CONCLUSIONS.

1.—It has been shown that although propylene is stated by Lebedew not to polymerize in the presence of activated Floridin, it does polymerize in the presence of the latter if kept under pressure.

2.—The factors influencing the polymerization of olefines by activated Floridin are:

(*a*) *Temperature.*—Inasmuch as the reaction is exothermic and a large amount of heat is liberated, proper cooling of the activated Floridin is essential for best results.

(*b*) *Pressure.*—Pressure was essential to polymerize a simply substituted ethylene, namely propylene, and in the case of isobutylene, an asymmetrical doubly substituted ethylene, which polymerizes readily at ordinary pressure, the polymerization reaction is increased if the system is put under pressure.

(*c*) *Time of Contact with Activated Floridin.*—Propylene under pressure with activated Floridin for two months had formed some dimer while at the end of year no dimer was present. Isobutylene when passed through a short column of activated Floridin formed some dimer but when the length of the column was materially increased only higher polymers were found.

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A DISCUSSION OF THE PHARMACOPŒIAL SPECIFICATIONS FOR CRESOL.*

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After the publication of the U. S. P. X a certain agitation was manifested to have either the present specifications for U. S. P. Cresol changed or else to have a new high boiling Cresylic Acid incorporated into the book in addition to the present Cresol. The discussion was opened by manufacturers of saponified cresol solutions from cresylic acids of higher boiling range than that outlined in the U. S. P. Their principal arguments for the change are four in number, namely: (1) Cresylic Acids of higher boiling range than 195–205° C. possess greater germicidal values than U. S. P. Cresol, (2) they are less corrosive to tissues, (3) they are cheaper and (4) there is a greater available supply of them on the market. Certainly, if true, these are a very valid set of arguments. Since Solution Cresol Compound, U. S. P. now enjoys quite an extensive use as a germicide by members of the medical profession especially, the question of a change in its specifications will no doubt have to be considered before the publication of the next U. S. P. A large number of saponified cresol solutions purporting to be U. S. P. products but which do not contain Cresol corresponding to the specifications of the U. S. P. X have appeared on the market. In order to maintain the dignity of the U. S. P. as a legal standard it becomes necessary to have any solutions erroneously labeled as U. S. P. removed from the market or else to have the U. S. P. specifications changed to include them. It has not been the policy of U. S. P. revision com-

* Scientific Section, A. PH. A., St. Louis meeting, 1927.

mittees of the past to change the text of the book to conform with the whims of any certain group of manufacturers. Few of us would want to see any such policy adopted by future committees yet all, no doubt, want to see future Pharmacopœias reach the highest state of excellence possible, and any genuine improvement of the book should be more than welcome. It is with a discussion, in a general way, of the advisability of changing the present specifications of Cresol that this paper is concerned. The writer is engaged in laboratory manufacturing both Compound Solution of Cresol, U. S. P. and a similar solution of higher boiling acids under its own trade name, and it has been his privilege during the past two years to investigate many different types of cresylic acid in addition to U. S. P. cresols and supposed-to-be U. S. P. cresols on the market.

The first of the arguments for a change of Cresol specifications seems to be the strongest. That is the argument that the high boiling acids produce a solution of greater germicidal efficacy than the present Cresol. The contention is, if high boiling acids produce a solution that is more efficient as a germicide, why not use high boiling acids? And if true, and our present methods of determining germicidal values indicate that it is, this is an excellent argument. Some members of the Fungicide Department of the Bureau of Chemistry submitted a report to the Pharmacopœial Revision Committee in which they showed this to be the case with the two organisms *B. typhosis* and *Staph. aureus*. Whether this is the case with all organisms is not known. But since high boiling cresols give a higher phenol coefficient by the methods for determining phenol coefficients in general use, it seems very probable that they are more efficient as disinfectants.

The second argument, that the higher boiling cresols are less corrosive to tissues, has not been definitely proven to the writer's knowledge. It is a generally accepted fact that the ortho, meta and para cresols are less corrosive than ordinary benzo phenol. Whether or not the higher boiling cresols, xylenols, etc. are still less corrosive the writer is not in a position to state. But it really makes no practical difference since the very fact of the general acceptance of Compound Solution Cresol, U. S. P. speaks highly of it as an efficient and harmless disinfectant.

