

LECON WOO¹ , Samuel Y. Ding²,
Michael T. K. Ling² and Stanley P. Westphal²

**FURTHER STUDIES ON OXIDATIVE INDUCTION TEST
ON MEDICAL POLYMERS**

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ABSTRACT: We have published previously initial results on the application of the oxidative induction test to a wide variety of medical polymers. This is a continuation and further elaboration on the earlier study.

For medical flexible PVC compounds, the traditional measure of degree of degradation by color formation was found to correlate to measured oxidative induction times. Furthermore, three distinct regimes were also detected. In the initial phase of degradation, little color formation was detected for significant decreases in the induction time. This is followed by a nearly linear regime. Finally in the terminal regime, where the stabilizer were nearly exhausted the color increased exponentially. This observation is interpreted by the established mechanism of PVC degradation.

In another series with polyolefins, several subtle phenomena that may have utility in either optimizing the stabilization package or predicting long term shelf life were observed. It was found at typical experimental temperatures above 200°C, significant antioxidant losses occurred. Much better shelf life predictions can be obtained by collecting data at lower temperatures. And the inflection point on the activation energy plot corresponds to the antioxidant volatilization temperature.

These and other recent results will be presented to illustrate the utility of this versatile test.

KEYWORDS: Oxidative Induction Test, OIT, PVC, polyolefins.

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1 Baxter Distinguished Scientist, Baxter Healthcare, Round Lake, IL 60048.

2 Senior Engineeing Specialist, Baxter Healthcare.

INTRODUCTION:

We have previously studied the utility of the oxidative induction test applied to many of the medical polymers (1). It was found that in numerous cases, if a clear induction point can be found, important insights can be generated on polymer stability, antioxidant formulation effectiveness, as well as in product and process performances. In this study, we will continue by examining several systems in further detail in the hopes of gaining additional information about optimizing the product or process.

EXPERIMENTAL:

ASTM Procedure D3895-80 is followed in the main, except air is used instead the pure oxygen, and both the isothermal oxidative induction time (OIT) and temperature scanning induction temperature were used. The oxidative induction test was conducted on a Dupont 1090 thermal analyzer with 910 differential scanning calorimetry (DSC) cell. Normally this test has two modes of measurement, that is, oxidative induction temperature and oxidative induction time. Oxidative induction temperature measures the onset of auto-oxidative reaction while the temperature is scanning at a preset rate. For this mode of testing, usually a thin and flat specimen, typically about 2 mg or less, was prepared and placed in an open aluminum sample pan and secured on the thermoelectric disk of the DSC cell. The sample was then scanned at a rate of 20°C/min from ambient to 300°C or higher in an air purging stream of 100 ml/min. The second method, the oxidative induction time, is a relative measure of the degree or level of stabilization of the material tested. The specimen preparation is the same as in the continuous temperature scanning method, except for scanning in a nitrogen gas environment to the preset isothermal testing temperature. Once temperature equilibrium has been established, the controller automatically switches purge gas to air or oxygen at the same purging rate. The changeover point to air or oxygen purge is taken as the zero time of the experiment. The oxidative induction stability of tested samples is assessed by monitoring an abrupt exotherm or endotherm departure from the baseline as indicated by figure [1] (2).

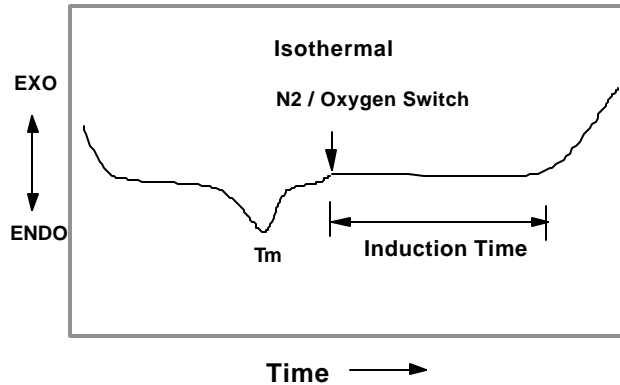


Figure 1, OIT tracing from Differential Scanning Calorimeter.

