Master Chemical Corporation
501 West Boundary
Perrysburg, OH 43551-1200 USA
Tel: 419-874-7902
www.masterchemical.com

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Via Electronic Mail

Dr. Yun Xie
NTP Designated Federal Official
Office of Liaison, Policy, and Review
P.O. Box 12233, MD-K2-03
Research Triangle Park, North Carolina 27709

Re: National Toxicology Program's Technical Report for TRIM®VX

Dear Dr. Xie:

Master Chemical Corporation ("MCC") submits the following comments, along with a review ("Review") of the National Toxicology Program's ("NTP") draft Technical Report ("Report") on toxicological studies of TRIM®VX for which the peer review panel will meet on February 16, 2016. The undersigned, Dr. Steven M. Florio, PhD as Master Chemical Corporation's Chief Technical Officer performed the Review as it relates to VX product specific comments and as to comments relating to chemical information. Dr. Patricia Beattie, PhD, DABT, Vice President Scientific Development, SciVera LLC., Charlottesville, VA performed the Review as it relates to toxicological issues and carcinogenic issues on behalf of MCC. Both this letter and Dr. Beattie's Review contain comments and suggestions, submitted for consideration by NTP as it finalizes its Report.

This letter presents a summary of MCC's comments and more detailed comments presented in the order of NTP's Report by page. This letter also refers to four appendices which are attached as well. Dr. Beattie's comments are organized by subject. In both cases, page references to the NTP draft Report are included where appropriate. A number of the comments relate to more than a single page.

MCC developed and started to market TRIM®VX ("VX") in 1983. VX is the Metal Working Fluid ("MWF") which was nominated for the toxicological testing under this program. MCC has discontinued the manufacture and sale of VX.

Summary Comments by Master Chemical Corporation

The following are the comments of Master Chemical Corporation reported by the undersigned Dr. Florio as part of MCC's during its review of the NTP report (NTP TR 591) on toxicology and carcinogenicity studies with TRIM® VX ("VX"), a soluble oil metalworking fluid (MWF).

Generally, the NTP Report on VX represents a serious effort by NTP to analyze MCC's product and submit that specific product to inhalation testing. Presumably, the well intentioned goal of NTP's selection process was to conduct a study of a "soluble oil" MWF product which would produce results and conclusions which might inform the public regarding toxicology and carcinogenesis issues involved in MWFs or which might be applicable to the MWF industry generally.

The information set forth in the Report demonstrates that NTP spent considerable time and resources on this study including efforts to reverse engineer VX to determine its chemical composition. Unfortunately, as will be discussed throughout these comments, the Study efforts failed to overcome a number of inherent serious structural problems involved in this Study. As a result, the Study findings as to toxicology and carcinogenetic activity caused by VX should be classified as "**Inadequate Study"**. The problems with this VX Study include the following:

1. VX was designed by MCC as a specialized niche product targeted to solve a unique and very difficult metal working problem, i.e. providing lubrication and cooling in the "heaviest duty machining operations" which operate under extreme pressures. This means that VX was never intended to achieve a "high production volume" and it never did. As a result, VX has never had a "large number of occupationally exposed workers". Since VX was first developed in the early 1980's, many of the chemicals utilized in its formulation are no longer used in common practice by MCC or by other manufacturers. Also, the VX formulation is well-known for its inability to control fungal growth; in fact, it shows the worst performance of all of Master Chemical's products in that regard, and serves as a negative control when evaluating fungal resistance. Thus, VX is a poor representative of the broad class of soluble oil MWFs among MCC's soluble oil products or the soluble oil products industry wide.

2. The formulation of VX, like many metal working fluids, is complex, consisting of 17 separate but interactive components. As such, VX has exhibited its own complex and unusual challenges. The underlying chemistry was developed by MCC in 1983 and the formula has remained unchanged since that time. Thus, the VX chemistry is now 33 years old. This product is not representative of MCC soluble oil products currently in the marketplace. NTP itself has characterized VX as "unique among the six soluble oils" considered by NTP for this Study.

