

**MULTI-STAKEHOLDER TECHNICAL CONSULTATION:  
PROPOSED SUBGROUPING OF AROMATIC AZO- AND BENZIDINE-BASED SUBSTANCES**

**SUMMARY REPORT**

**March 20, 2012  
Ottawa, ON**

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## INTRODUCTION

The Chemicals Management Plan (CMP) was announced by the Government of Canada in December, 2006. The CMP is a comprehensive program designed to enhance the protection of the health of Canadians and their environment from harmful chemicals. Detailed information on the CMP is available at the following website: [www.chemicalsubstanceschimiques.gc.ca](http://www.chemicalsubstanceschimiques.gc.ca).

Moving forward in the CMP, a key initiative is the Substances Groupings Initiative. This initiative began with a Notice of Intent for the aromatic azo- and benzidine-based substance group, published on June 5, 2010. On October 8, 2011 an announcement of planned actions to assess and manage, where appropriate, the risk posed by certain substances to the health of Canadians and the environment, that applies to this group and eight additional groups of substances, was published in the *Canada Gazette*, Part I: Vol 145, No. 41 - October 8, 2011.

The aromatic azo- and benzidine-based substances grouping, consists of 358 substances which were identified as priorities for action through the categorization process. To address this class of substances, the Government of Canada proposed subgroups to cluster substances based on structural similarities, common functional uses and applications and physical-chemical properties. A technical consultation on the proposed subgroups was carried out on March 20, 2012 in Ottawa, with the specific objective of obtaining stakeholder input on the proposed subgrouping approach for the 358 substances<sup>1</sup>. The charge questions were formulated around the specific topics (overall subgrouping approach and subgroup specific questions) and sent to the participants in advance of the meeting. Participation included individuals from industry, environmental and health non-governmental organizations and aboriginal groups, as well as academia. Representatives from Health Canada (HC) and Environment Canada (EC) attended as participants/presenters as well as observers/note takers.<sup>2</sup> The consultation meeting consisted of a series of presentations from HC and EC. Presentations were followed by breakout sessions with charge questions and plenary discussion periods.

This report is a summary of stakeholder feedback and commentary. Feedback and comments are presented as we have understood them and are not reported verbatim. In many cases, the comments summarized below are feedback based on information presented at the workshop. These presentations are available upon request<sup>3</sup>.

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<sup>1</sup> See Appendix A for consultation meeting agenda.

<sup>2</sup> See Appendix B for a list of participants.

<sup>3</sup> Please contact [Substances@ec.gc.ca](mailto:Substances@ec.gc.ca).

## Presentation 1: BACKGROUND & CONTEXT

Stakeholder comments/questions included:

- **Clarification was sought as to the percentage of commercially available dyes which have data.** *Government representatives indicated that summary of data availability posted on the Chemical Substances website is based on publicly available data, and additional information is expected from the s.71 submissions for data that are not published.*
- **Clarification was sought on the basis for the focus on dermal route of exposure given that other jurisdictions have focussed on reductive breakdown with respect to the lower GI tract or sediments.** *Government representatives indicated that data show that skin bacteria are capable of azo reductive cleavage as well and, therefore, the dermal route will also be considered.*
- **It was recognized that the presentation on risk management actions in other jurisdictions was not comprehensive.**
- **A concern was expressed that the assessment activity did not appear to encompass occupational scenarios.** *Government representatives indicated that data from occupational settings inform the assessments conducted under the CMP, and that officials from Health Canada's National Office of WHMIS participate in the internal review process, but that characterization of occupational exposure and risk is beyond the scope of the assessments.*
- **A comment was made regarding high tech applications of azo dyes,** but none of the participants were aware of such applications.
- **Government representatives clarified that the number of assessment reports for groupings in the Substance Grouping Initiative will vary. For the azo grouping more than one assessment report is envisioned.**
- **A comment was made regarding the role of decisions in other jurisdictions vis-à-vis decision-making under CEPA 1999.** *Government representatives indicated that actions in other jurisdictions were a selection consideration in establishing the current round of priorities under the CMP. The importance of obtaining the science-basis for the action and the supporting documentation was noted.*
- **A comment was made that bioaccumulation should be considered closely for human health, e.g. vulnerable populations** such as a child eating and drinking food and beverages containing azo dyes daily, which poses a different kind of bioaccumulation than in the environment.
- **Consideration should be given to sulfanilic acid, one of the metabolites,** which has been shown to produce hyperactivity and learning deficits.

