LETTERS TO THE EDITOR

Re: Radiation Absorbed Doses from Iron-52, Iron-55, and Iron-59 used to Study Ferrokinetics

As a first step in the installation of the MIRD model for the metabolism of iron (*1*) into a general model (*2*) used to calculate retention, excretion, and doses for radiation-protection purposes, the compartment residence times obtained for the model with the numerical differential equation integrator FORSIM (*3*) have been compared with those reported by Robertson et al. using the SAAM-25 integrator (*1*). The purposes of this comparison were to ensure that the model was properly installed, and to see what effects the three simplifying assumptions used by Robertson et al. have on the calculated activity in organs, and hence dose. The assumptions used by Robertson et al. are:

1. Excretion of radioiron can be ignored.

Residence times in compartments (see Table 1) have been calculated both without (FORSIM) and with (FOR-EXC) excretion included. The transfer rate constant for excretion from the plasma was estimated to be 0.14 from data summarized in Reference Man (*4*), assuming a total excretion rate from this compartment of 0.5 mg/day. Losses from bleeding or from desquamated intestinal cells have been ignored. By comparing the residence times for FORSIM and FOR-EXC (Table 1), it can be seen that ignored excretion results only in an overestimation of the residence time by about 20% in the worst case (Fe-55).

2. The relatively constant lifetime (120-day intervals) of red blood cells (RBC) can be adequately modelled by transferring all of the activity in the RBC to the rapid-storage compartment (rapid) at 120 day intervals.

Implementation with the FORSIM model can use this approximation or a more refined version, in which the amount of radioiron transferred from the bone marrow compartment to the RBC compartment on day T is used as the rate (suitably corrected for decay) of transfer of radioiron from the RBC compartment to the rapid-storage compartment on day T + 120. The results obtained with this latter approximation are given in Table 1.

3. The numerical integration need be carried out only to ten physical half-lives for Fe-52 and Fe-59, and to 400 days for Fe-55, after which time the retention of Fe-55 in each compartment is governed only by radioactive decay.

The integration to ten half-lives is a good approximation, since essentially all the activity has decayed by this time. After 400 days, however, less than ½ of the Fe-55, ($T_{1/2}$ = 1000 d) has decayed, and neither the slowly equilibrating tissue (slow) compartment nor the RBC compartment has reached equilibrium. The results (FORSIM and FOR-EXC) in Table 1 are for integrations to ten physical half-lives for all three radioirons. If the integration is stopped at T = 400 days, different results are obtained, but they do not agree with those taken from Ref. (*1*). However, when all of the approximations are used simultaneously, the results (FOR-APR, Table 1) are in reasonable agreement with those of Ref. (*1*), except for RBC and marrow for Fe-52.

The conclusion that can be drawn from the calculations performed using the model as implemented in FORSIM to test the effects of the assumptions is that they do not have a large effect on residence time. However, even if all the approximations are taken into account, there are still minor differences between the results obtained with FORSIM (FOR-APR) and those given in

TABLE 1. RESIDENCE TIME BY COMPARTMENTS* (hr)

	1(Plasma)	2(ECF)	3(Rapid)	4(Slow)	5(Marrow)	6(RBC)
			Fe-52, Mn-52m			
MIRD†	2.2	1.1	1.9	0.023	6.7	0
FORSIM	2.2	1.1	1.9	0.023	5.0	1.7
FOR-EXC	2.2	1.1	1.9	0.022	4.9	1.7
FOR-APR	2.2	1.1	1.9	0.023	5.0	1.7
			Fe-55			
MIRD†	22	23	270	6100	130	28,000
FORSIM	37	57	820	7900	320	25,000
FOR-EXC	30	47	670	6500	260	21,000
FOR-APR	14	22	270	6100	120	28,000
			Fe-59			
MIRD†	6.9	7.2	36	50	39	1400
FORSIM	4.4	6.7	35	48	37	1400
FOR-EXC	4.3	6.5	34	47	36	1400
FOR-ARP	4.4	6.7	35	48	37	1400

* See Reference 1 for description of the compartments.

