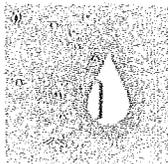


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Chemical Category					
COLORANTS					

ETAD



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Ecological and Toxicological Association of the Dye-stuffs Manufacturing Industry

*FYE-AX-0688-0621 INITIAL
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000582080N

CONTAINING REPORT

84-88000137

Your Ref.

Our Ref. PR/an

CH-4005 Basel, June 3, 1988

Dear Sirs,

Report T 2015-E - Copy No. 32
Executive Summary on the ETAD Project T 2015 - Toxicological Testing of
Major Colorants

Attached we are sending you the finished report on the second phase of our
investigation including a list of the structures of the coded colorants.

As you are aware the member companies of our association has so far not
been informed which commercially available products were actually tested
and which test results relate to which product.

We are now communicating this information to all our member companies to
enable them to decide what notification or other measures, if any, are
required or appropriate.

We trust our report is of interest to you.

Yours sincerely,

ETAD

Dr. R. Anliker
Executive Secretary

Dr. P. Rudolf
Legal Counsel

Encls.

cc: Dr. E.A. Clarke
USOC of ETAD (without enclosure)

ETAD



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Seq. A

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REPORT CATEGORY: ~~CONFIDENTIAL~~

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R E P O R T T 2015-E

Executive Summary on the

ETAD Project T 2015

Toxicological Testing of
Major Colorants

Author : Dr. E. Löser

Approved by: Toxicological Subcommittee of ETAD
Prof. Dr. G: Kimmerle, TSC Chairman *G. Kimmerle*

Date: March 8, 1988

Approved for Issue:

Date: April 15, 1988

Dr. R. Anliker *R. Anliker*
Executive Secretary of ETAD

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EXECUTIVE SUMMARY

on the

ETAD Project T 2015

Toxicological Testing of Major Colorants

The ETAD Project T 2015 includes a total of forty colorants and was initiated with the aim of combining information about possible genotoxic potential of these major colorants step by step.

STEP 1

Step 1 of this project consisted of:

- Ames testing of all colorants (ETAD member companies) with samples of technical quality using a standard protocol and including at least the following *Salmonella typhimurium* strains:
TA 1535, TA 100, TA 1537 and TA 98.
- Retesting of purified samples of some selected colorants (ETAD member companies) which gave positive results in the initial test using at least those strains which showed positive response.
- Compilation of analytical data for all colorants (ETAD member companies).
- Literature search (ETAD Secretariat).

Results of Step 1

A survey for the results of the Ames tests performed with all forty major colorants and with the selected purified samples is given in the appended tables. According to this compilation twenty-one colorants gave negative results in the Ames test for samples of technical grade. Nineteen were positive in at least one strain. Out of these nineteen compounds eight caused only frameshift mutations, whereas only two compounds caused solely base-pair substitutions.

The remainder induced both types of mutations. Taking into account that *S. typhimurium* TA 100 is also sensitive to frameshift mutagens due to its marker mutation it can be speculated, that the majority of the positive colorants were frameshift mutagens, because only five compounds reverted additionally TA 1535.



Out of these nineteen positive colorants nine were retested after purification. Whereas three of them were still mutagenic, five colorants gave negative results. Therefore, the mutagenic activity of these five compounds has to be accounted for to impurities and not to the colorant itself.

More detailed informations may be found in the ETAD Report T 2015-B "Results from the Salmonella/microsome mutagenicity assay", and in the ETAD Report T 2015-D "Amendment to Report T 2015-B".

STEP 2

Step 2 of this project consisted of selecting various Step 1 compounds for in vitro mammalian point mutation assay testing.

Twenty-one compounds giving negative results already when tested in technical quality and six compounds giving negative results after purification need no further testing for point mutagenic effects in mammalian cells. Also colorants No. 6 and 35 needed no further testing.

For compound No. 6 no further tests were recommended since literature data fulfilled the requirements of Step 2. However, these findings were conflicting and need a very careful review.

Also for colorant No. 35 no further testing was recommended because the negative findings for the purified sample were confirmed by literature data and findings of BASF. In addition a negative micronucleus test was found in the literature, too. Therefore the recommendations of the "ad hoc Working Group" were satisfied by these data.

In contrary, the positive compounds need further testing for point mutagenic effects in mammalian cells to examine the relevance of the positive effect in bacterial cells.

However, three of these colorants need no further testing at all:

Compound No. 4 was extensively tested in mutagenicity assays with conflicting results. Therefore further testing would not change the present situation.

