DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
FOOD AND DRUG ADMINISTRATION
WASHINGTON, D.C. 20204

sure to include
G.F. 16 in presm. tobacco test
Write Thompson for method on lead
+ review 40 ac

October 20, 1966

Dr. Jula Gordon, Chairman
The Committee of the Progressive
Hair Dye Industry
Rooms 510-511
60 East 42nd Street
New York, New York 10017

Dear Dr. Gordon:

We have completed the review of the experimental data and other material submitted by you on September 1, 1965 in support of your request for provisional listing of lead salt hair colors. We regret the inordinate delay in this reply.

We have concluded that the data submitted is inadequate to demonstrate safety of lead salt hair colors in general or of the particular preparations tested. The work thus far carried out, rather than demonstrating safety, raises certain questions which will require additional investigation.

The 90 day rabbit intact skin study shows a nearly tenfold increase in bone lead content for the high test level as against the controls. The inference must be made that there is absorption and partial storage of lead in the bones. However, it is not clear from the data submitted whether the animals were suitably restrained at all times during the study. There is therefore the possibility of ingestion from self-grooming and licking of residual material off the back in which case the results of the study would be invalid. If ingestion by self-grooming was prevented, then the only conclusion that can be drawn is that there is significant penetration through the intact skin. If this conclusion is valid, it would not be in the public interest to list lead salt hair colors.

You have reported the lead content of urine samples from 105 regular users of lead salt hair coloring products. We do not feel that the urine lead content alone is a sufficiently reliable indication of lead absorption.

Relatively recent reports in the literature -- PHS Publication #1440, March 1966 for example -- have caused us to reassess the type and extent of studies which we believe are necessary for permanent listing. We

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have also concluded that the data needed to obtain provisional listing is the same as would be required for permanent listing. It is not our intention therefore to provisionally list lead salt hair colors.

We believe results from the following investigations should be available before listing can be considered.

(1) Acute oral toxicity

(2) Animal skin application - percutaneous absorption tests on intact (30 day) and abraded (20 day) skin of rabbits according to the methods of Draize. There should be safeguards at all times during the study against possible self-grooming and ingestion of lead by the rabbits. At sacrifice, skin at site of application and major organs including bone marrow and lymph nodes should be examined gross and histopathology. Liver and kidneys should be examined & search be made for characteristic inclusion bodies. Hemograms should be obtained. Urine and blood should be analyzed for lead levels periodically throughout the study. Bone (femur), liver, kidneys should be analyzed for deposited lead levels. If there is any indication of an increase in these levels, this would be evidence of absorption and we believe this would preclude the use of lead salts as hair colors.

(3) Rabbit eye test - standard rabbit eye irritation test in the unwashed eye and eyes washed at 2 and 4 seconds.

(4) Human tests - for skin irritancy, sensitization, and urine and blood lead levels. A controlled test should consist of 200 subjects with the hair color applied as recommended on the label for a period of 3 months. For meaningful base line values, the subjects should not have used a lead hair color previous to this test. The scalp should be examined periodically and at the end for skin reaction. Analysis of urine and blood lead levels should be made periodically -- at the start, during, and at the conclusion of the tests.

Since there may be differences in toxicity depending on the complete formulation, the investigations outlined above should be done for each formula-type product of your cosmetic manufacture.

In addition to the toxicological data needed we will need the following chemical data.

(1) Manufacturing process - This should include a detailed description of the facilities and reaction or mixing conditions including temperature, time, pH, etc.

(2) The quantitative [illegible] specification of the impurities.

(3) Methods of analysis for each component of the formulation.

(4) Stability data of the finished formulation.

The toxicological and chemical information described above are the minimum we believe necessary. As you can readily understand, review of the submitted data may raise other questions which can be answered only by further investigations.

Please advise us if it is your intention to proceed with the investigations using the items described above. We will be glad to discuss with you further details of proposed procedures.

Sincerely yours,

Kenneth A. Fenaroli

Kenneth A. Fenaroli, Director
Division of Color Certification
and Evaluation