3. VX has a known short shelf life (12 months) and has a well-documented history of chemical and biological instability. VX is prone to, (i) emulsion settlement into zones (de-homogenization) within very short time periods (See Appendix 1, Dr. Florio's Comments which document settlement of VX within 4 months of manufacture based on significant specific gravity variations between samples from the top and from the bottom of a drum of VX Product.), (ii) Chemical degradation and decomposition as it approaches and exceeds its shelf life

particularly depending on storage and handling conditions (Again, see Appendix 1, Dr. Florio's Comments which document measurable chemical degradation of VX within 11 months of manufacture), and (iii) susceptibility to fungal growth (Detailed as well in Appendix 1, Dr. Florio's Comments). These problems with the product are common knowledge in the industry and are tolerated by MCC and its customers only because of VX's very limited application and because of VX's extraordinary lubricity in its specific niche applications. These problems are mitigated in the market place by MCC and its customers by closely monitoring "in use" product conditions for known problems, just-in-time supply efforts which assure concentrate product freshness, frequent testing, routine product addition and supplementation ("topping off") and recharging as needed to assure fresh working solutions at all times.

4. The rigorous chemical analysis of VX conducted by NTP and well documented in the Study itself, establishes that the VX product used by NTP (the "Tested Product") in both the 3 month Study and the 2 year Study had already experienced serious chemical degradation by the time of its use in the inhalation exposures described in the NTP Study. Further, the lot of Tested Product used in the 2 year Study exceeded its useful shelf life just 6 months into the 2 year exposure period. The NTP chemical analysis clearly shows through NTP's "Measured Components" (Table 1, page 34) that there was significant composition variation between the Tested Product used in the 3 month Study and the Tested Product used in the 2 year study (even though MCC's formulation remained unchanged during this time). The most that the Study can state is that, "The composition of both lots of Tested Product was <u>similar</u> based on analysis (Table 1) (page 34)." The two lots should have been virtually identical assuming consistent high quality test methods. (Further, as will be described in detail in the comments below, comparing either lot of the Tested Product to a fresh batch of VX demonstrates that neither lot of the Tested Product is chemically equivalent to fresh VX Product). Based on NTP's Measured Components, certain conclusions are inescapable: (i) the two lots of Tested Product each was found to include some, but not all, of the Components which make up a fresh batch of VX, and (ii) even where correct Components were found to be present in the Tested Product, there were numerous significant variations in the percentage or ratios of the Measured Components in the Tested Product compared to the actual components of fresh VX.

   These significant differences between the Measured Components of the Tested Product and fresh VX establish chemically that at least one of the following experimental errors occurred with the product testing: (i) settlement of the soluble oil emulsion had occurred in the Tested Product prior to the sampling (de-homogenization) resulting in a random physical sample of the settled Components during the Study, (ii) chemical degradation and decomposition reactions leaving by products in amounts described in the listing of the Measured Components, that

were inconsistent with the fresh VX Product, and (iii) fungal growth may have occurred in the Tested Product during storage or testing, which could have changed the chemistry of the Measured Components of the Tested Product (the NTP Study specifically states that it conducted ongoing bacterial and fungi tests during the study but has declined to provide any of those test results.) In short, the Tested Product which NTP used in this study was not chemically equivalent to MCC's VX Product.

Summarizing, the Study findings as to carcinogenetic activity caused by VX should be classified as "**Inadequate Study"**. From the outset, NTP's process for selecting the product for this test was flawed. VX was intentionally designed over thirty years ago by MCC for limited use in specific extreme and severe applications. Instead of being typical or "representative" of soluble oil MWFs, VX is an older generation product which is complex, chemically interactive and unusually unstable with respect to fungal growth in the world of soluble oils. NTP characterized VX as "unique among the six soluble oils" considered for the Study. VX is well known to have a short shelf life and instability issues. For these reasons, VX should never have been selected as the soluble oil representative product for the long term inhalation study. Having been selected by NTP, no measures were taken by NTP as part of the Study methodology to assure that fresh VX was supplied and used as the study progressed. The analysis by NTP establishes that ratios of Measured Components varied widely between the 2 batches of Tested Product used in the 2 studies even though MCC's formula was not changed. This fact by itself invalidates any exposure-based findings of the study.