Often, if the reaction follows a simple zero order kinetics, induction time measured at various temperatures can be used to construct an Arrhenius plot, expressed as $\log(\text{OIT}^{-1})$ versus T^{-1} , to obtain information on the oxidation reaction kinetics. Mathematically, the rate constant K , which is proportional to OIT^{-1} , may be expressed in the Arrhenius form as:

$$K = K_0 e^{(-\Delta E/RT)} \quad (1)$$

where K_0 is the pre-exponential factor, ΔE the activation energy of the reaction, R is the gas constant, and T is the absolute temperature in degrees Kelvin. The slope of the $\log K$ vs. T^{-1} plot is then the activation energy divided by R .

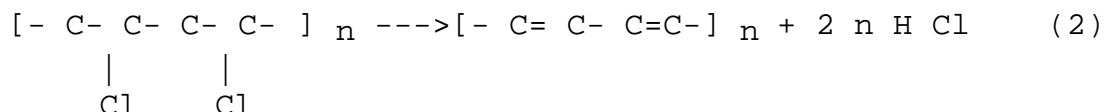
Specimens less than 100 microns in thickness were used through out this study to ensure homogenization. Inhomogeneity could result in multiple oxidative transitions, therefore, it should be avoided. Inhomogeneity usually arises from skin and core of molded sections, spatial variations in composition or thermal histories. With thin sections and small sample sizes, all of the inhomogeneities are likely to be resolved, and differentiation of skin and core, thermal histories made possible and meaningful.

PVC FORMULATIONS

Polyvinyl chloride is a unique polymer providing wide property spans in the medical field by simply adjusting the level of plasticizers in the formulation. In selecting different base polymers, the intrinsic stability of the

neat polymer is an important consideration. The intrinsic stability arises from the perfection of the polymer main-chain, head to head additions, degrees of unsaturation and is mainly a function of the polymerization process conditions during manufacturing. Since various imperfections will lead to greater tendencies toward degradation and the formation of impurities and extractibles, it is important for medical applications to minimize them.

The degradation of the PVC is primarily a cationic dehydrochlorination chain reaction [Eq. 2], and most stabilizing schemes are directed toward the elimination of labile reaction sites and the sequestration of the hydrogen chloride as soon as it is produced to avoid further catalyzing neighboring groups.



In a study to compare suspension PVC resins from different suppliers. We noted that based on various factors, for example, polymerization temperature, size of the reactor and agitation, type of initiator and suspension agents, and degree of conversion and whether chain transfer agents are used to control molecular weight, various chain ends and chain imperfections would be created (Figure [2]). These factors should lead to measurable differences in the oxidative induction time.

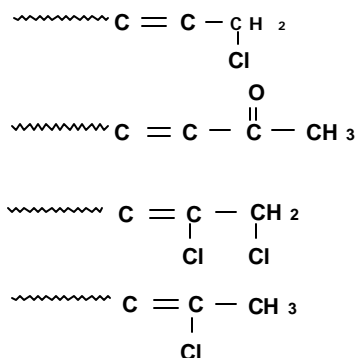


Figure 2, Suspension PVC Chain ends, Ref (3).

As reported in the earlier study, the dependence of the PVC thermal stabilities measured as OIT was found to exhibit a rather sharp maximum respect to the concentration of the primary stabilizer, a Calcium Zinc stearate at about 0.2 phr or about 0.13%, for the system studied, while an extremely linear relationship was found for the secondary stabilizer, in this case an epoxidized oil (Fig. [3]). In summary, the PVC stability function spanned a three dimensional design space schematically depicted in Fig.[4]. The utility of graphs such as Figure [4] in polymer stabilization system development is readily apparent.

