THE INVESTIGATION OF PRESENT-DAY DEFINITIONS AND CONCEPTS OF MAXIMUM ALLOWABLE CONCENTRATIONS IN NORTH AMERICA

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SIGNIFICANCE OF IMPURITY IN TECHNICAL INDUSTRIAL PRODUCTS

While the effect of added or remaining impurity is to decrease the toxicity of technical formulations when the impurity is of lower toxicity, the work of the author and co-workers[1] on aldrin and dieldrin and of Ingles[2] on chlordane, for example, demonstrated that the presence of process by-products in technical preparations of these insecticides greatly increased their toxicity. Subsequent investigation showed these impurities to be many times as toxic as the pure compound.

The synergistic action of certain non-toxic additives must be considered, *e.g.*, piperonyl butoxide on pyrethrin.

In America, technical products are tested even when the toxicity of the principal active ingredient is known.

TIME OF EXPOSURE

This is understood to mean duration of exposure. Maximum allowable concentrations (M.A.C.'s) are a product of concentration, toxicity and length of exposure. In America the latter is realistically set as an 8-hour day and a 5-day week. The M.A.C. must be low enough to prevent any observable ill effect.

MEDIUM OR TEMPORARILY INCREASED CONCENTRATION

A medium increase in concentration may be tolerated for a short time in the case of low and medium toxicity compounds, provided it does not cause the average to exceed the M.A.C.

The probable effect of short peak exposures is estimated from a knowledge of toxicity. If the process is one which emits irregular levels of toxicant, several samplings spaced through the working day may be required.

TOXIC EFFECT CAUSED BY DISCOMFORT

Discomfort places a stress on the body and will increase susceptibility to the poison in question or, indeed, to any other poison. M.A.C.'s are based on discomfort only when this occurs below the toxic level.

M.A.C.'s based on discomfort are usually below those based on toxicity, *e.g.*, where an unpleasant odour occurs at low concentration.

ACUTE EFFECT, CHRONIC EFFECTS AND ACCUMULATIVE EFFECTS

The M.A.C. is a value which is based on the long-term effect of the toxicant at a comparatively low level. When a short exposure causes observable effects, the environment is too dangerous for continued contact.

Acute toxicity tests are valuable for establishing the relative toxicities of compounds.

Chronic or long term exposure tests are the ones which are most valuable in establishing M.A.C.'s.

Accumulative effects may be considered those which are left after all reversible symptoms have had their effect. The final condition after a long-term exposure is the accumulative effect.

Definitions are as follows:

acute: short or sharp;
chronic: of long duration;
accumulative: heaped up.

M.A.C. IN PHYSICAL STRAIN

Stress of any kind (physical or mental) adds an extra burden to the body and reduces its ability to combat toxic materials.

Under extreme conditions of heat, cold, physical exertion, *etc.*, the M.A.C. should be lowered.

M.A.C. IN SIMULTANEOUS OCCURRENCE OF SEVERAL TOXIC SUBSTANCES

This has been studied under the heading of toxicity of mixtures and is perhaps the most complex problem in the M.A.C. field.

Before the M.A.C. can be estimated, it is necessary to establish by animal experimentation whether similar joint action, independent joint action, antagonism or synergism occur and to obtain some idea of the magnitude of their effect.

If the individual toxicities of the constituents of a mixture and the relative percentages in which they are present are known, simple mathematical calculations will give the overall toxicity, provided the toxicities have similar joint action (see Appendices A and B).

If the action is independent joint action, antagonism *or* synergism, the calculation given in Appendix A and B must be modified by that in Appendix C.

THE EXTENT TO WHICH IT IS NECESSARY TO CONSIDER INDIVIDUAL SENSIBILITY OF PEOPLE WHEN DETERMINING M.A.C.

The M.A.C. is based on average response with a margin for safety.

If the worker has a known allergy he must be placed on other work.

Certain exposures render people allergic to other things. Generally, however, the working population is more homogeneous and healthy than average.

References

[1] W. L. Ball, Kingsley Kay and J. W. Sinclair. " Observations on toxicity of aldrin ", *A.M.A. Arch. Ind. Health*, **7**, 292 (1953)

[2] L. Ingle. " A revised concept of chlordane toxicity to warm-blooded animals ", Paper presented to Chemical Specialties Manufacturing Association, New York, Dec. 1954

APPENDIX A

M.A.C. calculations for mixtures

Calculation of the M.A.C. of a mixture of two or more substances which exercise similar joint action if the individual M.A.C.'s and the relative concentrations of the ingredients are known can be made as follows:

Assume that a known mixture of substances is released into a working atmosphere.

Let $A, B, C, \ldots N$ represent the substances and $a, b, c \ldots n$ the percentages in which they were present in the original mixture.

Then, as the M.A.C. is a reciprocal, high values representing low toxicity, the following calculation applies:

$$\text{M.A.C. of mixture} = \frac{1}{1/A \times a/100 + 1/B \times b/100 + 1/C \times c/100 + \ldots + 1/N \times n/100}$$

$$= \frac{1}{a/100A + b/100B + c/100C + \ldots + n/100N}$$

$$= \frac{1}{1/100\,(a/A + b/B + c/C + \ldots + n/N)}$$

The equation can be further simplified, but its derivation then becomes obscure.

Example:

$$\text{Let } A = 100 \text{ and } a = 50$$
$$B = 200 \quad b = 20$$
$$C = 300 \quad c = 30$$

substituting in the equation gives:

$$\text{M.A.C. of mixture} = \frac{1}{1/100\,(50/100 + 20/200 + 30/300)}$$

$$= 143.$$

APPENDIX B

M.A.C. calculation for mixture based on the fraction or percentage of M.A.C. in which ingredients are present

It is sometimes important to be able to estimate how much of two or more toxicants may be permitted together in a working atmosphere.

This estimate may be made by calculating the fraction or percentage of its M.A.C. in which each constituent exists. If the total of these fractions or percentages does not exceed 1 or 100 respectively, the atmosphere may be assumed to be safe provided there is no synergism.

Example:

Suppose that benzene of M.A.C. 25 and toluene of M.A.C. 200 are present to the extent of 10 and 100 parts/million respectively. How much xylene of M.A.C. 200 could be added without creating a dangerous atmosphere?

Calculation:

$$10 \text{ is } \frac{10}{25} \text{ of benzene's M.A.C.}$$

$$100 \text{ is } \frac{100}{200} \text{ of toluene's M.A.C.}$$

$$\text{The total is } \frac{80 + 100}{200} = 90\% \text{ of an M.A.C.}$$

Therefore 10% (20 parts/million) of xylene could safely be permitted.

APPENDIX C

M.A.C. calculation for a mixture when synergism is present

Suppose that two of the constituents of a mixture are synergistic in action on each other. From animal experimentation it is possible to calculate how much their combined toxicity exceeds the expected or additive one. This value may then be applied as a correction to the M.A.C.

Let the M.A.C. of A be 100 and that of B be 200.

Assume that the toxicity of the mixture is 50 per cent greater than would be expected, due to synergism. If the toxicants are present in a 50/50 ratio without synergism:

50 per cent of the M.A.C. of A and 50 per cent of the M.A.C. of B could safely be present.

That is:

$$50 + 100 = 150 \text{ parts/million.}$$

Because of synergism this figure should be reduced by multiplying by

$$\frac{100}{150} \text{ which gives 100 parts/million.}$$

If antagonism occurred to the same extent, the M.A.C. would be raised by the same ratio.