## Presentation 2: THE PROPOSED APPROACH TO SUBGROUPING

Stakeholder comments/questions included:

- Bioavailability should be an important consideration in subgrouping.
- As concern with some parent substances have been identified, both parents and metabolites should be considered in assessments.
- Potential risk to consumers versus potential risk due to industrial use should be considered separately.
- Once the assessment is concluded, communication needs to be conducted in a manner that consumers understand, to avoid misinterpretations of the assessment outcomes.
- Care should be taken in determining implications of the presence of a metal in the subgrouping approach. An example from the categorization exercise was given in which sorting based on metal moiety (e.g., sodium and potassium salts placed in one group and other salts in a different group) resulted in the substances that were more inherently soluble not meeting the categorization criteria and those that were less soluble did.
- Solubility and enzymatic breakdown potential are not necessarily the same even if substances are structurally similar in a structurally related group. *Government representatives noted that consideration of breakdown potential will be made for each structurally related group. If empirical data are available, substances in the group may be compared to determine if there is good alignment in breakdown potential. When structures are highly similar, they may have similar breakdown potential; however, it is acknowledged that small structural differences could lead to substantial differences in breakdown potential in certain cases.*
- Clarification was sought on whether Government would be interested in receiving leachability and fastness data. *Government representatives indicated that they would be.*
- It was noted that it would be important to consider cumulative risk, and that moving forward with groupings rather than substance by substance assessments in the CMP better accommodates this.
- It was noted that the terminology needs to be consistently applied for clarity.

### Charge Question 1: What do you see as the strengths of the proposed subgrouping approach?

- With respect to subgrouping the pigments based on Chemical Category and Application Class, the approach was considered appropriate.
- From the dye industry perspective, it is a standard textbook defensible way to group the substances.
- Accommodates consideration of cumulative risk.
- Grouping of similar applications was identified as a strength.
- Consideration of approaches of other jurisdictions was identified as a strength.
- Recognition that the approach breaks group into manageable subgroups.
- Accommodates streamlining and efficiency.

- Allows for subgroup, and as appropriate substance-specific, conclusions.
- Like that dyes and pigments will be grouped separately.

**Charge Question 2. Are there limitations to the proposed subgrouping approach and if so, how do you recommend to address them?**

- Does not focus on hazard and risk (e.g., subgrouping by aromatic amine breakdown product).
- Some compounds have multiple uses – unclear how these will be addressed (e.g., some food dyes are in Azo Acid Dyes Subgroup while only one food dye is in Azo Food Dyes).
- Proposed approach does not address purity levels.
- Other types of degradation are not being addressed.
- Ingestion should be considered a more important route of exposure than dermal route.
- Exposure to children should be considered, especially for metabolites of azo dyes.
- Consideration should be given to filling data needs through provisions in *CEPA 1999*.
- Potential breakdown products need to be better understood as concern lies in them.
- Clarity sought on how exposure factors into the subgrouping approach.

**Charge Question 3. Are there other subgrouping approaches that you would like to recommend?**

- Consider subgrouping according to potential aromatic amines breakdown product, and then apply the proposed approach. One organization indicated they were compiling information on potential breakdown products and would share with Government representatives shortly. Government indicated they had undergone a similar exercise and look forward to the additional input.

**Presentation 3: SUBGROUP BY SUBGROUP WALKTHROUGH**

This session was designed to go through Subgroups one-by-one to address charge questions 4 and 5:

**Charge Question 4:** Should any substance belong to a different subgroup than proposed? If so, please provide the rationale.

**Charge Question 5:** Should any substances be considered within the same structurally related grouping? If so, please provide the rationale.

**OVERARCHING COMMENTS**

- All CAS RNs, DSL names and structures need to be verified:
  - The National Chemical Inventory should be consulted.
  - Counter ions should be displayed in structures with correct charge notation.

- Some substances are not complete in showing all associated atoms.
- Some substances are used in large volumes as food colourants. There was a recommendation that all food colourants be considered together.

### **Monoazo pigments**

- The text description for “structurally related group” needs to be chemically more descriptive.
- Substances in the same Structurally Related Group should be based on the coupling component rather than by the number and position of naphthalene rings. (i.e. the Beta-Oxynaphthoic Acid ("BONA") lake pigments<sup>4</sup> identified as substances CAS No. 12238-31-2, CAS No. 17852-99-2, CAS No. 7023-61-2, CAS No. 71832-83-5, and CAS No. 6417-83-0 should be grouped together and the 2-naphthylamine-l-sulfonic acid pigment lakes identified as substances CAS No. 5160-02-1, CAS No. 6372-81-2, CAS No. 83249-60-9).
- Some substances containing chlorine atoms may be UVCBs as the exact positions of chlorine may not be known.