Colorant No. 5 is a mixture of several components which may differ from company to company. The literature data are conflicting and may partly be due to different compositions. Therefore, further testing on one distinct batch would not clarify the situation. The main component of this compound is also reported to be a frameshift mutagen and a clastogen *in vitro*.

Compound No. 9 was produced by ACNA only. Since ACNA gave up the dyestuff production this product is no more of any importance.



Compound No. 34 was in the meantime deleted by ICI.

The compounds No. 22 and 24, both azoic coupling components, were also not considered for retesting in Step 2.

Due to these considerations only seven compounds need further testing.

Results of Step 2

Seven compounds which gave positive results in the Ames test were assayed in point mutation tests in mammalian cells in vitro. Among them were three azo dyes (colorants No. 3, 14 and 15), three anthraquinone dyes (colorants No. 8, 31 and 33) and one chrysazine dye (colorant No. 32). For compounds No. 3, 8, 14 and 31 a V79/HGPRT^{**} test was performed. Whereas colorants No. 3, 8 and 14 were proven as nonmutagenic in this assay, compound No. 31 was still mutagenic.

Colorant No. 15 was tested in the CHO/HGPRT^{**} assay whereas colorants No. 32 and 33 were evaluated using the L5178Y TKK+/-assay^{***}. In contrary to compound No. 15 which gave negative results both dyes tested in the mouse lymphoma assay (ML) were mutagenic.

SUMMARY

Nineteen of forty tested dyes gave positive results in the Ames test. Nine of them were retested after purification. Three purified dyes gave still positive results so that thirteen of forty tested dyes were finally positive in the Ames test. Seven of these thirteen dyes were tested for point mutagenic effects in mammalian cells in vitro. Of these seven compounds three gave positive results in the mammalian gene mutation assay in vitro.

Azo dyes tested for point mutagenic effects in mammalian cells in vitro were all non mutagenic. Two of three anthraquinone dyes as well as the chrysazine dye were mutagenic under these conditions.

- * Chinese hamster V79 cell
hypoxanthine-guanine-phosphoribosyl transferase locus mutation assay
- ** Chinese hamster ovary cell
hypoxanthine-guanine-phosphoribosyl transferase locus mutation assay
- *** Mouse lymphoma L5178Y cell
thymidine kinase locus mutation assay

ETAD Project T 2015

Survey of results

com- pound num- ber ETAD T 2015	Ames result		Results of point- mutation tests in mammalian cells in vitro
	with technical sample	with purified sample	
1	+ 9	-	
2	-		
3	+ 8,9	w 3,9	- V79
4	+ 8,9		
5	+ 7,8		
6	-		
7	-		
8	+ 7,8,9	w0,7,9,97	- V79
9	+ 8,9		
10	-		
11	-		
12	+ 0,7,8	-	
13	-		
14	+ 0,9		- V79
15	+ 0,9	+ 0,9	- CHO
16	-		
17	-		
18	-		
19	-		
20	-		

continued; codes see last page

ETAD Project T 2015
 Survey of results (continued)

com- pound num- ber ETAD T 2015	Ames result		Results of point- mutation tests in mammalian cells in vitro
	with technical sample	with purified sample	
21	-		
22	+ 9		
23	-		
24	+ 5,0,7,9		
25	-		
26	-		
27	+ 0	-	
28	-		
29	+ 0	-	
30	-		
31	+ 7,9		+ V79
32	+ 5,0,7,9		+ ML
33	+ 5,0,7,9		+ ML
34	+ 5,0,7,9		
35	+ 5,0,7,9	-	
36	-		
37	-		
38	+ 0,7,9	-	
39	-		
40	-		

codes see last page

Codes used in Table

-	=	negative response
+	=	positive response
w	=	weak positive response
5	=	strain TA 1535
7	=	strain TA 1537
8	=	strain TA 1538
9	=	strain TA 100
98	=	strain TA 98
97	=	strain TA 97

