated by modeling the super-subject dataset along with each subject's SA_p at the corresponding time. Model-predicted values for *FaS* used in these calculations were 2.40 at 3 d (n=11), 0.622 at 28 d (n=9), 0.618 at 29 d (n=1), and 0.614 at 30 d (n=1). Based on paired comparisons, TBS predictions were not significantly different at 3 d versus the later times. The geometric mean TBS for this subgroup of SCD-HbSS subjects was 252 µmol (range, 162–406 µmol) at 3 d and 248 µmol (range, 151–433 µmol) at 28 d. RID, retinol isotope dilution; SA_p, retinol specific activity in plasma; SCD-HbSS, sickle cell disease hemoglobin SS type; TBS, vitamin A total body stores.

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Supplemental WinSAAM Deck

```
A SAAM31          CHOP SCM ALL PRE-RX SS  [08-APR-2023]
C 2EV DI; LOSS SPLIT 50/50; INPUT INTO DT(3)
c DECK FOR MSS FIG 1
C FD ADJU >3D VS TIME AS DISCUSSED IN MSS
C UPDATED [13C10]ROH ANALYSIS FROM 17-OCT-19
H PAR
CC TRACER
   IC(3)    1.0
   DT(3)     2.627307E-01
   DN(3)    8
   L(4,3)   0.75
   L(0,3)=1-L(4,3)
   L(5,4)    9.643918E-01
   L(6,5)    4.675106E+00
   L(5,6)    3.123267E-02
   L(10,6)   1.650246E-03
   L(7,5)    2.954719E+00
   L(5,7)    2.439266E-01
C L(8,5)=(DR/2)/M(5)
   L(8,5)   0.234
   DT(8)    0.052
   DN(8)    8
   L(10,8)  1.0
CC PARALLEL TRACEE
   UF(13)=1.73078
   DT(13)=DT(3)
   DN(13)   8
   L(14,13)=L(4,3)
   L(0,13)=L(0,3)
   L(15,14)=L(5,4)
   L(16,15)=L(6,5)
   L(15,16)=L(5,6)
   L(20,16)=L(10,6)
   L(17,15)=L(7,5)
   L(15,17)=L(5,7)
   L(18,15)=L(8,5)
   DT(18)=DT(8)
   DN(18)   8
   L(20,18)=L(10,8)
   IC(13)=0.454729
   IC(14)=1.34601
   IC(15)=2.77
   IC(16)=393.823
   IC(17)=33.5534
   IC(18)=0.0337
H DAT
105                                        FSD=0.05
            TIME (d)      FD
            0             0
            0.296629663   0.021174952
```

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```
            0.383482966   0.043957318
            0.529109414   0.06960207
            1.042291763   0.070569
105                                     FSD=0.025
            2.998148553   0.014841528
105                                     FSD=0.05
            5.033566367   0.009483225
            7.023935806   0.007910541
            14.16594578   0.004449613
            21.44515146   0.004123146
            28.32947454   0.004377299
CC  COMPARTMENT SIMULATIONS
104
            0.0
2           0.1                         50
2           1.0                         23
2           10                          7
105
            0.0
2           0.1                         50
2           1.0                         23
2           10                          7
106
            0.0
2           0.1                         50
2           1.0                         23
2           10                          7
107
            0.0
2           0.1                         50
2           1.0                         23
2           10                          7
114
            0.0
2           0.1                         50
2           1.0                         23
2           10                          7
115
            0.0
2           0.1                         50
2           1.0                         23
2           10                          7
116
            0.0
2           0.1                         50
2           1.0                         23
2           10                          7
117
            0.0
2           0.1                         50
2           1.0                         23
2           10                          7
CC S FOR COMP 6 + 7
125G(25)
```

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```
XG(25)=(F(5)/F(15))/((F(6)+F(7))/(F(16)+F(17)))
             1.0
2            0.5                              18
2            1.0                              18
2            10                               7
CC Fa*S
126G(26)
XG(26)=(F(6)+F(7))*G(25)
             1.0
2            0.5                              18
2            1.0                              18
2            10                               7
```