CRC-12/3: Benzidine

*The Chemical Review Committee,*

*Recalling* Article 5 of the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade,

*Having* *reviewed* the new notifications of final regulatory action for benzidine submitted by Canada and Jordan,[[1]](#footnote-1) replacing the previous notifications from those countries,

1. *Concludes* that the new notification of final regulatory action for benzidine submitted by Canada meets the criteria set out in Annex II to the Convention;

2. *Adopts* the rationale for the Committee’s conclusion on the notification for benzidine submitted by Canada set out in the annex to the present decision;[[2]](#footnote-2)

3. *Notes* that as only one notification of final regulatory action in respect of benzidine meets the criteria set out in Annex II to the Convention it will take no further action at the current time.

Annex to decision CRC‑12/3

Rationale for the conclusion by the Chemical Review Committee that the notification of final regulatory action submitted by Canada in respect of benzidine meets the criteria of Annex II to the Rotterdam Convention

1. The notification on benzidine and benzidine dihydrochloride from Canada has been verified by the Secretariat as containing the information required by Annex I to the Rotterdam Convention. This notification underwent a preliminary review by the Secretariat and Bureau, who evaluated whether or not the notification appeared to meet the requirements of the Convention. The notification, supporting documentation and results of the preliminary review were made available to the Chemical Review Committee for their consideration (document UNEP/FAO/RC/CRC.12/6, UNEP/FAO/RC/CRC.12/6/Add.1, UNEP/FAO/RC/CRC.12/6/Add.2, UNEP/FAO/RC/CRC.12/4). Information on trade in benzidine is provided in the information collected by the Secretariat in document UNEP/FAO/RC/CRC.12/INF/4.

(a) Scope of the notified regulatory action

1. Canada had previously taken regulatory action on benzidine and benzidine dihydrochloride through the Prohibition of Certain Toxic Substances Regulations, 2003, which had been notified to the Secretariat and subsequently considered by the Chemical Review Committee as having met all criteria in Annex I and Annex II (UNEP/FAO/RC/CRC.12/6/Add.1). The subsequent Prohibition of Certain Toxic Substances Regulations, 2005, added flexibility over the 2003 regulations, and a new notification of final regulatory action was submitted by Canada and replaces the earlier notification.
2. The notified regulatory action relates to benzidine (CAS 92-87-5) and benzidine dihydrochloride (CAS 531‑85‑1) and their industrial uses (for example, as intermediates in the manufacture of dyes and pigments). Benzidine and benzidine dihydrochloride were listed in Schedule 2 of the Prohibition of Certain Toxic Substances Regulations, 2005, which prohibits their manufacture, use, sale, offer for sale and import. The regulations do not apply to benzidine and benzidine dihydrochloride that are:

* Contained in a hazardous waste, hazardous recyclable material or non-hazardous waste;
* Contained in a control product (e.g., pesticide);
* Present as a contaminant in a chemical feedstock used in a process from which there are no releases of the substance and provided that the substance is destroyed or completely converted in that process to a substance that is not a toxic substance listed in the regulations; or,
* Used in a laboratory for analysis; in scientific research; or, as a laboratory analytical standard.

1. In addition, the regulations do not apply in respect of the manufacture, use, sale, offering for sale or import of benzidine or benzidine dihydrochloride for the following permitted uses:

* Staining for microscopic examination, such as immunoperoxidase staining, histochemical staining or cytochemical staining;
* Use as a reagent for detecting blood in biological fluids;
* Use in a niacin test to detect some microorganisms;
* Use as a reagent for detecting chloralhydrate in biological fluids.

1. The regulations also establish a permit system that provides a mechanism for temporarily exempting certain applications of a substance listed in the regulations. A permit may be granted only if the minister for environment is satisfied that there is no technically or economically feasible alternative or substitute available for the substance. In addition, the minister must be satisfied that measures have been taken to minimize or eliminate any harmful effects of the substance on the environment and human health. Finally, the applicant must provide an implementation plan that identifies specific timelines for eliminating the substance. Each permit lasts for 12 months and may be renewed only twice (UNEP/FAO/RC/CRC.12/6 sect. 2.3.2 of the Canadian notification).