NTP conducted a detailed analysis of the Tested Product periodically during the two year Study ("at least every six months"). MCC has demonstrated through the use of FTIR (one of the same techniques utilized by NTP to evaluate Tested Product stability) that degradation of the product occurs during normal storage. MCC has requested NTP's periodic analysis results to assist MCC in gauging the extent and speed of the Tested Product deterioration, but this request was denied. The Measured Components found in the Tested Product indicate that the batches of VX used in both studies had experienced settlement and had chemically degraded. While the study states that NTP also has other test data (such as bacteria and fungi test results, storage conditions, efforts at mixing, etc.) which would shed light on these issues, NTP has declined to release this other information as well. Based on the limited information released by NTP to date, the Tested Product was NOT MCC's VX Product or chemically equivalent to MCC's VX Product.

For these reasons and based on the more detailed comments set forth below, the Study results are invalid as to MCC's VX Product. Any "exposure dosage" related conclusions are invalid on their face. Further, the Study results cannot validly be applied generally to soluble oil Metal Working Fluids. The Study findings as to toxicology and carcinogenetic activity caused by VX should be classified as "**Inadequate Study"**.

Detailed Page by Page Comments

The following are detailed Comments on the draft Report organized on a page by page basis. In addition, the following Appendices are attached:

Appendix 1: Comments by Dr. Steven M. Florio, PhD, MCC Chief Technology Officer
Appendix 2: Comments by Dr. Patricia Beattie, PhD, DABT, Vice President Scientific Development, SciVera LLC., Charlottesville, VA
Appendix 3: VX Data & Information Sheet published by MCC
Appendix 4: NTP's "Metal Working Fluids: Strategy for Toxicological Evaluation dated August 17, 2005"
Appendix 5: A Letter from Independent Lubricant Manufacturers Association ("ILMA") sent a letter to NIEHS, dated October 21, 2005.

Page 7: The statement in the 1st Paragraph that, "VX was nominated … for study … because of its high production volume, the large number of occupationally exposed workers…" is factually incorrect and misleading. This should be corrected or deleted and replaced entirely with correct information.

VX was designed by MCC as a specialized niche product targeted to solve a unique and very difficult metal working problem, i.e. the "heaviest duty machining operations" including applications operating under extreme pressures. See the attached promotional Data & Information Sheet (Appendix 3) published by MCC. VX is not recommended for light to medium duty machining. A 5% to 10% working concentration is recommended for moderate to Heavy Duty machining which are the most common applications for which this product is approved. A 10% to 20% working concentration is recommended for Very Heavy Duty machining on "soft" materials and "lower speed operations". Lower speed operations typically would involve less mist and thus less operator inhalation exposure than higher speed operations.

VX has never been a "high production" product. Because of its niche application, it has never had a "large number of occupationally exposed workers." Over the past five calendar years, VX sales have represented less than twelve one hundredths of one percent (.12%) of MCC's annual sales in North America.

NTP's records of this study actually confirm and acknowledge the fact that VX is an extraordinarily unique formulation among MWFs and even among the sub category of soluble oils. NTP and NIOSH published their "Metal Working Fluids: Strategy for Toxicological Evaluation dated August 17, 2005" (Appendix 4). At page 4 and page 5, NTP lists candidate products considered by NTP and classifies each of the candidates as a "Soluble Oil", a "Semi-Synthetic" or a "Synthetic" MWF. At page 6 and page 7 of Appendix 4, NTP sets forth various conclusions relating to the results of its chemical analysis of potential test products and describes its conclusions which led to the

nomination or elimination of specific products in the various categories for further testing. At page 7, Item 3, NTP states:

> "3) Select Trim VX as unique among the six soluble oils."

