CPMA
COLOR PIGMENTS
MANUFACTURERS
ASSOCIATION, INC.

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Dr. C. W. Jameson
Report on Carcinogens
National Toxicology Program
MD EC-14
79 Alexander Drive (East Campus)
P.O. Box 12233
Research Triangle Park, NC 27709

Re: Comments of the Color Pigments Manufacturers Association, Inc. for the 10th Report on Carcinogens Concerning the Review of Lead and Lead Compounds and Lead Chromate Pigments

Dear Dr. Jameson:

I am writing on behalf of the Color Pigments Manufacturers Association, Inc. ("CPMA"), with respect to the National Toxicology Program ("NTP") call for public comment for the 10th Report on Carcinogens with respect to the review of lead and lead compounds. 65 Fed. Reg. 17889. The CPMA is an industry trade association representing small, medium and large color pigment manufacturers throughout Canada, Mexico and the United States, accounting for approximately 95% of the production of color pigments in these countries.

Color pigments are widely used in product compositions of all kinds, including paints, inks, plastics, glass, synthetic fibers, ceramics, colored cement products, textiles, cosmetics, and artists' colors. Color pigment manufacturers located in other countries with sales in Canada, Mexico and the United States and suppliers of intermediates to the pigments industry are also members of the association. These comments are provided on behalf of the Lead Chromate Committee. The Lead Chromate Committee addresses and represents the views of the CPMA with respect to issues directly involving the production and use of lead chromate classes of pigments.

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The language included in the call for public comments indicates that new evidence points to the carcinogenicity of all lead compounds. The CPMA, on behalf of the Lead Chromate Committee, believes that this assertion is unsubstantiated as it is applied to lead chromate pigments in the scientific literature. The often cited letter to the editor of the Scandinavian Journal of Environmental Health by Vainio, H., Vol. 32, p. 1-3 (1997), provides no new studies or evidence to support carcinogenicity characterization for lead chromate compounds. Indeed, with new information including a comprehensive update study by the International Lead and Zinc Research Organization ("ILZRO") planned shortly, this consideration is, at best, premature. The CPMA on behalf of the lead chromate subcommittee, supports the conclusion reached by ILZRO in its comments to NTP. Based on an extensive review of the literature, ILZRO concludes that since the International Agency for Research on Cancer completed the evaluation of the carcinogenicity of lead in 1987, data generated since that time make it even less probable that lead functions as a human carcinogen.

There are no studies of worker exposure specific to lead chromate pigments which reasonably conclude that lead chromate pigments are carcinogenic. There are, however, several studies of workers in the lead chromate industry which are specific to lead chromate exposures and do not show these pigments to be carcinogenic. Animal studies of lead chromate pigments support this view. Like many other metal compounds, there is a tendency among scientists to assume that if any one compound of an element is carcinogenic, then all compounds of that element are automatically carcinogenic. Recent trends in research are finding that chemical speciation, even with the same valence state, illicits different biochemical reactions. Hence the general assumption that all compounds will illicit the same response is simply incorrect in every case.

INTRODUCTION

The NTP should differentiate lead chromate pigments, from the more soluble lead compounds. As these comments will demonstrate, lead chromate pigments have been extensively tested and researched for decades. These pigments are well known in terms of their properties, toxicity and reactions.

When properly used, these pigments are proven safe. Based on their cost and superior performance, these pigments are the coloring materials of choice for many articles in commerce. Due to their extremely low solubility, lead chromate pigments are significantly less bioavailable than other more soluble compounds and should not be restricted in rules that target bioavailable compounds.

The following discussion will review the chemistry, uses and toxicity of lead chromate pigments.

LEAD CHROMATE PIGMENTS

There are two main lead chromate pigment color groups. The yellow varieties are known as chrome yellow pigment, classified by the Colour Index as C.I. Pigment Yellow 34. Color shades range from greenish-yellow to red shade yellow. The orange varieties, molybdate orange pigments, are classified by the Colour Index as C.I. Pigment Red 104. Colors range from yellow shade to red shade orange. (The Colour Index (C.I.) is published by the Society of Dyers and Colourists.)

