ANNEXES

ANNEX 1

REPORTS AND OTHER DOCUMENTS RESULTING FROM PREVIOUS MEETINGS OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

1. **General principles governing the use of food additives** (First report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Report Series, No. 15, 1957; WHO Technical Report Series, No. 129, 1957 (out of print).
2. **Procedures for the testing of intentional food additives to establish their safety for use** (Second report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Report Series, No. 17, 1958; WHO Technical Report Series, No. 144, 1958 (out of print).
3. **Specifications for identity and purity of food additives (antimicrobial preservatives and antioxidants)** (Third report of the Joint FAO/WHO Expert Committee on Food Additives). These specifications were subsequently revised and published as **Specifications for identity and purity of food additives**, Vol. I. **Antimicrobial preservatives and antioxidants**, Rome, Food and Agriculture Organization of the United Nations, 1962 (out of print).
4. **Specifications for identity and purity of food additives (food colours)** (Fourth report of the Joint FAO/WHO Expert Committee on Food Additives). These specifications were subsequently revised and published as **Specifications for identity and purity of food additives**, Vol. II. **Food colours**, Rome, Food and Agriculture Organization of the United Nations, 1963 (out of print).
5. **Evaluation of the carcinogenic hazards of food additives** (Fifth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Report Series, No. 29, 1961; WHO Technical Report Series, No. 220, 1961 (out of print).
6. **Evaluation of the toxicity of a number of antimicrobials and antioxidants** (Sixth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Report Series, No. 31, 1962; WHO Technical Report Series, No. 228, 1962 (out of print).
7. **Specifications for the identity and purity of food additives and their toxicological evaluation: emulsifiers, stabilizers, bleaching and maturing agents** (Seventh report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 35, 1964; WHO Technical Report Series, No. 281, 1964 (out of print).
8. **Specifications for the identity and purity of food additives and their toxicological evaluation: food colours and some antimicrobials and antioxidants** (Eighth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 38, 1965; WHO Technical Report Series, No. 309, 1965 (out of print).
9. **Specifications for identity and purity and toxicological evaluation of some antimicrobials and antioxidants**. FAO Nutrition Meetings Report Series, No. 38A, 1965; WHO/Food Add/24.65 (out of print).
10. **Specifications for identity and purity and toxicological evaluation of food colours**. FAO Nutrition Meetings Report Series, No. 38B, 1966; WHO/Food Add/66.25.

11. **Specifications for the identity and purity of food additives and their toxicological evaluation: some antimicrobials, antioxidants, emulsifiers, stabilizers, flour treatment agents, acids, and bases** (Ninth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 40, 1966; WHO Technical Report Series, No. 339, 1966 (out of print).
12. **Toxicological evaluation of some antimicrobials, antioxidants, emulsifiers, stabilizers, flour treatment agents, acids, and bases**. FAO Nutrition Meetings Report Series, No. 40A, B, C; WHO/Food Add/67.29.
13. **Specifications for the identity and purity of food additives and their toxicological evaluation: some emulsifiers and stabilizers and certain other substances** (Tenth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 43, 1967; WHO Technical Report Series, No. 373, 1967.
14. **Specifications for the identity and purity of food additives and their toxicological evaluation: some flavouring substances and non nutritive sweetening agents** (Eleventh report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 44, 1968; WHO Technical Report Series, No. 383, 1968.
15. **Toxicological evaluation of some flavouring substances and non nutritive sweetening agents**. FAO Nutrition Meetings Report Series, No. 44A, 1968; WHO/Food Add/68.33.
16. **Specifications and criteria for identity and purity of some flavouring substances and non-nutritive sweetening agents**. FAO Nutrition Meetings Report Series, No. 44B, 1969; WHO/Food Add/69.31.
17. **Specifications for the identity and purity of food additives and their toxicological evaluation: some antibiotics** (Twelfth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 45, 1969; WHO Technical Report Series, No. 430, 1969.
18. **Specifications for the identity and purity of some antibiotics**. FAO Nutrition Meetings Series, No. 45A, 1969; WHO/Food Add/69.34.
19. **Specifications for the identity and purity of food additives and their toxicological evaluation: some food colours, emulsifiers, stabilizers, anticaking agents, and certain other substances** (Thirteenth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 46, 1970; WHO Technical Report Series, No. 445, 1970.
20. **Toxicological evaluation of some food colours, emulsifiers, stabilizers, anticaking agents, and certain other substances**. FAO Nutrition Meetings Report Series, No. 46A, 1970; WHO/Food Add/70.36.
21. **Specifications for the identity and purity of some food colours, emulsifiers, stabilizers, anticaking agents, and certain other food additives**. FAO Nutrition Meetings Report Series, No. 46B, 1970; WHO/Food Add/70.37.
22. **Evaluation of food additives: specifications for the identity and purity of food additives and their toxicological evaluation: some extraction solvents and certain other substances; and a review of the technological efficacy of some antimicrobial agents**. (Fourteenth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 48, 1971; WHO Technical Report Series, No. 462, 1971.
23. **Toxicological evaluation of some extraction solvents and certain other substances**. FAO Nutrition Meetings Report Series, No. 48A, 1971; WHO/Food Add/70.39.
24. **Specifications for the identity and purity of some extraction solvents and certain other substances**. FAO Nutrition Meetings Report Series, No. 48B, 1971; WHO/Food Add/70.40.