Thus, NTP's analysis concluded that VX was unique among MWFs generally and beyond that, VX was entirely unique when compared to all other Soluble Oil products considered for the Study. Interestingly, (and evidencing the internal contradictions of the Nomination process) on this same page 7, Item 6, NTP states the following when considering Clearedge 6519:

> "6) Eliminate Clearedge 6519 because it is unique among MWFs and, therefore, not representative."

The inconsistent, arbitrary and capricious nature of NTP's Nomination process is starkly visible when these two conclusions are compared. One product, VX is characterized not just as unusual or complex, but "as unique among the six soluble oils". Amazingly, this "uniqueness" is the apparent basis for the selection of VX by NTP. The other product, Clearedge 6519 is eliminated "because it is unique". NTP states the correct, logical and obvious conclusion leading to the elimination of Clearedge 6519: It is unique and "therefore not representative". There is simply no way to reconcile these two clearly inconsistent treatments of products in the nomination process. NTP selected VX for further study in its Nomination process even though it should have been eliminated from consideration just as Clearedge 6519 was eliminated. NTP cannot now deny its own previously published conclusions and its stated underlying Study assumptions. Whatever the Study results of VX, "VX is unique among the six soluble oils" and "therefore, not representative" of Soluble Oil products manufactured by MCC or by other companies in the MWF industry. For the reasons set forth herein including the instability of the unique niche formulation of VX, the NTP Study results are invalid as to VX. However, even if the results had been valid, because of its uniqueness, VX is "not representative" of soluble oil MWFs.

There are other NTP files which support the conclusion that the VX formulation is unique and document the fact that NTP was put on notice of the very limited shelf life of VX. In response to NTP's "Metal Working Fluids: Strategy for Toxicological Evaluation dated August 17, 2005" (Appendix 4) and its nomination decisions, the trade association, Independent Lubricant Manufacturers Association ("ILMA") sent a letter to NIEHS, dated October 21, 2005 on behalf of its members (including MCC) who manufacture the Nominated products (Appendix 5). This letter documents meetings between ILMA and NTP regarding the Study and provides additional product and manufacturer specific information. As stated in the letter at page 1 (Appendix 5) "To assist NTP in designing further studies", ILMA agreed to provide technical product specifications on shelf life and fluid stability, [and] insights on dilution…" At page 2, the letter sets forth a matrix addressing the "shelf life and product stability" for the nominated fluids including VX. In

reviewing the matrix, what is said about MCC's product and what is said about the other manufacturers' products is important. MCC's VX product has a more limited shelf life of just 12 months compared to the Castrol product's 24 month shelf life. In the ILMA letter, MCC also notes a range of temperature for stability purposes that is more limited than any of the other manufacturer's products: "Concentrates are stable within a range of 50° F to 90° F". Castrol's temperature stability range for its nominated product is twice that of VX: "40° F to 120° F". The nominated Milacron product stability range is broader still: "stable in ambient temperatures". Thus, NTP clearly knew in advance that the 2 year time period for the inhalation study was longer than the VX shelf life. This would have been the case even NTP had secured freshly manufactured VX at the start of the Study. In fact, the actual lot used in the study was already 9 months old at the time of the first test subject exposure in the 3 Month Study and 6 months old at the time of the first exposure in the 2 Year Study (Table 2, page 42 of the Study).

Page 14: The explanation of the findings needed to support a finding of "Clear evidence of carcinogenic activity" includes a requirement that the Study results are "showing a dose-related" relationship between the tested chemical and one or more specific carcinogenic effects. The definitions for "Some evidence" and "Equivocal evidence" also require findings that the carcinogenic effects are "chemical related". As noted in the Summary and in the detailed Comments from Dr. Steven M. Florio (Appendix 1), there are chemical inconsistencies in the Tested Product from batch to batch and between either Tested Product batch and the composition of fresh VX.