Chrome yellow pigments are solid crystal compositions of lead chromate and sulfate. Shade is primarily controlled by sulfate content bound within the crystal lattice. Molybdate orange pigments are solid compositions of lead chromate, sulfate and molybdate. Shade is controlled more by crystal form and use than by composition.

Improved lightfastness, weatherability and use properties, such as ease of dispersion and low dusting characteristics, are obtained by surface treatment. In some applications, further improvement in performance stability can be obtained by encasing the base pigment with a continuous, dense, amorphous shell of silica. This encapsulation treatment significantly improves color durability and performance properties. An ancillary benefit of encapsulation is a significant reduction in solubility, since the barrier provided by the amorphous silica coating inhibits contact with the core pigment.

MANUFACTURING PROCESS

Naturally occurring lead chromate, the mineral crocoite, is not suitable as a pigment, and cannot be economically converted to pigment use. Instead, lead chromate colored pigments are produced by aqueous precipitation chemistry to effect the desired solid crystal compositions which determine color and shade. Surface treatments to improve pigment performance properties, such as lightfastness, weatherability and dispersibility, are accomplished as part of the synthesis technology.

Generally, several process steps are employed to produce lead chromate pigments: initial precipitation, involving reacting an aqueous solution of lead nitrate and a solution of sodium bichromate containing the requisite amount of sulfate ion (and molybdate ion for molybdate orange production), followed by crystal development, treatment, isolation, drying, pulverization and standardization. Worker exposures to lead and hexavalent chromium are monitored and controlled through all stages of pigment production under the worker health agencies and rules common to all industrial nations.

CHROME YELLOW AND MOLYBDATE ORANGE PIGMENTS AND THEIR USE IN INDUSTRY

Lead chromate pigments are among the most versatile of all pigments, offering many desirable properties, such as: bright, clean color shades; high opacity or hiding; good lightfastness; good rheology in coating vehicles, and excellent non-bleeding properties in solvents.

The color range extends from the greenish (primrose) yellow through lemon yellow and medium yellow to the orange and red region of the spectrum.

Grades Available

Lead chromate pigments may be subdivided into four categories:

(1) Regular Lead Chromate Pigments. These pigments are characterized by cleanliness of shade and high color strength. They are the least stabilized grades for fastness properties, tending to darken with exposure to weather over time. Their heat stability for thermal application is only moderate.

(2) Predarkened Lead Chromate Pigments. Less pure in color than the regular grades, they exhibit greatly enhanced weatherability and increased heat stability. They are particularly suited for industrial paints and plastics applications.

(3) Silica-Encapsulated Lead Chromate Pigments. These pigments are characterized by further reduced solubility and cleanliness of shade, with significantly lower color strength than the regular grades. They possess improved chemical resistance and heat stability in plastics, permitting them to be used in plastics at processing temperatures of approximately 300 degrees Centigrade.

(4) Special Varieties of Weather Resistant Pigments. These pigments provide excellent resistance to sulfur dioxide, and find particular application in highly industrial settings or areas subject to acid rain fallout. In addition, they possess most of the properties of the pre-darkened pigments, including good weatherability and heat stability. They also exhibit considerably lower soluble lead content, which significantly reduces possible hazards to the environment.

Uses of Lead Chromate Pigments

Lead chromate pigments are widely used throughout the paint and plastics industries, because of their excellent combination of properties. Lead chromate pigments offer valuable safety application attributes such as high visibility when used in traffic paint striping for highways and airports, and safety identification paints on buses, ambulances and fire trucks. These pigments also provide infrared radiation absorption in camouflage coatings for the military. Examples of military paints which have specified lead chromate pigments include camouflage lacquer, basic silico lead chromate primer, acrylic nitrocellulose camouflage lacquer, modified alkyd lusterless camouflage enamel and semigloss rust-inhibiting enamel.[1]

Paint and Coatings Industry

The largest consumer of lead chromate pigments is the paint and coatings industry, which uses these pigments in a variety of industrial coatings.

Traffic marking yellow is generally based on the medium chrome yellow pigment, and constitutes the largest single market end-use area for the pigment.

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[1] These titles are from the Federal and Military specifications utilizing lead chromate and molybdate orange pigments and current as of March 13, 1991.