25. **A review of the technological efficacy of some antimicrobial agents**. FAO Nutrition Meetings Report Series, No. 48C, 1971; WHO/Food Add/70.41.
26. **Evaluation of food additives: some enzymes, modified starches, and certain other substances: Toxicological evaluations and specifications and a review of the technological efficacy of some antioxidants** (Fifteenth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 50, 1972; WHO Technical Report Series, No. 488, 1972.
27. **Toxicological evaluation of some enzymes, modified starches, and certain other substances**. FAO Nutrition Meetings Report Series, No. 50A, 1972; WHO Food Additives Series, No. 1, 1972.
28. **Specifications for the identity and purity of some enzymes and certain other substances**. FAO Nutrition Meetings Report Series, No. 50B, 1972; WHO Food Additives Series, No. 2, 1972.
29. **A review of the technological efficacy of some antioxidants and synergists**. FAO Nutrition Meetings Report Series, No. 50C, 1972; WHO Food Additives Series, No. 3, 1972.
30. **Evaluation of certain food additives and the contaminants mercury, lead, and cadmium** (Sixteenth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 51, 1972; WHO Technical Report Series, No. 505, 1972, and corrigendum.
31. **Evaluation of mercury, lead, cadmium and the food additives amaranth, diethylpyrocarbamate, and octyl gallate**. FAO Nutrition Meetings Report Series, No. 51A, 1972; WHO Food Additives Series, No. 4, 1972.
32. **Toxicological evaluation of certain food additives with a review of general principles and of specifications** (Seventeenth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 53, 1974; WHO Technical Report Series, No. 539, 1974, and corrigendum (out of print).
33. **Toxicological evaluation of some food additives including anticaking agents, antimicrobials, antioxidants, emulsifiers, and thickening agents**. FAO Nutrition Meetings Report Series, No. 53A, 1974; WHO Food Additives Series, No. 5, 1974.
34. **Specifications for identity and purity of thickening agents, anticaking agents, antimicrobials, antioxidants and emulsifiers**. FAO Food and Nutrition Paper, No. 4, 1978.
35. **Evaluation of certain food additives** (Eighteenth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 54, 1974; WHO Technical Report Series, No. 557, 1974, and corrigendum.
36. **Toxicological evaluation of some food colours, enzymes, flavour enhancers, thickening agents, and certain other food additives**. FAO Nutrition Meetings Report Series, No. 54A, 1975; WHO Food Additives Series, No. 6, 1975.
37. **Specifications for the identity and purity of some food colours, enhancers, thickening agents, and certain food additives**. FAO Nutrition Meetings Report Series, No. 54B, 1975; WHO Food Additives Series, No. 7, 1975.
38. **Evaluation of certain food additives: some food colours, thickening agents, smoke condensates, and certain other substances**. (Nineteenth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Nutrition Meetings Series, No. 55, 1975; WHO Technical Report Series, No. 576, 1975.
39. **Toxicological evaluation of some food colours, thickening agents, and certain other substances**. FAO Nutrition Meetings Report Series, No. 55A, 1975; WHO Food Additives Series, No. 8, 1975.