NTP's own chemical analysis lists NTP's "Measured Components" (Table 1, page 34) in the 2 Tested Product lots used in the Studies. This shows significant composition variations between the lot of Tested Product used in the 3 month Study and the lot of Tested Product used in the 2 year study (even though MCC's formulation remained unchanged during this time). The most that the Study can state is that, "The composition of both lots was "similar" based on analysis (Table 1)." They should have been the "same" if not virtually identical assuming that NTP used consistent and accurate test methods. If the testing methodology resulting in the Table 1 information was unreliable or inconsistent, this should be disclosed. As Dr. Florio in Appendix 1 comparing either lot of Tested Product to a fresh batch of VX demonstrates that the neither of the tested materials is chemically equivalent to fresh VX product. Based on NTP's Measured Components, certain conclusions are inescapable: (i) the two lots of Tested Product each include some, but not all, of the Components which make up a fresh batch of VX, and (ii) even where correct Components were present in the tested products, there were numerous significant variations in the percentage or ratios of the Measured Components in the Tested Product compared to the actual components of fresh VX.

More details and specific information on the "dose-related" disconnect are found in MCC's comments regarding Page 32 and Table 1 below.

Because of the wide variations in the Measured Components documented by NTP, any "exposure dosage" related conclusions are invalid on their face. Further, the Study results cannot validly be applied generally to soluble oil Metal Working Fluids. The Study findings as to carcinogenetic activity caused by VX should be classified as "**Inadequate Study"**.

Page 19: Paragraph 1 includes a statement that, "Generally, the concentrated soluble [oil] metalworking fluids are diluted prior to use with water…" This statement is correct and is certainly true of VX which has a low water content. Importantly, this is exactly the issue which was raised by ILMA's October 21, 2005 letter (Appendix 5) at page 2 as follows:

> "Dilution
>
> Soluble oil product concentrates … generally do not contain water in the product concentrate. As a result, any change in product chemistry (including the possible reaction of water with other chemical components in the product concentrate) that might occur upon dilution would not occur if the soluble oil product concentrate were to be directly aspirated. Thus, in order to assure that animals are exposed to fluids representing conditions [and the chemicals] representing conditions as close as possible to those of machinists, ILMA recommends that any soluble oil product be first diluted one part fluid concentrate to 20 parts of deionized before exposure."

In other words, chemical reactions that occur upon dilution change the chemical composition of the tested product. (This point was made by ILMA well in advance of the actual inhalation exposures.) Using the concentrate prevents these chemical changes from occurring and thus changes the chemical-related and the dose-related results which are fundamental to establishing valid findings of carcinogenic activity in soluble oil MWFs. In spite of NTP's acknowledgement of this issue, and ILMA's specific caution on this point, NTP's Study of VX failed to make any dilution of VX before the exposure or to take any other measures to adjust for any change in chemistry that was not permitted to occur. For this reason as well, the findings as to VX should be "Inadequate Study".

Page 20: The second full paragraph mentions bacterial and fungal contamination and the potential inhalation impacts of such contaminants. This passage references the potential impact of such contaminants on workers. ILMA's October 21, 2005 letter (Appendix 5) at page 2 noted this same concern and recommended to NTP, based on 15 years of research, that the NTP Study should include in the study exposures containing some of the known contaminants for comparison with fresh MWFs. NTP failed to do this. MCC's information also points to the impact such contaminants could have on the degradation of VX and VX's unique susceptibility to fungal growth. No consideration of this factor. NTP claims to have monitored bacterial and fungal levels during the tests but NTP does not indicate the levels of these contaminants found in the Tested Products.

Page 21: The second full paragraph suggests that MCC typically recommends diluting concentrate VX 5% to 20% in water before use. This makes the above referenced point that MCC does not recommend direct use of the concentrate for any application. However, the stated working solution range is incomplete and misleading. MCC only recommends working solutions as high as 10% to 20% for "very heavy duty" machining on "soft" materials and "lower speed operations". Recommended working solutions for more typical "Moderate-duty machining" is 5% - 7% and "Heavy-duty machining" 7% - 10% (See Appendix 3).