### **Benzidine-based Dyes**

#### **Benzidine Acid Dyes:**

- Substances CAS No. 72252-59-6 and CAS No. 70210-28-5 are trisazo compounds which are usually classified as direct dyes rather than acid dyes.

#### **Benzidine Direct Dyes:**

- Structures of benzidine direct dyes often exist in copper-complexes particularly those molecules containing dianisidine.
- Only three of the substances in this group are strictly “benzidine-based dyes”: Direct Red 28 (CAS No. 573-58-0), Direct Brown 95 (CAS No. 16071-86-6) and Direct Black 38 (CAS No. 1937-37-7). It was noted that these three substances are entirely off the market. The other dyes in this group are based on benzidine congeners. While the properties of dyes based on benzidine and benzidine congeners are similar, it was recommended to separate them further (benzidine-based dyes and benzidine congener based dyes).
- The substances should be grouped by their potential cleavage products (e.g. dyes based on methoxy congeners of benzidine should be placed in the same group).

#### **Benzidine Basic Dyes:**

- Behaviour of the two substances in this grouping (CAS No. 298-83-9 and CAS No. 1871-22-3) (whether they act in the same manner or not) is not known and requires additional evaluation.
- For CAS No. 298-83-9, clarification was sought as to whether the tetrazole ring is considered an azo group, and whether the ring would be subject to cleavage. Government

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<sup>4</sup> An azo pigment lake, alternatively referred to as a “toner” or a “lake,” is a salt-type pigment formed by precipitating a water-soluble anionic monoazo substance with a metal cation.

representatives noted that moving into the assessment phase, potential for cleavage would be further evaluated.

### **Azo Solvent Dyes**

- CAS No. 2653-64-7 (Pigment Red 40) in “Monoazo Pigments” is also named “Solvent Red 4” meaning that this substance could be a solvent dye or a pigment based on intended application (different forms of the same substance).
- CAS No. 63281-10-7 appears to be very different structurally than the other substances in this Subgroup. The structural groups indicate that it may be more water-soluble than other solvent dyes (i.e., ethoxy group present). Its name does not indicate that it is a solvent dye.

### **Azo Acid Dyes**

- CAS No. 1934-21-0 appears to be Tartrazine (Food Yellow 4 or FD&C Yellow 5), a colourant widely used in foods. Recommend considering all food colourants together.
- Metal complexes of these acid dyes containing chromium, iron or cobalt exist. These complexes should include metal ions to be precise. Also note that there are examples of acid dyes that do not contain a sulfonic acid group (*in reference to the description of acid dyes on slide 12 of Deck 3*).
- CAS No. 102616-51-3 and CAS No. 85223-35-4 are the same substance. Recently, CAS No. 102616-51-3 has been replaced by CAS No. 85223-35-4 in the CAS Registry.

### **Azo Direct Dyes**

- The structure for CAS No. 71033-21-1 needs to be corrected (the correct structure should be very similar to the structure of CAS No. 10114-47-3). The molecule should not be “bound through” the sulfonate group although the exact location of the sulfonate group is unknown.
- CAS No. 1325-37-7 and CAS No. 65150-80-3 are not azo dyes and do not have known structures (different from structures being available but not being disclosed).

### **Azo Reactive Dyes**

- Reactive Black 5 (CAS No. 17095-24-8) is a large data-rich substance that was fully registered under REACH in 2010. A full REACH dossier on this substance should be accessed and used for read-across with similar substances in this subgroup.
- The potential for human exposure to the reactive dyes which are chemically reacted with the fibre would be expected to be limited. Reactive dyes bind rapidly to the fibre and they have high fixation once bound and should exhibit very little washing or leaching out. Under alkaline laundering conditions, a reacted group containing vinyl may be susceptible to



cleavage (i.e., “reverse reaction”). However, this may not have much relevance to general population exposure.

- Fastness data would be an important piece of information for the assessment and should be considered.

### **Azo Basic Dyes**

- It was noted that there is a mix of quaternary salts and amines in this Subgroup. Clarification was sought as to whether there was a significant difference in the exposure potential and solubility of these two types of substances. A participant noted that in terms of solubility, for the amines, they may be protonated to provide a cationic site for uptake into the substrate. As the pH of the environment increases, the water solubility would be expected to decrease. For the quaternary salts, the substances have permanent charges.