40. **Specifications for the identity and purity of certain food additives**. FAO Nutrition Meetings Report Series, No. 55B, 1976; WHO Food Additives Series, No. 9, 1976.
41. **Evaluation of certain food additives** (Twentieth report of the Joint FAO/WHO Expert Committee on Food Additives). FAO Food and Nutrition Meetings Series, No. 1, 1976; WHO Technical Report Series, No. 599, 1976.
42. **Toxicological evaluation of certain food additives**. WHO Food Additives Series, No. 10, 1976.
43. **Specifications for the identity and purity of some food additives**. FAO Food and Nutrition Series, No. 1B, 1977; WHO Food Additives Series, No. 11, 1977.
44. **Evaluation of certain food additives** (Twenty-first report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 617, 1978.
45. **Summary of toxicological data of certain food additives**. WHO Food Additives Series, No. 12, 1977.
46. **Specifications for identity and purity of some food additives, including antioxidant, food colours, thickeners, and others**. FAO Nutrition Meetings Report Series, No. 57, 1977.
47. **Evaluation of certain food additives and contaminants** (Twenty-second report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 631, 1978.
48. **Summary of toxicological data of certain food additives and contaminants**. WHO Food Additives Series, No. 13, 1978.
49. **Specifications for the identity and purity of certain food additives**. FAO Food and Nutrition Paper, No. 7, 1978.
50. **Evaluation of certain food additives** (Twenty-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 648, 1980, and corrigenda.
51. **Toxicological evaluation of certain food additives**. WHO Food Additives Series, No. 14, 1980.
52. **Specifications for identity and purity of food colours, flavouring agents, and other food additives**. FAO Food and Nutrition Paper, No. 12, 1979.
53. **Evaluation of certain food additives** (Twenty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 653, 1980.
54. **Toxicological evaluation of certain food additives**. WHO Food Additives Series, No. 15, 1980.
55. **Specifications for identity and purity of food additives (sweetening agents, emulsifying agents, and other food additives)**. FAO Food and Nutrition Paper, No. 17, 1980.
56. **Evaluation of certain food additives** (Twenty-fifth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 669, 1981.
57. **Toxicological evaluation of certain food additives**. WHO Food Additives Series, No. 16, 1981.
58. **Specifications for identity and purity of food additives (carrier solvents, emulsifiers and stabilizers, enzyme preparations, flavouring agents, food colours, sweetening agents, and other food additives)**. FAO Food and Nutrition Paper, No. 19, 1981.
59. **Evaluation of certain food additives and contaminants** (Twenty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 683, 1982.

60. **Toxicological evaluation of certain food additives**. WHO Food Additives Series, No. 17, 1982.
61. **Specifications for the identity and purity of certain food additives**. FAO Food and Nutrition Paper, No. 25, 1982.
62. **Evaluation of certain food additives and contaminants** (Twenty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 696, 1983, and corrigenda.
63. **Toxicological evaluation of certain food additives and contaminants**. WHO Food Additives Series, No. 18, 1983.
64. **Specifications for the identity and purity of certain food additives**. FAO Food and Nutrition Paper, No. 28, 1983.
65. **Guide to specifications General notices, general methods, identification tests, test solutions, and other reference materials**. FAO Food and Nutrition Paper, No. 5, Rev. 1, 1983.
66. **Evaluation of certain food additives and contaminants** (Twenty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 710, 1984, and corrigendum.
67. **Toxicological evaluation of certain food additives and contaminants**. WHO Food Additives Series, No. 19, 1984.
68. **Specifications for the identity and purity of food colours**. FAO Food and Nutrition Paper, No. 31/1, 1984.
69. **Specifications for the identity and purity of food additives**. FAO Food and Nutrition Paper, No. 31/2, 1984.
70. **Evaluation of certain food additives and contaminants** (Twenty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 733, 1986, and corrigendum.
71. **Specifications for the identity and purity of certain food additives**. FAO Food and Nutrition Paper, No. 34, 1986.
72. **Toxicological evaluation of certain food additives and contaminants**. WHO Food Additives Series, No. 20. Cambridge University Press, 1987.
73. **Evaluation of certain food additives and contaminants** (Thirtieth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 751, 1987.
74. **Toxicological evaluation of certain food additives and contaminants**. WHO Food Additives Series, No. 21. Cambridge University Press, 1987.
75. **Specifications for the identity and purity of certain food additives**. FAO Food and Nutrition Paper, No. 37, 1986.
76. **Principles for the safety assessment of food additives and contaminants in food**. WHO Environmental Health Criteria, No. 70. Geneva, World Health Organization, 1987 (out of print). The full text is available electronically at www.who.int/pcs.
77. **Evaluation of certain food additives and contaminants** (Thirty-first report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 759, 1987 and corrigendum.
78. **Toxicological evaluation of certain food additives**. WHO Food Additives Series, No. 22. Cambridge University Press, 1988.
79. **Specifications for the identity and purity of certain food additives**. FAO Food and Nutrition Paper, No. 38, 1988.
80. **Evaluation of certain veterinary drug residues in food** (Thirty-second report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 763, 1988.