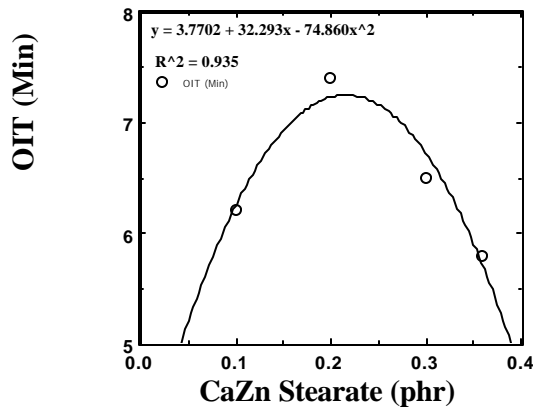


Figure 3, PVC OIT Dependence on CaZn Stearate

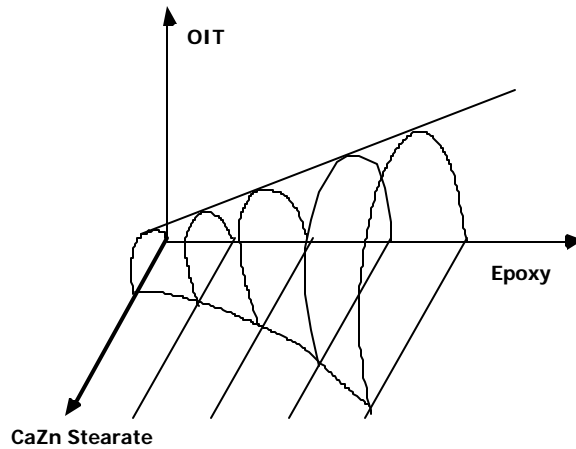


Figure 4, 3-Dimensional Schematic of PVC Stability

Base (neat) PVC polymer powder do not exhibit a sharp OIT onset. However, a semi-micro scale solution formulation of PVC, calcium zinc stearate, and plasticizers with epoxydized oil was found to simulate PVC compounds produced on large scale mixers and melt extrusion lines

Briefly, identical formulations as in a commercial formulation was replicated in a fractional gram scale, except a solvent tetrahydrofuran was used to solution blend all ingredients. After the solvent has been thoroughly removed in a vacuum oven, the resulting film was made more homogenous by repeated folding and compression molding at a relatively low temperature of about 180°C. The OIT data at 230 °C are show in Figure [5] with the standard deviation shown as the error bars.

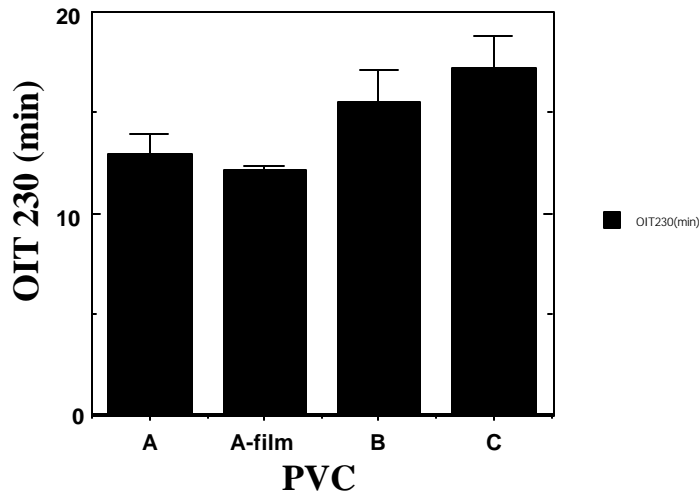


Figure 5, PVC Resin Stability Comparison

Figure 5 also compares the formulation stability from resin supplier A prepared by two methods, the semi-micro laboratory method and a large scale extruded film. The slightly extended induction time from the laboratory sample clearly indicated the less extensive thermal and shear history compared with extrusion. However, the significantly greater standard deviation also reflected less homogeneity. In a similar way, one can state that resins from suppliers B and C are significantly more stable inherently without going through a large scale compounding and extrusion step.

In another series suspension PVC powder from Supplier A with different molecular weights were similarly compared for their inherent stability, and their OIT at 230°C plotted against the molecular weight, or the number of chain ends per unit volume. When the results in Figure [6] were examined, it was noticed that the sample at about 110K dalton Mw exhibited an anomalously high stability as the

one would expect from the concentration imperfections from chain ends. However, an inquiry into the PVC manufacturing process revealed that for this polymer, the molecular weight was controlled by the addition of a chain transfer agent. Since the chain transfer agent would invariably "cap" the reactive chain-ends, enhanced inherent stability was achieved. This example clearly revealed that when a series of polymers of similar compositions were compared under identical conditions, very subtle, often chemically difficult to determine structural differences can be obtained by OIT.