Because of strict international limitations on the level of lead allowed in household paints and toys, lead chromate pigments are not and cannot be used in this area. The wide variety of industrial paints using lead chromate pigments includes automotive finishes, industrial and agricultural equipment, baking enamels and air-dried finishes.

Plastics Industry

The plastics industry is the second largest consumer of lead chromate pigments. Because the pigments become totally encapsulated in plastic during processing, they are effectively isolated from the environment. Consequently, exposure to lead and chromium from plastic articles colored with regular lead chromate pigments is not a problem. Because of limitations in their heat stability, regular lead chromate pigments are largely confined to those plastics that are processed at temperatures of up to approximately 230 degrees centigrade. Above this temperature, there is a tendency for the pigments to darken, depending on the time of exposure to the higher temperatures, the type of plastic and the method of processing. The silica encapsulated grades can be used up to approximately 300°C.

The combination of working properties and value-in-use provides the plastics market with a unique material that can be used in many applications, such as automotive interiors, packaging, rust resistant furniture and electronic housings.

Miscellaneous Uses

Lesser quantities of lead chromate pigments are used in a variety of other industries, including the coloring of rubber, paper and flooring compounds. Although their usage has declined in recent years, significant volumes continue to be used.

EXPOSURE TO PIGMENT MATERIALS DURING AND FOLLOWING USE

Questions regarding exposure risks can most meaningfully be answered by defining exposure as "biological exposure", and considering that the toxicity of metals is related to solubility, which in turn is related to bioavailability and ecotoxicity. While lead chromate pigments are strictly for industrial use and not intended or regulated for use in contact with biological systems, assessing use-risk based on bioavailability is the prudent scientific way to determine exposure and risks.

The bioavailability, or the "...extent of systemic absorption of a xenobiotic[2]..." is related to the chemical's solubility within the organism. To cause physiological harm, the metal constituent must be soluble in the bloodstream. Therefore, speciation of compounds on the basis of solubility-bioavailability should be the scientific approach to regulation.

When these pigments are further encapsulated in paint and plastic resins, leachability of lead and chromium drops to an almost undetectable level. Therefore, they exhibit even lower levels of toxicological concern from environmental routes.

TOXICITY OF LEAD CHROMATE PIGMENTS

Introduction

An analysis of exposures must differentiate between the various speciation forms of lead and chromium which may be the subject of the exposure. Exposure can be in the form of free metallic lead and chromium or of compounds of lead and chromium with widely differing chemical and physical properties. Health effects from exposure to a substance are related to the bioavailability of the substance, which in turn is linked to solubility.

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[2] Xenobiotic is defined as any chemical foreign to the body

The toxicity of metals such as lead and chromium is dependent upon the metal being in a form which renders it biologically available, either through ingestion or inhalation. Biological availability will only occur if the metal is capable of being solubilized in the appropriate biological fluid, e.g., stomach acid. Toxicity is, therefore, related to the solubility of the metal.

There are wide differences in the solubility and toxicity of lead and chromium compounds. For example, lead carbonate, known as "white lead," and used extensively over forty years ago as a cheap white pigment for house paints, is almost totally solubilized in stomach acid. Ingestion of this pigment, or paint containing the pigment, results in lead being dissolved, and therefore becoming bioavailable, causing lead poisoning.

In sharp contrast, lead chromate pigments are extremely insoluble substances with very low solubility in simulated stomach acid. Technical developments by pigment manufacturers have produced modified versions of the pigment with further reduced solubility.

Lead chromate pigments are some of the most extensively studied chromium compounds, for toxicity and for potential risk for specific use applications. Investigations which demonstrate that the use of these insoluble pigments do not pose unreasonable risks for significant exposure to lead or chromium are highlighted below.

Animal Feeding Studies for Oral Toxicity

CPMA sponsored 90-day feeding studies with rats[3] and beagle dogs[4] evaluated the toxic effect of lead based pigments. Lead chromate was found to be substantially less toxic than lead carbonate (white lead). It is not surprising that this finding correlates well with the acid solubility differences between lead carbonate and the significantly less soluble lead chromate.