(b) Annex II paragraph (a) criterion

*(a) Confirm that the final regulatory action has been taken in order to protect human health or the environment;*

1. The task group confirms that the regulatory action was taken to protect human health (UNEP/FAO/RC/CRC.12/6, sect. 2.4.2 of the Canadian notification).
2. In Canada, benzidine was used primarily as an intermediate in the manufacture of dyes and pigments. It is not produced in Canada, and although it may have been imported in small amounts between 1980 and 1987, there no longer appears to be any manufacture or industrial use of these substances in Canada. Benzidine and benzidine dihydrochloride are currently allowed for certain specified uses as described above (UNEP/FAO/RC/CRC.12/6, sect. 2.3.1 of the Canadian notification).
3. The risk evaluation provided in the supporting information from Canada notes that benzidine is a non-threshold carcinogen. The results of a number of epidemiological studies and supporting data from case reports and series regarding workers occupationally exposed to benzidine have provided clear evidence for the carcinogenicity of benzidine in humans. The observed associations were noted as having been very specific, in that occupational exposure to benzidine has been associated with increased risk of, or death due to, cancer of the bladder. Although environmental exposure of the general population of Canada was not estimated, the non-threshold nature of the adverse effects was clearly noted. Consequently, any level of exposure carries a risk of adverse effects on human health and the regulatory action was put in place as a precautionary measure to protect the health of Canadians (UNEP/FAO/RC/CRC.12/6/Add.2, Priority Substances List Assessment Report (Benzidine) – 1993).
4. The Committee confirms that the criterion of paragraph (a) of Annex II is met.

(c) Annex II paragraph (b) criteria

*(b) Establish that the final regulatory action has been taken as a consequence of a risk evaluation. This evaluation shall be based on a review of scientific data in the context of the conditions prevailing in the Party in question. For this purpose, the documentation provided shall demonstrate that:*

*(i) Data have been generated according to scientifically recognized methods;*

*(ii) Data reviews have been performed and documented according to generally recognized scientific principles and procedures;*

1. The notification states that the final regulatory action was based on a risk or hazard evaluation. In the notification, reference is made to the following documents:

* Priority Substances List Assessment Report (Benzidine) – 1993;
* ChemFinder.com Database and Internet Searching ([www.chemfinder.com](http://www.chemfinder.com)).

1. The notifying Party also provided the following documents, which are compiled in document UNEP/FAO/RC/CRC.12/6/Add.2:

* Focused summary outlining the regulatory action on benzidine in Canada;
* Regulatory Impact Analysis Statement for the 2003 regulatory action;
* Regulatory Impact Analysis Statement for the 2005 regulatory action.

1. A risk evaluation was carried out for benzidine and resulted in a finding of the substance being toxic to human health. The evaluation reviewed epidemiological studies as well as supporting data from case reports and series regarding workers occupationally exposed to benzidine. This provides clear evidence for the carcinogenicity of benzidine in humans. The observed association between the occurrence of bladder carcinoma and occupational exposure to benzidine meets the traditional criteria (consistency, strength, specificity, temporal relationship, exposure-response relationship and plausibility) for the assessment of causality in epidemiological studies.
2. All of the original studies that form the basis for determining whether benzidine is “toxic” under Canadian law are cited as references in the risk evaluation and are sourced from recognized journals and scientific bodies. These studies were critically evaluated by staff at Health Canada and Environment Canada. The environmental sections of the risk evaluation and sections related to the assessment of effects on human health were peer-reviewed, while the entire Priority Substances List Assessment Report (Benzidine) was reviewed and approved by the Environment Canada/Health Canada CEPA Management Committee (UNEP/FAO/RC/CRC.12/6/Add.2, Priority Substances List Assessment Report (Benzidine) – 1993).
3. The Committee confirms that the criteria in paragraphs (b) (i) and (b) (ii) of Annex II are met.