Page 33: The first paragraph on Page 33 discloses the lot numbers for the 2 lots of Tested Product: "Lot 101607N was used during the 3-month studies, and lot 011509N was used during the 2-year studies." MCC assigns lot numbers based on the date of production of the lot. Thus, Lot 101607N was produced on October 16, 2007. Lot 011509N was produced January 15, 2009. Based on these production dates, the Tested Product used in the 3 Month Study was already 9 months old at the time of the first test subject exposure and was about at, or beyond, the end of its useful shelf life by the conclusion of that Study. The situation in the 2 Year Study was much worse: The Tested Product was already 6 months old at the time of the first exposure and it had reached the end of its useful life by the time that the 2 Year Study was only 25% complete. A full 75% of the exposures in the 2 Year Study were made with "out of date" or expired product. (Table 2, page 42 of the Study lists the actual first and last exposure dates for both Studies.)

Page 34: At the top of the page before Table 1, the Report makes the following conclusory statement about the 2 lots of Tested Product:

> "The composition of both lots was similar based on analysis (Table 1)."

This statement is either inaccurate or meaningless. The Study provides no definition of the word "similar" or what the word is intended to convey in this context. As set forth in Appendix 1, Table 1 itself shows a number of very significant variations between the 2 lots of Tested Product. During this time period there was no change in the formulation of VX. If the 2 lot were both fresh VX Product, and if the analysis methodology used by NTP was consistent, the results should have been virtually identical. Beyond this, as described in Appendix 1, neither Lot 101607N not Lot 011509N was the chemical equivalent of fresh VX Product.

Looking at Table 1 on page 34, various other problems with the results become apparent. First, the data set is entirely undated. The first study involved the acquisition of the Tested Product, test preparations and an additional 3 months of exposure. The second study involved the acquisition of the Tested Product, test preparations and an additional 2 years of exposure. NTP has provided no information when the information set forth in Table 1 was gathered as to each Tested Product: Before the study, during the study or after the study. For all that has been disclosed, the data could represent averages of scores

of tests conducted at various times. Below Table 1 on Page 34, the Study asserts that periodic testing was conducted throughout the Exposure period "at least every 6 months during the 2-year studies." The results of these periodic analyses have been specifically requested by MCC. This request has been denied.

Another obvious problem on the face of Table 1 is that the "Measured Components total more than 100%: Column 1 totals 109.68% and Column 2 totals 110.08%. No explanation of this problem is provided. In fact, footnote a simply states that, "All values are percentages." These "percentages" are in most instances carried out to 2 decimal points suggesting considerable accuracy in the results of these analyses. Such accuracy is inconsistent with a presentation of components totaling 110%. No explanation is provided but presumably some of the Measured Components are double counted or are grossly inaccurate. This problem on its face makes any "dose related" findings impossible.

The rigorous chemical analysis of VX conducted by NTP and well documented in Table 1 and elsewhere in the Study establishes that Tested Product used in both the 3 month Study and the 2 year Study had already experienced serious chemical degradation by the time of its use in the inhalation exposures described in the NTP Study. The lot of Tested Product used in the 2 year Study exceeded its useful shelf life just 6 months into the 2 year exposure period. The comparison of Table 1 with the fresh VX Product discussed in Appendix 1 shows that there was significant composition variation between the Tested Product used in the 3 month Study and the Tested Product used in the 2 year study (even though MCC's formulation remained unchanged during this time). Further, comparing either lot of the Tested Product to a fresh batch of VX demonstrates that neither lot of the Tested Product is chemically equivalent to fresh VX Product. Based on NTP's Measured Components, certain conclusions are inescapable: (i) the two lots of Tested Product each was found to include some, but not all, of the Components which make up a fresh batch of VX, and (ii) even where correct Components were found to be present in the Tested Product, there were numerous significant variations in the percentage or ratios of the Measured Components in the Tested Product compared to the actual components of fresh VX.