Bioavailability Studies

A rat feeding study[5] comparing the bioavailability of lead from lead carbonate, lead chromate pigment and silica encapsulated lead chromate pigment showed that the more acid insoluble compounds were significantly less bioavailable than lead carbonate, with the silica encapsulated lead chromate pigment being the least bioavailable.

Lethal Dose, LD:50

The LD:50, a measure of acute oral toxicity, for chrome yellow and molybdate orange pigments in rat feeding studies, is greater than 10,000 mg/Kg, which is considered nontoxic.

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[3] Kennedy, G.L. Jr., M.L. Keplinger, R.J. Wingender, E.E. Christofano and J.C. Calandra: Abstracts: Toxicity of Lead Chromate Pigments and Tissue and Residues Following 90 Days Feeding to Albino Rats. Toxicol. Appl. Pharmacol. 37:160, 1976.

[4] Christofano, E.E., G.L. Kennedy Jr., D.E. Gordon, M.L. Keplinger and J.C. Calandra: Abstract: Toxicity of Lead Chromate Pigments and Tissue Residues Following 90 Days Feed to Beagle Dogs. Toxicol. Appl. Pharmacol. 37:161, 1976

[5] T.C. Clapp, T.H. Umbreit, R.J. Meeker, D.S. Kosson, D. Gray: Bioavailability of Lead and Chromium from Encapsulated Pigment Materials, Bull, Environ. Contam. Toxicol. 461271-275, 1991

Workplace Studies

The concentration of lead and chromium in the air of four paint factories producing and using paints containing lead chromate pigments (not more specifically identified) was measured at various stages of the process. Exposure levels were found to be minimal.[6]

Blood level data on operators in paint plants spraying paint containing lead chromate pigments revealed levels of lead in the range of background levels in the non-exposed population.[7]

The European Manufacturers of Lead Chromate and Molybdate Pigments Association reported[8] on the findings of a symposium of the German Paint Institute in Berlin. Attention was drawn to the comparatively small number of occupational illnesses that could be regarded as directly attributed to paint and ink materials.

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6 Cowley, "Controlling Lead Chromes in the Work Place," Fatipec, 1984.

7 Cowley, C.D., "Living With Lead Legislation", J. Oil Col. Chem. Ass. 62, 1982

8 The European Manufacturers of Lead Chromate and Lead Molybdate Pigments E.V., Cartstrat 21, D-6000 Frankfurt am Main 1, West Germany, American Paint & Coatings Journal, 1984

Consumer Product Safety Commission ("CPSC")

In the United States, since the 1977 limitation on the content of household paint to less than 0.06% lead, the CPSC has investigated the use of lead and chromium pigments in consumer products, outside of the scope of the original ban. Specifically reviewed was the use of color pigments containing these metals in consumer products. The report, issued April 12th, 1982, states:

> "...the analysis indicates that it is unlikely that the levels of lead and chromium in printed products under the Commission's jurisdiction present a significant health risk. Accordingly, the staff recommends no further investigation of toxic heavy metal pigments in printed products".[9]

Epidemiology Studies

The IARC Monograph on the "Evaluation of Carcinogenic Risks to Humans" reports that, "studies carried out in the Federal Republic of Germany, France, the Netherlands, Norway, the UK and the USA of workers in the production of chromate pigments have also consistently shown excess risks for lung cancer ... excess risk for lung cancer has been clearly established in facilities where zinc chromate was produced although other chromium pigments were also generally made in these plants. A small study in the UK of workers producing lead chromate pigments showed no overall excess for lung cancer."[10]

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[9] Gerber, A.I. - Project Manager, Chemical Hazards Program, Health Sciences, U.S. Consumer Products Safety Commission. Internal Memorandum "Toxic Heavy Metal Pigments in Printed Products," April 12, 1982.

[10] IARC, 1980, "Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Some Metals and Metallic Compounds", Vol. 23, pp. 205-323, IARC, Lyonn, France.

Most of available epidemiological studies on chromate pigment manufacture involved mixed exposures to chromium-containing compounds, in particular to zinc chromate which was often made in the same factory as the lead chromate. In these cases, it is not possible to draw conclusions about the carcinogenicity of lead chromate due to the likelihood of co-exposures to zinc chromate.