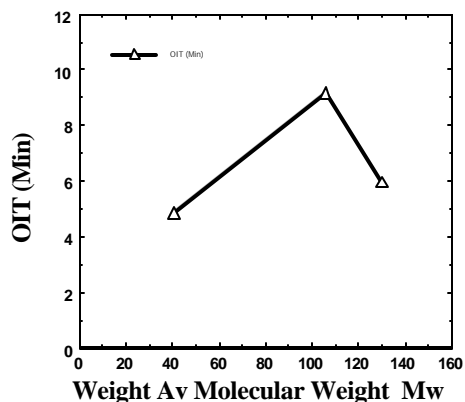


Figure 6, Supplier A PVC OIT vs Mw

In another series, PVC films subjected to a standard heat aging test were used. In the heat aging test, film samples were conditioned in a circulating hot air oven at 190 C for various times and the resultant color formation is an indication of relative processing stability. In this case ASTM test of yellowness index (4) was used as the determination of color. The basis of color came from the cationic dehydrogenation degradation mechanism for PVC. As hydrogen chloride is liberated from the PVC matrix, it coordinates onto a neighboring tertiary carbon (most reactive), forming a very stable allylic carbonium ion, before eliminating another HCl molecule to propagate the reaction. In so doing, a series of conjugated dienes (poly-enes) were formed. Since the electrons on these conjugated dienes can freely move over the entire length of the conjugated diene, an one dimensional electron well resulted. As the diene increases in length, the energy levels and the absorption spectra of the free electron begin to move from UV toward the visible wavelengths. As the absorption spectra increase in intensity from the short wave length direction, the originally clear PVC film

starts to appear yellow to dark yellow, orange, red, and finally black as the degradation progresses.

When the yellowness index of these films were compared with OIT measured at 230C, a very good correspondence was obtained (Fig[7]).

Not only one can uniquely determine the degree of the degradation compared to the color formation as evidenced by the fit of the data, subtle indications arising from the mechanisms of the degradation are also evident. Figure [7] clearly indicates that the degradation of the PVC proceeds in three distinct phases.

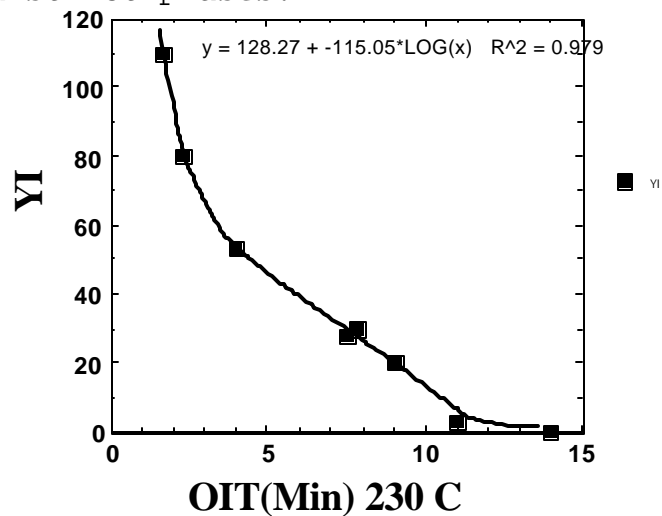


Figure 7, PVC OIT, COLOR CORRELATION

In the initial phase, significant induction time were lost without detectable color formation. The second phase indicated a more or less linear dependence of OIT with color. And the final phase, as the stabilizer becoming exhausted and numerous poly-ene sequences simultaneously moving in from the ultraviolet, the color formation becomes exponential before total destruction. The first and initial phase deserves further comment. If, in the absence of significant and detectable color, extensive degradation reaction can take place as measured by OIT, the consequence on chemical extractibles must be extensive. This may offer a rapid and effective screening method on chemical and leachable testing.

In terms of color formation, a simplified mechanism based on the poly-ene sequences can be formulated.

POLYOLEFINS

Due to their inherent cleanliness and cost/performance, polyolefins are desirable medical polymers. Since these are the polymers the original OIT test were established by researchers in the Bell Telephone Laboratories, we are taking a more detailed examination on the effectiveness. Gugamus(5) discussed the lack of correlation between OIT measurements on polypropylene and long term oven aging results. The oven aging results were obtained by onsets of embrittlement over up to 14 weeks of oven aging at 135°C. However, a close examination of the data (Figure [8]) indicated that only a single data point was out of place. With the offending data removed, the data fit improved from a correlation coefficient of 0.49 to 0.69 (figure [9]), a remarkable improvement indeed. Since the embrittlement assessment are known to be subjected to large errors, most of the data scatter in figure [8] was expected to have come from the oven aging test.