*(iii) The final regulatory action was based on a risk evaluation involving prevailing conditions within the Party taking the action;*

1. Canada determined that benzidine was toxic to human health and cited the non-threshold nature of its carcinogenic effects, that is, that any level of exposure carries a risk of adverse effects to human health. The results of a number of analytical epidemiological studies as well as supporting data from case reports and series regarding workers occupationally exposed to benzidine provide clear evidence for the carcinogenicity of the substance in humans. The observed associations have been very specific, in that occupational exposure to benzidine has been associated with an increased incidence of, or death due to, cancer of the bladder – almost exclusively transitional cell carcinoma. Although quantitative information on exposure to benzidine was not assessed in any of the available analytical epidemiological studies, a relationship between qualitative measures of exposure and an increased incidence of bladder cancer was reported in two studies Although the data are limited, there is evidence indicating that a reduction in (occupational) exposure to benzidine was associated with a decrease in the incidence of bladder carcinoma.
2. As a result, and although environmental exposure of the general population was not estimated, the regulatory measures were put in place to protect the health of Canadians. Previously allowed use in the manufacture of dyes and pigments was prohibited by the regulatory action, thereby removing this possible route of occupational exposure and release to the Canadian environment. This approach is consistent with the objective that exposure to non-threshold carcinogens be reduced wherever possible and obviates the need to establish an arbitrary de minimis level of risk.
3. Consequently, the Committee confirms that the criterion in paragraph (b) (iii) of Annex II is met.
4. The Committee confirms that the criteria of paragraph (b) of Annex II are met.

(d) Annex II paragraph (c) criteria

*(c) Consider whether the final regulatory action provides a sufficiently broad basis to merit listing of the chemical in Annex III, by taking into account:*

*(i) Whether the final regulatory action led, or would be expected to lead, to a significant decrease in the quantity of the chemical used or the number of its uses;*

1. The estimated quantity of benzidine and benzidine dihydrochloride produced, imported, exported and used in Canada prior to the regulatory action was provided (1995 and 1996), showing only a small amount of production (UNEP/FAO/RC/CRC.12/6, sect. 2.5.1 of the Canadian notification).
2. At the time of the regulatory action, benzidine and benzidine dihydrochloride had limited use in Canada. The regulatory action prohibited all manufacture, use, sale, offer for sale and import with certain, specified exceptions (UNEP/FAO/RC/CRC.12/6, sects. 2.5.3.1 and 2.3 of the Canadian notification).
3. As a result, the number of uses in Canada was reduced. Further, the regulations were introduced as a precautionary measure and would lead to a decrease in the quantities of the chemicals potentially used in Canada.
4. Therefore the Committee confirms that the criterion in paragraph (c) (i) is met.

*(ii) Whether the final regulatory action led to an actual reduction of risk or would be expected to result in a significant reduction of risk for human health or the environment of the Party that submitted the notification;*

1. Citing the substances as non-threshold carcinogens, the severe restriction notified by Canada would be expected to lead to a significant reduction in risk to Canadians by reducing the chance for release and exposure.
2. The Committee confirms that the criterion in paragraph (c) (ii) is met.

*(iii) Whether the considerations that led to the final regulatory action being taken are applicable only in a limited geographical area or in other limited circumstances;*

1. Canada cites in its notification that other states or regions using the substances in similar applications (manufacture of dyes and pigments) may find the regulatory action relevant (UNEP/FAO/RC/CRC.12/6 sect. 2.5.2 of the Canadian notification).
2. Given the substance is a non-threshold carcinogen, any state or region where exposure or release is possible may find the regulatory action relevant.
3. Therefore the Committee confirms that the criterion of paragraph (c) (iii) is met.

*(iv) Whether there is evidence of ongoing international trade in the chemical;*

1. Export notification summaries during the years 2011–2016, as provided by the European Union and made available to the Committee in document UNEP/FAO/RC/CRC.12/INF/4, suggest that some trade in benzidine is continuing.
2. Therefore the Committee confirms that the criterion of paragraph (c) (iv) is met.

(e) Annex II paragraph (d) criterion

*(d) Take into account that intentional misuse is not in itself an adequate reason to list a chemical in Annex III.*

1. There is no indication in the notification or supporting documentation that concerns for intentional misuse of benzidine or benzidine dihydrochloride prompted the regulatory action.
2. Based on the above point the Committee confirms that the criterion of paragraph (d) of Annex II is met.

(f) Conclusion

1. The Committee concludes that this notification of final regulatory action by Canada meets the criteria set out in Annex II to the Convention.

1. UNEP/FAO/RC/CRC.12/6. [↑](#footnote-ref-1)
2. The rationale annexed to the present decision replaces the rationale developed by the Committee at its first meeting (UNEP/FAO/RC/CRC.1/28, annex V, sect. C). [↑](#footnote-ref-2)