In those factories which made only lead chromate pigments, as reported by Davies in the UK in 1984, and by Cooper in the US in 1983, there was no evidence to indicate that lead chromate caused an increased incidence of cancer.[11] [12]

A recent epidemiological study of lead chromate workers in Japan, reported by Kano, Katsumi et al. in 1993, concluded that lead chromate pigments did not cause an excess risk for malignant tumors.[13]

Lead chromate pigments must be differentiated from zinc chromate pigments which are consistently shown to be carcinogenic in various studies. When zinc chromate and lead chromate exposures occur simultaneously, there appears to be a significant cancer hazard. However, when lead chromate alone is the source of chromium exposure, a significant carcinogenic response has never been found.

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[11] Davies, J.M. Lung Cancer Mortality Among Workers Making Lead Chromate Pigments At Three English Factories: British Journal of Industrial Medicine, 41:158-169, 1984.

[12] Cooper, W.C. An Epidemiological Study of Lead Chromate Plants: Equitability Environmental Health, Inc. for the Dry Color Manufacturers' Association, March 1983.

[13] Kano, Katsumi, et. al. "Lung Cancer Mortality Among a Cohort of Male Chromate Pigment Workers in Japan", International Journal of Epidemiology, Volume 2, No. 1, 1993, pp. 16-22

Animal Studies

The IARC Monograph reports that "lead chromate and derived pigments have been tested by intrabronchial implantation in rats without producing a significant increase in the incidence of tumors. Lead chromate and derived pigments have also been tested in rats by subcutaneous and intramuscular injection producing malignant tumors at the site of injection and in one study, renal carcinomas. A study by intrapleural administration to rats could not be evaluated. No increase in tumor incidence was observed when lead chromate was administered intramuscularly to mice." It was also reported that a single subcutaneous injection of basic lead chromate produced a high incidence of local sarcomas in rats. It should be pointed out that basic lead chromate is chemically different from lead chromate pigment.

The injection studies referred to were carried out by Hueper in 1961[14], Maltoni et. al. in 1974[15] and Furst et. al. in 1976[16]. It is argued that tests involving intramuscular, intrapleural or subcutaneous injection techniques are of questionable relevance in relation to human workplace exposure conditions in industry, whereas tests involving implantation in rat lung, as carried out by Levy et. al. in 1986[17], are relevant to inhalation in industrial exposures. These latter studies indicated no increased incidence of tumors for lead chromate although other more soluble chromates exhibited varying degrees of carcinogenicity.

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[14] Hueper, W.C. and W.W. Payne. 1962. Experimental studies in metal carcinogenesis, Chromium, Nickel, Iron, Arsenic. Arch. Environ. Health, 5: 445-462

[15] Maltoni, C., Sinibaldi, C., and Chieco, P., 1974, "Subcutaneous sarcomas in rats following local injections of chromium orange and molybolenium orange." In: E. Davis & C. Maltoni (eds) Advances in Tumor Prevention, Detection and Characterization, Vol. 1, pp. 133-134. New York: American Elsevier Publishing Co., Inc.

[16] Furst, A., M. Schlauder, and D.P. Sasmore, 1976, Tumorigenic activity of lead chromate. Cancer Res., 36: 1779-1783.

[17] L.S. Levy, P.A. Martin, P.L. Bidstrup, "Investigation of the Potential Carcinogenicity of a Range of Chromium Materials on Rat Lung", British Journal of Industrial Medicine, Vol. 43, No. 4, pp. 243-256, 1986.

Genotoxicity Studies

The IARC Monograph on the "Evaluation of Carcinogenic Risks to Humans" reports that "---lead chromate and the derived pigments chromium orange, chromium yellow and molybdenum orange" induced DNA damage and gene mutation in bacteria but "often required preliminary dissolution in alkali or acids." Such studies were carried out by Nestman et. al. in 1979[18] and De Flora in 1981[19] where the lead chromate was "dissolved" in 0.5 N sodium hydroxide.