† Normal values from Table 6 of Ref. *1*.

TABLE 2. RESIDENCE TIME IN SOURCE ORGANS* (hr)

	Liver	Spleen	Red marrow	Heart	RBC	Residual
			Fe-52, Mn-52m			
MIRD†	0.22	0.037	8.7	0.18	0	2.8
FORSIM	0.31	0.12	7.1	0.32	1.4	2.8
FOR-EXC	0.30	0.12	7.0	0.31	1.3	2.7
FOR-APR	0.31	0.12	7.1	0.32	1.4	2.8
			Fe-55			
MIRD†	3400	2300	3300	2200	22,000	1400
FORSIM	3900	2500	4500	2000	20,000	1800
FOR-EXC	3200	2000	3700	1700	16,000	1500
FOR-APR	3400	2300	3300	2300	20,000	1400
			Fe-59			
MIRD†	87	78	150	110	1100	23
FORSIM	87	78	140	110	1100	20
FOR-EXC	85	76	140	110	1100	20
FOR-APR	87	78	150	110	1100	21

* See Ref. *1* for a description of the organs.

† Normal values from Table 4 of Ref. *1*.

Ref. (*1*). In order to see whether the SAAM-25 (*1*) or the FORSIM implementation of the model was at fault, the ratio of activity in several compartments after equilibrium is reached with a chronic input was calculated and compared with the ratio of residence times taken from Table 1. The reason for doing this is that the activity in a compartment from chronic intake at equilibrium is numerically equal to the integrated activity following a single intake (*5*).

Ratios considered are Compartments 5 to 6 for Fe-52 (equal to 2.9) and Compartments 1 to 2 for Fe-59 (equal to 0.66), as these will not be affected by the approximations. These values were calculated using the rate constants given in Table 3 of Ref. (*1*). A comparison of these values with those calculated with the SAAM-25 program (MIRD) and the FORSIM program from Table 1 indicates that it is the SAAM-25 program that is at fault.

The effect of the above-mentioned assumptions, and of the differences between the results calculated by SAAM-25 and FORSIM on dose, can be estimated by comparing the residence times in organs, as is done in Table 2. It can be seen that the differences in organ residence times, and hence organ doses, are significant only for Fe-52 and Fe-55. The largest difference for Fe-52 is for the residence time in the spleen, which in turn arises from the difference in the residence time for the RBC compartment (Table 1). The maximum difference for Fe-55 is less than 40%, which is probably less than the uncertainty resulting from individual variability in metabolism and organ size.

J. R. JOHNSON
D. W. DUNFORD
Chalk River Nuclear Laboratories
Chalk River, Ontario, Canada

REFERENCES

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Reply

In response to Johnson's and Dunford's letter regarding a comparison of their calculation of residence times in the iron model with those of the MIRD Committee, I would like to begin by welcoming this independent approach. A long-existing weakness of the use of the SAAM method of analysis has been the unavailability of competitive methods. The overall agreement obtained is, of course, also gratifying.

Some of the discrepancies noted are readily explained, others involve the philosophy of modeling.

In the first category is the absorbed dose to the RBC compartment from Fe-52 and Mn-52m. As was mentioned in the MIRD report (*1*) the delay time for iron in the marrow is 3 to 5 days. Because of this and the 8.2-hr half-life of Fe-52, no appreciable amount of Fe-52 reaches the circulating RBCs. Therefore, for Fe-52 the marrow should not be considered to be a well-mixed compartment, but should have a delay time, as is done for the RBCs. This delay however, did not seem to be important for Fe-55 and Fe-59. Although a simplification was implied but not explicitly stated in the MIRD report, rather than complicating the model we adopted the simple expedient of using a transfer rate of zero for the red marrow to RBC compartments when Fe-52 was con-