81. **Toxicological evaluation of certain veterinary drug residues in food.** WHO Food Additives Series, No. 23. Cambridge University Press, 1988.
82. **Residues of some veterinary drugs in animals and foods.** FAO Food and Nutrition Paper, No. 41, 1988.
83. **Evaluation of certain food additives and contaminants** (Thirty-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 776, 1989.
84. **Toxicological evaluation of certain food additives and contaminants.** WHO Food Additives Series, No. 24. Cambridge University Press, 1989.
85. **Evaluation of certain veterinary drug residues in food** (Thirty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 788, 1989.
86. **Toxicological evaluation of certain veterinary drug residues in food.** WHO Food Additives Series, No. 25, 1990.
87. **Residues of some veterinary drugs in animals and foods.** FAO Food and Nutrition Paper, No. 41/2, 1990.
88. **Evaluation of certain food additives and contaminants** (Thirty-fifth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 789, 1990, and corrigenda.
89. **Toxicological evaluation of certain food additives and contaminants.** WHO Food Additives Series, No. 26, 1990.
90. **Specifications for identity and purity of certain food additives.** FAO Food and Nutrition Paper, No. 49, 1990.
91. **Evaluation of certain veterinary drug residues in food** (Thirty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 799, 1990.
92. **Toxicological evaluation of certain veterinary drug residues in food.** WHO Food Additives Series, No. 27, 1991.
93. **Residues of some veterinary drugs in animals and foods.** FAO Food and Nutrition Paper, No. 41/3, 1991.
94. **Evaluation of certain food additives and contaminants** (Thirty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 806, 1991, and corrigenda.
95. **Toxicological evaluation of certain food additives and contaminants.** WHO Food Additives Series, No. 28, 1991.
96. **Compendium of Food Additive Specifications.** Joint FAO/WHO Expert Committee on Food Additives (JECFA). Combined specifications from 1st through the 37th Meetings, 1956-1990. FAO, 1992 (2 volumes).
97. **Evaluation of certain veterinary drug residues in food** (Thirty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 815, 1991.
98. **Toxicological evaluation of certain veterinary residues in food.** WHO Food Additives Series, No. 29, 1991.
99. **Residues of some veterinary drugs in animals and foods.** FAO Food and Nutrition Paper, No. 41/4, 1991.
100. **Guide to specifications—General notices, general analytical techniques, identification tests, test solutions, and other reference materials.** FAO Food and Nutrition Paper, No. 5, Ref. 2, 1991.
101. **Evaluation of certain food additives and naturally occurring toxicants** (Thirty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series No. 828, 1992.
102. **Toxicological evaluation of certain food additives and naturally occurring toxicants.** WHO Food Additive Series, No. 30, 1993.