### **Azo Mordant Dyes**

- Names of substances CAS No. 94276-35-4 and CAS No. 85029-57-8 of Table 1 “Azo Mordant Dyes” need to be complete.

### **Azo Food Dyes**

- A recent report from the Center for Science in the Public Interest provides a Top 8 - 10 list of food colourants, five of which are azo dyes. Some of the colourants listed in this recent report are Yellow 6 (produced in over 3500 lbs/years), Yellow 5 (Tartrazine), Red 40, Orange B and Citrus Red 2. While Yellow 6 is not on the list of 358 substances in this Grouping Initiative, Red 40 should be.
- One participant noted that she would like to obtain a list of food colourants used in Canada. Government representatives indicated that they would follow-up.

### **Aromatic Amines and Benzidine derivatives**

- A suggestion was raised as to whether all other potential aromatic amines theoretically produced by azo bond cleavage be considered together with these 23 aromatic amines in an “aromatic amine group”. Government representatives clarified that these 23 aromatic amines do not encompass all of the corresponding aromatic amines, rather they are priority substances under the CMP. This particular subgroup is not the same as the other subgroups and these substances are not assessed as one group. Other potential aromatic amines will also be considered in the assessment.
- While substance CAS No. 91-97-4 of “Benzidines” has a diisocyanate component, it does not mean that other isocyanate substances will be included in this Subgroup. This particular substance was included in this Subgroup based on the benzidine substructure rather than the isocyanate substructure. When a substance belongs to more than one subgroup, it will be looked at closely on a case-by-case basis.

## WRAP UP DISCUSSION ON THE PROPOSED APPROACH TO SUBGROUPING

Participants, including Government representatives, had further discussions on advantages and disadvantages of the proposed approach versus an aromatic amine breakdown product-oriented approach. Government representatives indicated a difficulty with a moiety-based approach is that, of the 358 substances in the grouping, analysis indicated approximately 200-300 theoretical/potential breakdown products, which presents a large number of substances on which to organize a subgrouping approach. Government representatives indicated they recognized that several substances may release a common aromatic amine of concern and that consideration of such a common moiety needs to be taken into consideration at some point in the approach. A comment was made that perhaps one approach versus the other might not be the path forward, but rather a combination of both would be most appropriate.

- **Clarification was sought on the proposed read-across approach, and considerations in terms of whether specific read-across was defensible.** Government representatives shared their preliminary thinking, and indicated that analogues within each structurally related group will be considered first, though in the absence of an appropriate analogue within the same structurally related group, other analogues would be considered (i.e., outside the 358 substances).
- **It was noted that the Government should be using s.71(1)(c) provisions of CEPA 1999 to have data generated when no data is available on a substance.** *Government representatives indicated that their approach is to make decisions based on available information, but that instances may arise moving forward in the CMP where data generation would have value.*
- **Government representatives confirmed that SNACs will be considered an option moving forward with this class assessment, as appropriate.**
- **Concern was expressed that the timelines of the Section 71 survey did not align with a REACH deadline.** Specifically, several substances on the list (15 to 20) are scheduled for full REACH registration in 2013 and several companies are currently preparing REACH dossiers. Focussing on both requirements is very challenging and a request was made to consider a delay in the timelines for the Section 71 survey. *Government representatives indicated that there is an option for a 2 month extension; and if data is not yet available for specific substances, it is sufficient to indicate when that data will be provided. Government representatives agreed to explore opportunities for flexibility.*
- **A recommendation was made that in some instances the focus should be on the amine rather than the coupling component.** Specifically, CAS No. 13515-40-7 in the monoazo pigments grouping is composed of two components: a coupling component and an amine that has been diazotized. As a practical matter, upon cleavage of the azo bond, the reintroduced coupling component will likely be a substance not in commerce, and it will lack any empirical data. The nitrogen atom of the regenerated coupling component would not be present.

- **It was noted that “cleavage potential” needs to be carefully examined.** Specifically, it was noted that all the metabolites and breakdown products being referred to are “theoretical”; that some of these theoretical breakdown products are structurally “strained” or not be able to be broken down by enzymes, or that such enzymes may not exist. Government representatives noted that as they move forward with assessment activity, this activity will be an early focus.
- **It was noted that the US EPA published SNURS<sup>5</sup> for this group of substances.**
- **Two references were provided for consideration of Government representatives.** One article examines the quality and quantity of data available for a group of azo substances; and a follow-up publication which encompasses structure-activity relationship analysis for the same group.