At present there can be no doubt of the validity of the third argument—that of price. The acid specified by the U. S. P. sells quite a bit higher than a good grade acid of any other boiling range.

Authorities seem to disagree on the fourth argument. There is perhaps more or less of a shortage of U. S. P. Cresol but any laboratory that can anticipate its needs for a short time in the future, experiences no difficulty in obtaining a sufficient stock. It is doubtful if an actual shortage of U. S. P. Cresol exists.

The U. S. P. at present defines Cresol as a mixture of the three isomeric cresols, having a specific gravity of about 1.038 and ninety per cent of which distills between the ranges of 195 and 205 degrees C. This specification of boiling range was made in consideration of the boiling points of ortho, meta and para cresol, which are about 190.8, 202.8 and 201.8 degrees, respectively. Having to meet certain solubility tests, specific gravity and narrow boiling range, U. S. P. Cresol as now defined becomes a fairly uniform product. "High boiling" cresylic acids on the market might be defined for our purpose to be any cresylic acid less than ninety per cent of which will have come over by the time a temperature of 205° C. has been reached. They are not defined legally except as to classification into

dutiable and duty-free products and are not liquids of uniform composition. They vary in boiling range, color, odor and solubility in soap solutions according to their method of manufacture. Phenol coefficients of their saponified solutions also vary. The variations of solubility, color and phenol coefficient are the ones most troublesome to a manufacturer of a saponified cresol solution. The solubility of a cresylic acid is no doubt in correlation with its boiling range but in the daily routine examination of the products of different manufacturers one finds many examples of acids of comparatively low boiling range making a solution inferior to that of a higher boiling acid. The following actual figures from the author's laboratory note book illustrate this point.

DISTILLATION RANGE—100-CC. SAMPLES.

No. 1.		No. 2.	
to 190° C. (corr.)	1 cc.	to 190° C. (corr.)	0 cc.
195°	1 cc.	195°	0 cc.
207°	5 cc.	207°	1 cc.
215°	68 cc.	215°	41 cc.
230°	98 cc.	230°	95 cc.

No. 1 would not make a clear saponified solution, No. 2 made a beautiful one. No. 2 was found by assay to contain ninety-nine per cent of phenols. This sort of solubility result is not at all uncommon. The writer regrets that since the routine examination of a cresylic acid is begun by actually making a saponified solution from it and, if this proves unsatisfactory, discarding the acid without further tests, except in special cases, he has more statistical data on cresylic acids that will make satisfactory solutions than on those that will not. But it is true to state that the solubility of a cresylic acid is influenced by other factors in addition to its actual boiling range. There are many different kinds of cresylic solutions on the market all known as "High Boiling Acids" and varying through wide ranges in physical properties.

This lack of uniformity of high boiling cresylic acids should be fully realized before attempting to make any change in the present pharmacopœial specifications for cresol. There are two possibilities for a change, namely: (1) official recognition of cresylic acids of varying and ununiform compositions, in which case the recognition would be more or less meaningless or (2) adoption of a new set of definite specifications for a different but still uniform acid. Since the main reason for the existence of the U. S. P. is to establish a standard of uniformity of medicinal products, it would seem that the latter type of change is the only justifiable one to be made. If a new uniform cresylic acid is adopted it will, if its compound solution meets with general approval and use, soon meet with economic conditions very similar to that encountered by the present Cresol. But the fact will still remain that it gives a higher phenol coefficient than the present Solution of Cresol Compound, U. S. P. Will it be wise to change from the present Solution, a solution that has met with extensive use and one with which the members of the medical profession are already familiar, for the sake of a difference in the phenol coefficient of the new product? If so, we should welcome the change, if not we should retain the present Cresol. In either case, in order to maintain the U. S. P. as a Standard and as *the* standard, strict conformity to its specifications should be enforced.—LABORATORY OF PARKE, DAVIS & CO., DETROIT, MICH.