Appendix 3

Informational submission by J. Lederberg in connection with Engineering Models of Biohazard of Microbiological Procedures

Although many elements of risk assessment are difficult to quantitate at the present time it is useful to outline models that help to identify critical factors. We may view contamination as a process of hindered diffusion. The eventual biohazard cost is, crudely C= S x T x R, where S is the level of environmental loading in the laboratory, T is the probability per organism of release outside the laboratory and R is the social cost per organism released. To a first approximation these are linear functions, i.e. the fate of each microbe is independent of others.

Each of these factors may be subdivided, and is subject to some manipulation in the interests of minimizing C. Thus R may be drastically reduced by biological variation: the choice of organisms which are discovered or engineered to be relatively incapable of doing harm even if released. In the context of molecular genetic research, these are the "disabled carriers".

Good laboratory practice is dedicated primarily to minimizing Se, the microbial load in the laboratory but outside the specific containers which house the organisms. The level Se depends on the total bioburden and on the procedures by which this is handled. 10^{10} organisms in a quiet flask offer less risk than 10^{6} organisms subject to inadvertent aerosolization.

The transmission factor, T, may be divided into a physical and a human component (Tp and Th respectively). The training of personnel is obviously of the first importance for a) reducing the interval loads, Se, b) for maintaining the parietal integrity (Tp) of the physical facilities, and c) for their personal hygiene, Th. Other measures like prophylactic immunization and clinical surveillance for early spotting of possible infection are also appropriate for given organisms.

We have relatively little quantitative, absolute information on these parametersbut some guesses are possible about relative risk - attenuation ratios, expressed in decibels (e.g. 25 db = $10^{-2.5}$). The numbers are rough guides only.

Disabled organisms in the most favourable cases can afford 100-120 db improvements, by theoretical calculation. This may be tempered by non-ideal behaviour and other uncertainties so that a conservative 60 db is assigned to this recourse in the figure.

We have little explicit information on the security factors of moderate-risk oriented facilities. It is possible that substantial economy and assurance is available through more informed choices in this area. Aerosol reduction and internal hygiene in the laboratory have already been discounted. Given the realities of human compliance it may be optimistic to expect more than another 40 db from moderate-cost facilities, and an additional 40-60 db from ultra-secure operations (involving, e.g. tele operator handling of cultures).

Note that 160-180 db may be achievable either with the use of safe carriers or with ultra-secure facilities.

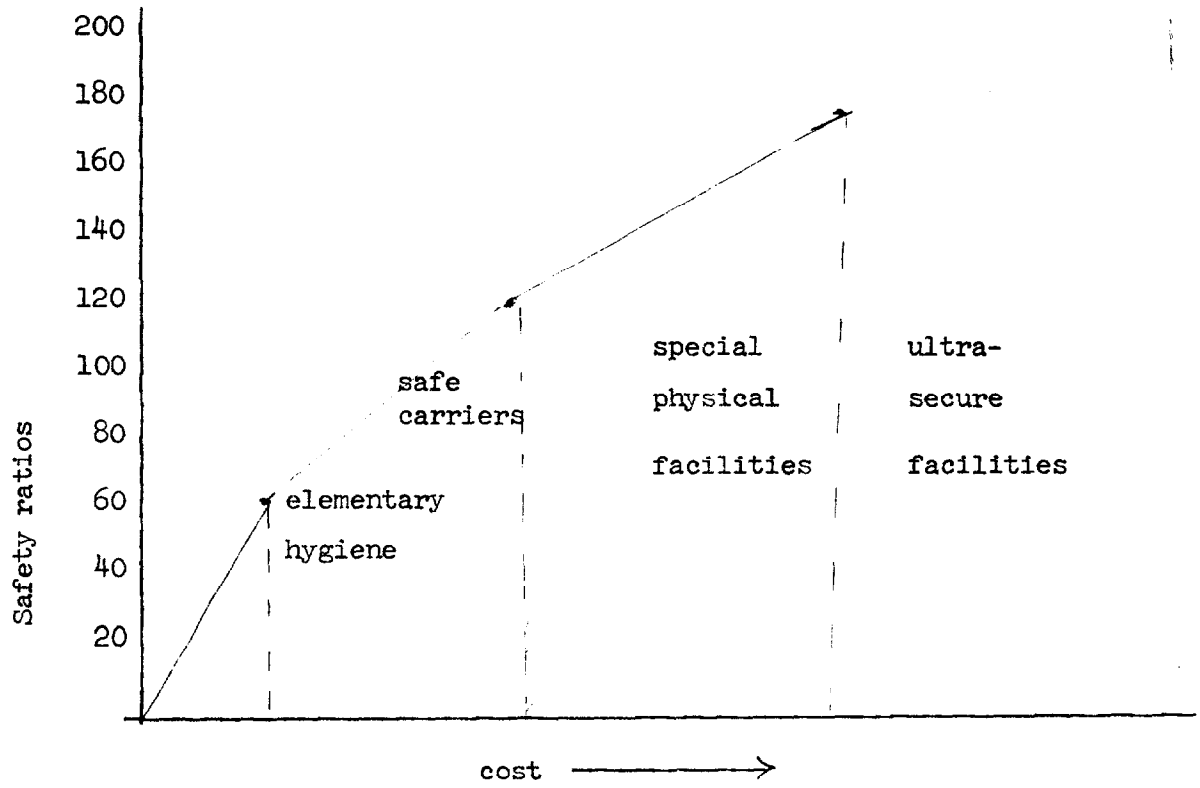
This attenuation, 10^{-16}, is indeed an astronomical safety factor. It is tantamount to reducing releases from, say, 10^{6} organisms per day to a probability of 10^{-10}. Another dollar's investment (which includes the foregoing of a like benefit) would be justified only in the remarkable case that the expected cost (not the worst case contingency) of releasing an organism were of the order 10^{9} dollars. (E.G. that the hazard of one such release exceeded the annual benefits of the world's public health programmes.)