103. **Compendium of food additive specifications: Addendum 1**. FAO Food and Nutrition Paper, No. 52, 1992.
104. **Evaluation of certain veterinary drug residues in food** (Fortieth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 832, 1993.
105. **Toxicological evaluation of certain veterinary drug residues in food**. WHO Food Additives Series, No. 31, 1993.
106. **Residues of some veterinary drugs in animals and foods**. FAO Food and Nutrition Paper, No. 41/5, 1993.
107. **Evaluation of certain food additives and contaminants** (Forty-first report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 837, 1993.
108. **Toxicological evaluation of certain food additives and contaminants**. WHO Food Additives Series, No. 32, 1993.
109. **Compendium of food additive specifications: Addendum 2**. FAO Food and Nutrition Paper, No. 52, Add. 2, 1993.
110. **Evaluation of certain veterinary drug residues in food** (Forty-second report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 851, 1995.
111. **Toxicological evaluation of certain veterinary drug residues in food**. WHO Food Additives Series, No. 33, 1994.
112. **Residues of some veterinary drugs in animals and foods**. FAO Food and Nutrition Paper, No. 41/6, 1994.
113. **Evaluation of certain veterinary drug residues in food** (Forty-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 855, 1995, and corrigendum.
114. **Toxicological evaluation of certain veterinary drug residues in food**. WHO Food Additives Series, No. 34, 1995.
115. **Residues of some veterinary drugs in animals and foods**. FAO Food and Nutrition Paper, No. 41/7, 1995.
116. **Evaluation of certain food additives and contaminants** (Forty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 859, 1995.
117. **Toxicological evaluation of certain food additives and contaminants**. WHO Food Additives Series, No. 35, 1996.
118. **Compendium of food additive specifications: Addendum 3**. FAO Food and Nutrition Paper, No. 52, Add. 3, 1995.
119. **Evaluation of certain veterinary drug residues in food** (Forty-fifth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 864, 1996.
120. **Toxicological evaluation of certain veterinary drug residues in food**. WHO Food Additives Series, No. 36, 1996.
121. **Residues of some veterinary drugs in animals and foods**. FAO Food and Nutrition Paper, No. 41/8, 1996.
122. **Evaluation of certain food additives and contaminants** (Forty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 868, 1997.
123. **Toxicological evaluation of certain food additives**. WHO Food Additives Series, No. 37, 1996.
124. **Compendium of food additive specifications, addendum 4**. FAO Food and Nutrition Paper, No. 52, Add. 4, 1996.

125. **Evaluation of certain veterinary drug residues in food** (Forty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 876, 1998.
126. **Toxicological evaluation of certain veterinary drug residues in food**. WHO Food Additives Series, No. 38, 1996.
127. **Residues of some veterinary drugs in animals and foods**. FAO Food and Nutrition Paper, No. 41/9, 1997.
128. **Evaluation of certain veterinary drug residues in food** (Forty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 879, 1998.
129. **Toxicological evaluation of certain veterinary drug residues in food.** WHO Food Additives Series, No. 39, 1997.
130. **Residues of some veterinary drugs in animals and foods**. FAO Food and Nutrition Paper, No. 41/10, 1998.
131. **Evaluation of certain food additives and contaminants** (Forty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 884, 1999.
132. **Safety evaluation of certain food additives and contaminants**. WHO Food Additives Series, No. 40, 1998.
133. **Compendium of food additive specifications: Addendum 5**. FAO Food and Nutrition Paper, No. 52, Add. 5, 1997.
134. **Evaluation of certain veterinary drug residues in food** (Fiftieth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 888, 1999.
135. **Toxicological evaluation of certain veterinary drug residues in food.** WHO Food Additives Series, No. 41, 1998.
136. **Residues of some veterinary drugs in animals and foods**. FAO Food and Nutrition Paper, No. 41/11, 1999.
137. **Evaluation of certain food additives** (Fifty-first report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 891, 2000.
138. **Safety evaluation of certain food additives**. WHO Food Additives Series, No. 42, 1999.
139. **Compendium of food additive specifications, addendum 6**. FAO Food and Nutrition Paper, No. 52, Add. 6, 1998.
140. **Evaluation of certain veterinary drug residues in food** (Fifty-second report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 893, 1999.
141. **Toxicological evaluation of certain veterinary drug residues in food**. WHO Food Additives Series, No. 43, 2000
142. **Residues of some veterinary drugs in animals and foods**. FAO Food and Nutrition Paper, No. 41/12, 2000.
143. **Evaluation of certain food additives and contaminants** (Fifty-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, 2000.
144. **Safety evaluation of certain food additives and contaminants**. WHO Food Additives Series, No. 44, 2000.
145. **Compendium of food additive specifications, addendum 7**. FAO Food and Nutrition Paper, No. 52, Add. 7, 1999.
146. **Evaluation of certain veterinary drug residues in food** (Fifty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, 2000.