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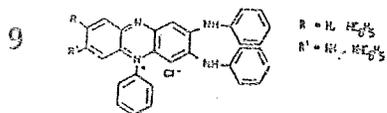
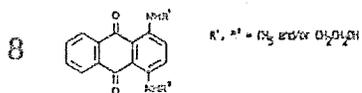
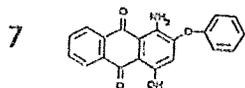
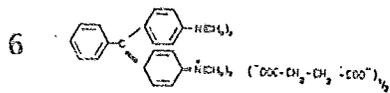
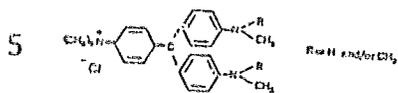
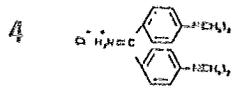
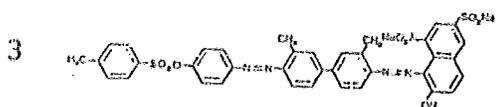
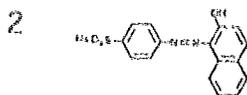
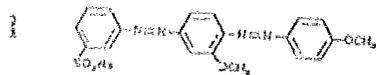


Code of Colorants of Report T 2015-E

T 2015-Code	CAS No.	C.I.No.	C.I. Name
1	71819-57-3	-	Acid Yellow 219
2	633-96-5	15510	Acid Orange 7
3	6459-94-5	23635	Acid Red 114
4	2465-27-2	41000	Basic Yellow 2
5	8004-87-3	42535	Basic Violet 1
6	2437-29-8	42000	Basic Green 4
7	17418-58-5	60756	Disperse Red 60
8	2475-46-9	61505	Disperse Blue 3
9	8004-98-6	50400	Solvent Blue 7
10	1326-82-5	53185	Sulphur Black 1
11	72496-81-9	13906	Acid Yellow 151
12	3351-05-1	26360	Acid Blue 113
13	1325-37-7	40000	Direct Yellow 11
14	83221-67-4	35435	Direct Black 22
15	1787-61-7	14645	Mordant Black 11
16	2512-29-0	11680	Pigment Yellow 1
17	6486-23-3	11710	Pigment Yellow 3
18	3520-72-7	21110	Pigment Orange 13
19	6535-46-2	12370	Pigment Red 112
20	11099-03-9	50415	Solvent Black 5
21	92-77-3	37505	Azoic Coupling Component 2
22	91-96-3	37610	Azoic Coupling Component 5
23	135-61-5	37520	Azoic Coupling Component 18
24	97-52-9	37125	Azoic Diazo Component 5
25	5102-83-0	21100	Pigment Yellow 13
26	5468-75-7	21095	Pigment Yellow 14
27	2425-85-6	12120	Pigment Red 3
28	5280-66-0	15865:4	Pigment Red 48:4
29	2580-78-1	61200	Reactive Blue 19
30	17095-24-8	20505	Reactive Black 5
31	3860-63-7	63305	Disperse Blue 26
32	12222-75-2	-	Disperse Blue 35
33	31810-89-6	63285	Disperse Blue 56
34	12270-38-1	-	Disperse Blue 122
35	482-89-3	73000	Vat Blue 1
36	81-77-6	69800	Vat Blue 4
37	130-20-1	69825	Vat Blue 6
38	128-58-5	59825	Vat Green 1
39	2475-33-4	70800	Vat Brown 1
40	131-92-0	69015	Vat Brown 3



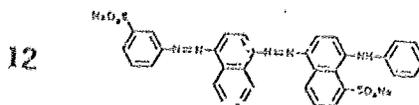
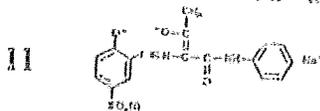
Structures of Colorants of Report T 2015-E



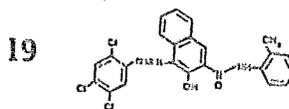
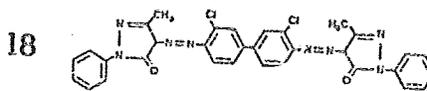
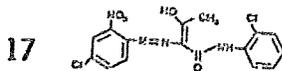
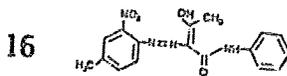
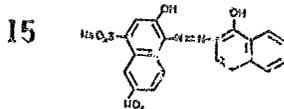
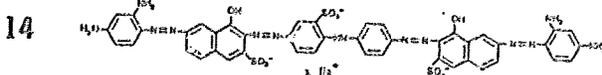
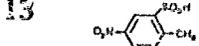
Reaction product of



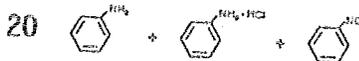
1:2 Co²⁺ complex of

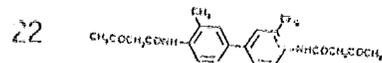
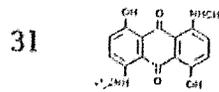


Self condensation product of:



Reaction product from catalytic redox condensation of:





32 partially methylated dianilinochrysanin (including some 6-substitution)