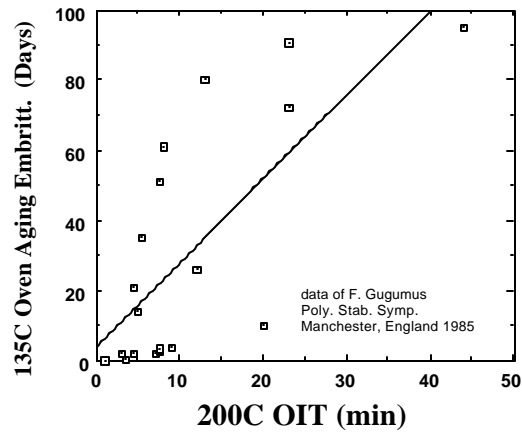


Figure 8 Polyolefin OIT Oven Stability Comparison

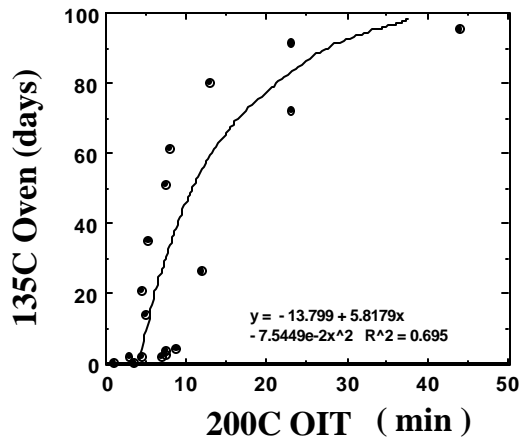


Figure 9, Replot of Figure 8 with one data point removed.

This combined with the very rapid nature(in minutes) of the OIT test, would tend to re-affirm the value of the OIT as a early predictor of the long term aging results.

In many of the OIT tests on polyolefin samples we have conducted, as the induction time is plotted in the Arrhenius fashion, a curious inflection in the activation enthalpy was frequently seen at relatively high temperatures. On the low temperature side of the line, a normal activation enthalpy is measured. On the high temperature high of the inflection, an anomalously higher activation enthalpy is measured. We speculated that the increase in apparent degradation rate is the volatilization of antioxidants at these high temperatures. For example, a highly stabilized structural polypropylene, the inflection occurred at 2.06 on the 1000/K scale, or about 210 C (Figure [10]).

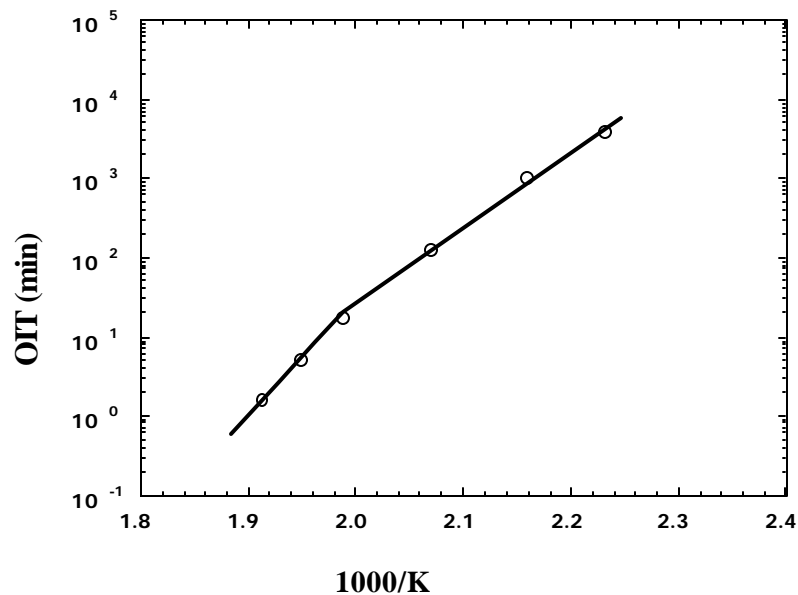


Figure 10, PP OIT vs. 1000/K

However, since the stabilizer package is not known, we can only suspect but not attribute the observation to the lost of antioxidants. In a similar series where we have specifically compounded 0.1% of Irganox-1010 (7) antioxidant in high density polyethylene (HDPE), an inflection point is clearly visible at about 2.015×10^{-3} or 200 C. Below 200C, an activation enthalpy of about 20 Kcal/mole is seen, while above 200C, a much higher activation enthalpy of about 60 Kcal/mole was seen. Bair(6) had