## NEXT STEPS

- The following were identified as next steps:
  - Government representatives will distribute the draft meeting summary and electronic copies of presentations within approximately 2 weeks.
  - Participants will provide Government representatives with any additional commentary on the proposed subgrouping approaches within approximately 2 weeks.
  - Government plans to incorporate input from this consultation into a draft science framework document, which is targeted for release in summer 2012. The intent is for this document to have a public comment period.
    - The CMP website will be updated at the time with more specific information on subgrouping and timing of publications of assessment reports (note: a subgrouping may have more than one assessment report).

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<sup>5</sup> Significant New Use Rules (<http://www.gpo.gov/fdsys/pkg/FR-2012-03-28/pdf/2012-7208.pdf>)

# Appendix A – Technical Consultation Meeting Agenda

## Technical Consultation Meeting

### Proposed Subgrouping of the Aromatic Azo- and Benzidine-based Substances

March 20<sup>th</sup>, 2012

Minto Suites Hotel (Salon Stanley)

185 Lyon Street North, Ottawa

#### Agenda

#### Objective of the Meeting:

To solicit input on the proposed subgrouping of the Aromatic Azo- and Benzidine-based substances

Time	Item	
8:30	Registration and Coffee	
9:00	Welcome and Objective of Meeting Review of agenda and approach Introductions	Christine Norman, Director, Health Canada Kathleen Connelly, Intersol Group
9:15	Background and Context Q&A	HC/EC Officials Participants
10:15	Health Break	
10:30	The Proposed Approach to Subgrouping the Substances Presentation Q&A Feedback <b>Charge Question 1.</b> What do you see as the strengths of the proposed subgrouping approach? <b>Charge Question 2.</b> Are there limitations to the proposed subgrouping approach and if so, how do you recommend to address them? <b>Charge Question 3.</b> Are there other subgrouping approaches that you would like to recommend?	HC/EC Officials Participants Participants
12:00	Lunch (not provided)	
13:00	Subgroup by Subgroup Walkthrough Description and rationale of each subgroup Feedback on each subgroup <b>Charge Question 4.</b> Should any substance belong to a different subgroup than proposed? If so, please provide the rationale. <b>Charge Question 5.</b> Should any substances be considered within the same structurally related grouping? If so, please provide the rationale. (Health Break 14:30 – 14:45)	HC/EC Officials Participants
16:00	Recap and Next Steps	Christine Norman, Director, Health Canada
16:30	Meeting Close	Kathleen Connelly, Intersol Group

## Appendix B – List of Participants

Name	Affiliation
Abel, Susan	Food and Consumer Product Association
Aikawa, Bio	Health Canada
Albert, Tawnia	Health Canada
Borkhoff, Joyce	Cantox/Intertek (ETAD <sup>1</sup> )
Bullock, Neil	Cantox/Intertek (ETAD)
Connelly, Kathleen	Intersol Group
Cran, Bruce	Consumers Association of Canada
de Leon, Fe	Canadian Environmental Law Association
Dornan, Laura	Environment Canada
Farago, Domenico	Health Canada
Freeman, Harold	College of Textiles, North Carolina State University
Griffiths, Adam	Health Canada
Helmes, Tucker	ETAD North America (ETAD)
Hill, Jonathan	Environment Canada
Kneen, Soha	Inuit Tapiriit Kanatami (ITK)
Madray, Sandra	Chemical Sensitivities Manitoba
Manarang-Pena,	Canadian Paints and Coatings Association
McElgunn, Barbara	Canadian Institute of Child Health / Learning Disabilities Association of Canada
Merritt, Glenn	Fitzpatrick & Merritt (CPMA <sup>2</sup> )
Montemayor, Beta	Canadian Cosmetic, Toiletry and Fragrance Association
Mott, Robert	Sun Chemical (CPMA)
Norman, Christine	Health Canada
Okonski, Sahsa	Environment Canada
Richardson, Mary	Crooked Creek Conservancy Society of Athabasca
Seenundun, Shayesta	Health Canada
Seibert, Earl	FlintGroup Pigments (CPMA)
Sharp, Donald	Assembly of First Nations
Tilli, Pat	Clariant (ETAD)
Whitall, Cheri	Health Canada
Wilke, Don	Canadian Consumer Specialty Products Association / Industry Coordinating Group for CEPA 1999

<sup>1</sup> Ecological and Toxicological Association of Dyes and Organic Pigments Manufacturers

<sup>2</sup> CPMA: Color Pigments Manufacturers Association, Inc.