This criterion exceeds (but not by a large margin) the expected hazard from the release of a single particle of any known infectious agent.

Thus it does leave some rationale for the interdiction of a range of high-risk low-benefit experiments for which still higher margins are for some reason unavoidable.

If the human population is assumed to be so vulnerable to a one-particle risk it should give occasion to reexamine the cost-effectiveness imperatives of other measures to reduce our vulnerability to natural sources of infection.

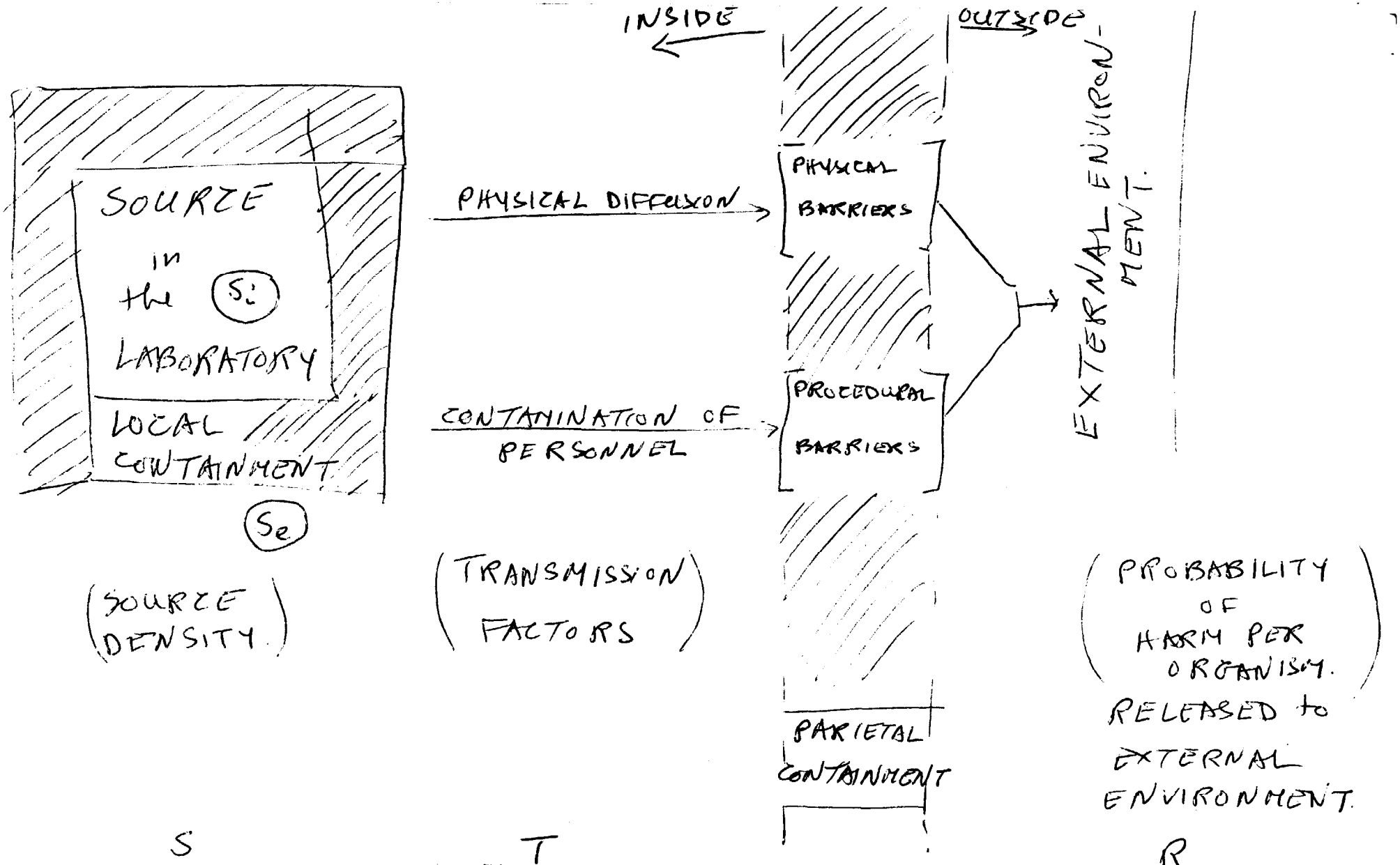
Careful practice and choice of equipment can easily reduce the Se/Si ratio by 40 db, and elementary hygiene can ameliorate T (Tp + Th) by at least another 20 db. This 10^6 fold reduction in risk is achievable at low cost by the application of the most elementary principles of laboratory hygiene (Appendix I). This is the most cost-effective part of the safety function.



To Recapitulate

10 db = 10^{-1} attenuation of risk

Costs per lab per worker per year	Component	safety increment	cumul approx.
$ 500 ——— $ 1000	Training safe equipment and internal barriers	40 20	60
1000 (amortized development costs)	safe carriers	60	120
4000	safe lab (sealing, ventilation)	40	180
20 000	ultra-secure lab	40	220 (160 (without safe carrier)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