published rate of volatilization of Irganox-1010 determined by thermal gravimetric analysis. Indeed, if one replots the data from the reference as a function of temperature, a strong upturn is seen at about 200 C (Figure [11]).

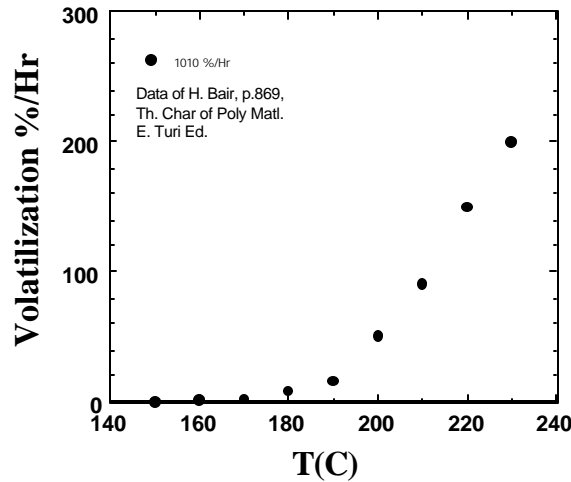


Figure 11, Phenonic Antioxidant Volatilization

Based on this we can conclude that these high temperature OIT inflection points are most probably caused by antioxidant volatilization. Following this line of reasoning, OIT data measured below the inflection, those free from the loss of antioxidants should be used for lower temperature property predictions.

In a similar way, a polypropylene sample with Ethyl-330 antioxidant was found to have a deflection at about 190C.

POLYESTER ELASTOMER

Polyester thermoplastic elastomers (TPE) based on polybutylene terephthalate (PBT) hard segment (8) and tetramethylene ether (PTMO) soft segments constitute an important class of medical elastomers because of their wide property range, solvent bonding capability, oxidative stability and processing ease. In a series of experiments film samples of 40D hardness were prepared on a 1 1/2 inch laboratory extruder at similar processing conditions but at varying thicknesses. Figure[12] presents the OIT activation enthalpy plot of two of the films. Both the 100 micron (4 mils) and 200 micron (8 mils) film exhibited identical activation enthalpies, indicative of identical

chemistry. A two layer composite of the thinner film also exhibited identical OIT of the thinner film. This indicates that the sample thickness of the OIT sample is not a primary variable for the induction times measured. However, between the two set of data, there was about a three fold difference. An inquiry into the details of the film extrusion process revealed that the thinner film was processed at slightly higher temperatures (193°C vs. 175°C). However, temperature alone could not account for the magnitude of the observed OIT discrepancy. It was concluded that the residence time in processing the thinner film must have been significantly longer than the 200 micron film. In other words, Figure [12] maps out a time temperature envelop for processing this particular polymer without significantly depleting the antioxidant package.

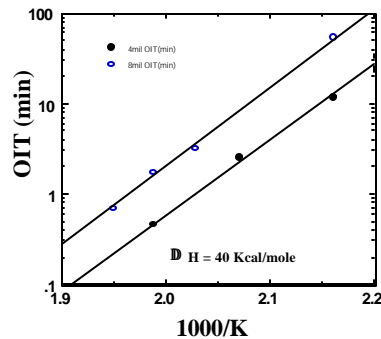


Figure 12, Polyester TPE Processing

SUMMARY:

In this continuation of an earlier study, we have examined in detail the application of the oxidative induction test to more polymer systems in the medical industry. In the case of flexible polyvinyl chloride (PVC), subtle effects of chain perfection were detected by using identical formulations. For polyolefins, it was found that a high temperature acceleration of the oxidation originated from the volatilization of antioxidants. And in comparing OIT's from a polyester thermoplastic elastomer, the processing temperature and residence time combination was identified as the principal variable in minimizing processing degradations.

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