We believe that the conclusions from these studies should be discounted since the validity of the methodology is highly questionable. The "solubilization" of lead chromate in alkali or acid causes the chemical breakdown of the lead chromate pigment crystal. This leads to the formation of soluble chromate ions. Thus the genotoxilogical effect is not caused by the insoluble lead chromate but rather its chemical by-products particularly soluble chromate ion.

More recently lead chromate pigments, both silica-encapsulated and non-encapsulated types, were investigated for mutagenicity by Connor and Pier in 1990[20] using the Ames test protocol without solubilization of the pigments. Lead chromate pigments and their silica-encapsulated counterparts were found to be non mutagenic. The effectiveness of silica-encapsulation was demonstrated by incorporation of a powerful chelating agent. In this study, encapsulated lead chromates could not be forcibly solubilized to promote mutagenic activity.

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[18] Nestmann, E.R. et. al. 1979. Detection of the mutagenic activity of lead chromate using a battery of microbial tests. Mut. Res., 66: 357-365.

[19] DeFlora, S. 1981. Study of 106 organic and inorganic compounds in the Salmonella/Microsome test. Carcinogenesis, 2: 283-298.

[20] T.H. Connor, S.M. Pier, Reduction of the Mutagenicity of Lead Chromate - Based Pigments by Encapsulation with Silica, Mutation Research, 245, pp. 129-133, 1990.

Solubility and Bioavailability

The toxicity of metal ions such as hexavalent chromium is dependent upon the metal ion being in a form which renders it biologically available either through ingestion or inhalation. Biological availability will only occur if the metal ion is capable of being solubilized in the appropriate biological fluid either in the lung or stomach. Toxicity is therefore related to the solubility of the metal ion.

There are extremely wide variances, by many orders of magnitude, in the solubilities of various hexavalent chromium compounds as the following table illustrates:

Compound	Solubility in water (cold)	Solubility Rating
Lead Chromate	5.8×10^{-4}g/litre	Very low solubility
Barium Chromate	4.4×10^{-3}g/litre	Very low solubility
Strontium Chromate	1.2g/litre	Slightly soluble
Zinc(Potassium)Chromate (the commercial pigment)	2.5-5.0g/litre	Slightly soluble
Potassium Chromate	49g/litre	Intermediate solubility
Calcium Chromate	163g/litre	Intermediate solubility
Potassium Dichromate	629g/litre	Highly soluble
Sodium Chromate	873g/litre	Highly soluble
Sodium Dichromate	1,800g/litre	Highly soluble

Ref: Handbook of Chemistry and Physics 53rd Edition

It has been suggested that only the chromate compounds of slight to intermediate solubility exhibit carcinogenic potential whereas chromates with very low or very high solubility do not.

Because of the tremendous difference in solubility (i.e. by a factor of tens of thousands) between lead chromate and the known carcinogenic chromates of zinc, strontium and calcium, it is inappropriate to classify all of these compounds as if they have the same bioavailability and hence toxicity.

The absence of clear evidence for the carcinogenicity of lead chromate is borne out by the epidemiological studies carried out by Davies in the UK, by Cooper in the US and by Kano, Katsumi et. al. in Japan in those factories which only manufactured lead chromate pigments and is further confirmed by the rat lung implantation studies of Levy.

CONCLUSION

The CPMA member companies provide vital lead chromate products that are important coloring materials in today's economy. Lead chromate pigments:

- have been extensively studied and are safe for persons and the environment when properly used.
- are not the pigments responsible for workplace cancer. This association is incorrect and based on an insufficient analysis, and failure to distinguish lead chromates from other more soluble and bioavailable compounds.

The broad brush approach described by NTP in the Report on Carcinogens has an unjustified impact on all industries using lead chromate pigments and other valuable products. Lead chromate colored polymers and paints are viable, important commercial products that are safe when used as intended under existing laws. Lead chromate pigments should not be described or listed as "known to be human carcinogens."

We hope this information is helpful in developing amended language which is fair and equitable to lead chromate pigments in future editions of the NTP Report on Carcinogens.

Please call me at the above number if there are any questions or comments. If necessary, we would welcome a meeting with you to discuss these issues.

Sincerely,

J. Lawrence Robinson
President

JLR:daa

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