

review a nomination and any comments received on the background document. The RG1 conducts a scientific review of the nomination applying the criteria and provides comments and makes its recommendations to the Director, NTP for listing or delisting it in the RoC.

NTP Executive Committee's Interagency Working Group for the RoC (RG2)

The RG2, a federal government interagency scientific review group, also conducts a scientific review of nominations to the RoC. The RG2 assesses whether relevant information for a nomination is available and sufficient for listing in or delisting from the RoC. The RG2 reviews the original nomination and all public comments received in response to the **Federal Register** announcement of the intent to review a nomination and any comments received on the background document. Upon completion of its review, the RG2 provides comments and makes its recommendations to the Director, NTP for listing or delisting the nominations in the RoC.

Board of Scientific Counselors RoC Subcommittee (External Peer Review)

The third step in the review process is external scientific peer review of the nominations by a standing subcommittee of the NTP Board of Scientific Counselors ("the RoC Subcommittee"). The RoC Subcommittee serves as an independent peer review group that assesses whether the relevant information available for a nomination is sufficient for listing or delisting it in the RoC. The RoC Subcommittee reviews nominations in an open public meeting. Prior to this public review, a notice is published in the **Federal Register** and NTP publications announcing the public meeting, a reminder of the availability of the background documents and soliciting public comment on the nominations. The notice invites interested groups or individuals to submit written comments and/or address the RoC Subcommittee during the public review meeting. The RoC Subcommittee reviews the original nomination and all public comments received in response to the **Federal Register** notices including the announcement of the intent to review a nomination and the announcement of the public meeting, any comments received on the background documents, and comments received at the public meeting. Upon completion of its review, the RoC Subcommittee provides comments and makes its recommendations for listing or delisting the nominations in the RoC.

Final Public Comment

Upon completion of the reviews by RG1, RG2 and the RoC Subcommittee, the NTP publishes in the **Federal Register** and NTP publications the nominations and the review groups' recommendations for each (to list, to delist, or not to list in the RoC), and solicits final public comment and input on the nominations.

NTP Executive Committee

The recommendations of RG1, RG2 and the RoC Subcommittee and all public comments received in response to all **Federal Register** announcements and the background documents are presented to the NTP Executive Committee for review and comment. The NTP Executive Committee reviews the information on the nominations and provides the Director, NTP its recommendations for listing or delisting them in the RoC.

NTP Director

The NTP Director receives the independent recommendations for the nominations from RG1, RG2 and the NTP Board RoC Subcommittee, the recommendation of the NTP Executive Committee and all public comments received concerning the nominations. The NTP Director evaluates this input and any other relevant information on the nominations and develops recommendations to the Secretary, Department of Health and Human Services (DHHS) regarding whether to list, delist, or not list the nominations in the RoC.

Secretary, Department of Health and Human Services

The NTP prepares a final draft of the RoC based on the NTP Director's recommendations and submits it to the Secretary, DHHS for review and approval. Upon approval of the RoC, the Secretary submits it to the U.S. Congress as a final document. The submission of the RoC to Congress constitutes publication of the report and it becomes available to the public at that time.

The NTP publishes a notice of the publication and availability of the latest edition of the RoC, indicating all newly listed or delisted agents, substances, mixtures or exposure circumstances in the **Federal Register** and NTP publications.

Report on Carcinogens

Criteria for Listing

Agents, Substances, Mixtures or Exposure Circumstances

Known To Be Human Carcinogen:

There is sufficient evidence of carcinogenicity from studies in humans, which indicates a causal relationship between exposure to the agent, substance, or mixture, and human cancer.

Reasonably Anticipated To Be Human

Carcinogen:

There is limited evidence of carcinogenicity from studies in humans, which indicates that causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding factors, could not adequately be excluded, or

there is sufficient evidence of carcinogenicity from studies in experimental animals, which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors (1) In multiple species or at multiple tissue sites, or (2) by multiple routes of exposure, or (3) to an unusual degree with regard to incidence, site, or type of tumor, or age at onset, or

there is less than sufficient evidence of carcinogenicity in humans or laboratory animals; however, the agent, substance, or mixture belongs to a well-defined, structurally related class of substances whose members are listed in a previous Report on Carcinogens as either known to be a human carcinogen or reasonably anticipated to be a human carcinogen, or there is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans.

Conclusions regarding carcinogenicity in humans or experimental animals are based on scientific judgment, with consideration given to all relevant information. Relevant information includes, but is not limited to, dose response, route of exposure, chemical structure, metabolism, pharmacokinetics, sensitive subpopulations, genetic effects, or other data relating to mechanism of action or factors that may be unique to a given substance. For example, there may be substances for which there is evidence of carcinogenicity in laboratory animals, but there are compelling data indicating that the agent acts through mechanisms which do not operate in humans and would therefore not reasonably be anticipated to cause cancer in humans.

Clarification of Criteria

Some questions have arisen regarding information from studies involving humans and how this is applied to the listing of a substance determined to be a "known human carcinogen". The "known human carcinogen" category