These significant differences between the Measured Components of the Tested Product and fresh VX establish chemically that at one or more of the following experimental errors occurred with the product testing: (i) settlement of the soluble oil emulsion had occurred in the Tested Product prior to the sampling (de-homogenization) resulting in a random physical sample of the settled Components during the Study, (ii) chemical degradation and decomposition reactions leaving by products in amounts described in the listing of the Measured Components, that were inconsistent with the fresh VX Product, and (iii) fungal growth may have occurred in the Tested Product during storage or testing, which could have changed the chemistry of the Measured Components of the Tested Product (the NTP Study specifically states that it conducted ongoing bacterial and fungi tests during the study but has declined to provide any of those test results. In short,

the Tested Product which NTP used in this study was not chemically equivalent to MCC's VX Product.

Appendix H to the Study: The problem throughout Appendix H to the Study is lack of details and information. Repeatedly in these pages, references are made to analyses, determinations, measurements and the collection of data. In few cases are any of the raw data actually disclosed. Raw data results that are disclosed are undated or the sampling and testing methods are not disclosed. Given the known chemical and biological instability of VX and the fact that the 2 year Study used Tested Product at 2.5 times its useful life, detailed information is essential if the Study results are to be conclusive or reliable. This information has been requested as well and has not been provided by NTP. It is difficult to understand how the NTP can ask a panel of peers to review its Study without providing this basic information.

Figure H2 is typical. It suggests that a "mixer" was used in the "Chemical Reservoir" during the study but no details are provided regarding this critical test component. It fails to disclose if the above referenced "Chemical Reservoir" was the original MCC supplied drum or if the Tested Product was transferred into a separate "Chemical Reservoir". In either case, how was the Test Product removed from the "Chemical Reservoir" for actual use in the exposure process? Was a fixed or floating intake point used in the reservoir? Did the reservoir share a room with the test subject or was it in an adjoining room? Again, fungal levels were "measured" but the results and levels of contamination have not been disclosed.

General Comments: Dr. Florio (in Appendix 1) and Dr. Beattie (in Appendix 2) set forth additional specific Comments. Dr. Florio's address VX Product and Chemical information primarily and Dr. Beattie's address primarily the toxicological issues and carcinogenic issues on behalf of MCC.

Conclusion

The Study findings as to toxicological and carcinogenetic activity caused by VX should be classified as "**Inadequate Study"**. The NTP's process for selecting the product for this test was flawed. VX was never an appropriate product for testing in the Study. VX is an older generation product which is "unique among the six soluble oils", complex, unusually unstable, both chemically interactive and with respect to fungal growth. It has a very short useful shelf life. NTP was advised in writing of the shelf life and stability issues well in advance of the Study and NTP took no measures in the design of the Study to deal with these known problems. The 2 year Study continued using a single batch of Tested Product until past the point at which the Tested Product reached 2.5 times its known useful shelf life.

The analysis by NTP set forth in the draft of the Study establishes that ratios of Measured Components varied widely between the 2 batches of Tested Product used in the 2 studies

even though MCC's formula was not changed. Dr. Florio's Comments (Appendix 2) establish differences between the Tested Product and fresh VX. These comments document the fact that the Product Tested by NTP was NOT the chemical equivalent of VX. This chemical discrepancy by itself invalidates any exposure-based findings of the study. A finding of "Clear Evidence" requires a "dose-related" increase in carcinogenic effects and this standard cannot be met by this Study. Even findings of "Some Evidence" or "Equivocal Evidence" require "chemical related" evidence of carcinogenic results. Again, with the problems inherent in this Study, such findings are simply not possible.

The information set forth in the draft Report demonstrates that NTP spent considerable time and resources on this study, but the Peer Review process requires an examination of the Study Results, not the time and effort spent on the Study. The Study findings as to toxicology and carcinogenetic activity caused by VX should be classified as "**Inadequate Study"**.

/S/ Steven M. Florio

Steven M. Florio, PhD
Chief Technology Officer

Master Chemical Corporation
501 West Boundary
Perrysburg, Ohio 43551-1200