147. **Toxicological evaluation of certain veterinary drug residues in food**. WHO Food Additives Series, No. 45, 2000.
148. **Residues of some veterinary drugs in animals and foods**. FAO Food and Nutrition Paper, No. 41/13, 2000.
149. **Evaluation of certain food additives and contaminants** (Fifty-fifth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series No. 901, 2001.
150. **Safety evaluation of certain food additives and contaminants**. WHO Food Additives Series, No. 46, 2001.
151. **Compendium of food additive specifications: Addendum 8**. FAO Food and Nutrition Paper, No. 52, Add. 8, 2000.
152. **Evaluation of certain mycotoxins in food** (Fifty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series No. 906, 2002.
153. **Safety evaluation of certain mycotoxins in food**. WHO Food Additives Series, No. 47/FAO Food and Nutrition Paper 74, 2001.
154. **Evaluation of certain food additives and contaminants** (Fifty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series No. 909, 2002.
155. **Safety evaluation of certain food additives and contaminants**. WHO Food Additives Series, No. 48, 2002.
156. **Compendium of food additive specifications: Addendum 9**. FAO Food and Nutrition Paper, No. 52, Add. 9, 2001.
157. **Evaluation of certain veterinary drug residues in food** (Fifty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series No. 911, 2002.
158. *Toxicological evaluation of certain veterinary drug residues in food* WHO Food Additives Series, No. 49, 2002.
159. ***Residues of some veterinary drugs in animals and foods.*** FAO Food and Nutrition Paper, No. 41/14, 2002.
160. *Evaluation of certain food additives* (Fifty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series No. 913, 2002.
161. *Safety evaluation of certain food additives and contaminants.* WHO Food Additives Series, No. 50, 2003.
162. *Compendium of food additive specifications: addendum 10.* FAO Food and Nutrition Paper No. 52, Add. 10, 2002.
163. *Evaluation of certain veterinary drug residues in food* (Sixtieth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 918, 2003.
164. *Toxicological evaluation of certain veterinary drug residues in food.* WHO Food Additives Series, No. 51, 2003.
165. *Residues of some veterinary drugs in animals and foods.* FAO Food and Nutrition Paper, No. 41/15, 2003.
166. *Evaluation of certain food additives and contaminants* (Sixty-first report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 922, 2004.
167. *Safety evaluation of certain food additives and contaminants.* WHO Food Additives Series, No. 52, 2004.
168. *Compendium of food additive specifications: addendum 11.* FAO Food and Nutrition Paper, No. 52, Add. 11, 2003.

169. *Evaluation of certain veterinary drug residues in food* (Sixty-second report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 925, 2004.
170. *Residues of some veterinary drugs in animals and foods.* FAO Food and Nutrition Paper, No. 41/16, 2004.
171. *Toxicological evaluation of certain veterinary drug residues in food.* WHO Food Additives Series, No. 53, 2005.
172. *Compendium of food additive specifications: addendum 12.* FAO Food and Nutrition Paper, No. 52, Add. 12, 2004.
173. *Evaluation of certain food additives* (Sixty-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 928, 2005.
174. *Safety evaluation of certain food additives* WHO Food Additives Series, No. 54, 2005.
175. *Evaluation of certain food contaminants* (Sixty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 930, 2005.
176. *Safety evaluation of certain contaminants in food.* WHO Food Additives Series, No. 55/FAO Food and Nutrition Paper, No. 82, 2005.
177. *Evaluation of certain food additives* (Sixty-fifth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 934 2005.
178. *Compendium of food additive specifications: addendum 13.* FAO Food and Nutrition Paper, No. 52, Add.13 (in prepration).

ANNEX 2

ABBREVIATIONS USED IN THE MONOGRAPHS

ADI	acceptable daily intake
ALT	alanine aminotransferase
APM	aminopeptidase
AUC	area under the curve (concentration–time)
BSO	buthionine sulfoximine
bw	body weight
CAS	Chemical Abstracts Services
CoA	coenzyme A
CYP450	cytochrome P450
D002	mixture consisting of C24 (13.2%), C26 (15.3%), C28 (17.5%), C30 (26.6%), C32 (17.0%) and C34 (2.2%) fatty alcohols
EC_{50}	median ? concentration
F	female
F_1	first filial generation
F_2	second filial generation
FAD	flavin adenosine dinucleotide
FAO	Food and Agricultural Organization of the United Nations
GLP	good laboratory practice
γ-GT	γ-glutamyltransferase
GSH	reduced glutathione
GST	glutathione *S*-transferase
HPLC	high-performance liquid chromatography
IPCS	International Programme on Chemical Safety
IU	international unit
JECFA	Joint FAO/WHO Expert Committee on Food Additives
K_m	Michaelis-Menten constant
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LEU	lecitase unit
LOEL	lowest-observed-effect level
M	male
NA	not avuilable
NAT	*N*-acetyltransferase
ND	no intake data reported
NOEL	no-observed-effect level
NR	not reported
N/R	not required for evaluation because intake of the substance was determined to be of no safety concern at Step A3 of the Procedure

NRU_{50}	median reduction in neutral red uptake
OECD	Organisation for Economic Co-operation and Development
OR	odds ratio
P	parent generation
PAPS	3´-phosphoadenosine-5´-phosphosulfate
pK_a	
ppm	parts per million
QA	quality assurance
S9	9000 × *g* microsomal frcation of rat liver
SD	standard deviation
SPF	specific-pathogen-free
t	time
UDPGA	UDP-glucuronic acid
UDPGT	UDP-glucuronosyltransferase
v/v	volume for volume
V_{max}	maximum volume
WHO	World Health Organization
w/w	weight for weight

ANNEX 3

PARTICIPANTS IN THE SIXTY-FIFTH MEETING OF THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

Geneva, 7–16 June 2005

Members

Professor J.R. Bend, Faculty of Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada

Professor Y. El-Samragy, Food Science Department, Ain Shams University, Cairo, Egypt

Dr Y. Kawamura, National Institute of Health Sciences, Tokyo, Japan

Dr A. Knaap, National Institute of Public Health and the Environment, Bilthoven, The Netherlands

Dr P.M. Kuznesof, US Food and Drug Administration, College Park, Maryland, United States

Dr J.C. Larsen, Danish Institute of Food and Veterinary Research, Søborg, Denmark (*Joint Vice-Chairman*)

Dr A. Mattia, US Food and Drug Administration, College Park, Maryland, United States

Mrs I. Meyland, Danish Institute of Food and Veterinary Research, Søborg, Denmark (*Chairman*)

Dr G. Pascal, Institut National de la Recherche Agronomique, Paris, France

Dr M. Veerabhadra Rao, Central Laboratories Unit, United Arab Emirates University, Al Ain, United Arab Emirates

Dr J. Schlatter, Swiss Federal Office of Public Health, Zürich, Switzerland

Dr P. Verger, Institut National de la Recherche Agronomique, Paris, France

Mrs H. Wallin, National Food Agency, Helsinki, Finland

Dr D.B Whitehouse, Bowdon, Cheshire, United Kingdom

Secretariat [1]

Dr P.J. Abbott, Food Standards Australia New Zealand, Canberra, Australia (*WHO Temporary Adviser*)

Dr A. Bruno, Joint FAO/WHO Food Standards Programme, Secretariat of the Codex Alimentarius Commission, Food and Agriculture Organization of the United Nations, Rome, Italy

Dr R.C. Cantrill, American Oil Chemists' Society, Champaign, Illinois, United States (*FAO Consultant*)

Dr R. Charrondiere, Food and Nutrition Division, Food and Agriculture

[1] Unable to attend: Dr Z. Olempska-Beer, Center for Food Safety and Applied Nutrition, US Food and Drug Administration, College Park, Maryland, USA; Dr Monica Olsen, Food and Nutrition Division, Food and Agriculture Organization of the United Nations, Rome, Italy

Organization of the United Nations, Rome, Italy (*FAO Staff Member*)

Dr M.deL. Costarrica, Food and Nutrition Division, Food and Agriculture Organization of the United Nations, Rome, Italy (*FAO Staff, Acting FAO Joint Secretary*)

Dr M. DiNovi, US Food and Drug Administration, College Park, Maryland, United States (*WHO Temporary Adviser*)

Dr C.E. Fisher, Hatfield, Hertfordshire, United Kingdom (*FAO Consultant, Acting FAO Joint Secretary*)

Dr C.A. Lawrie, Food Standards Agency, London, United Kingdom (*FAO Consultant*)

Dr C. Leclercq, National Research Institute for Food and Nutrition, Rome, Italy (*FAO Consultant*)

Dr G. Moy, Food Safety Department, World Health Organization, Geneva, Switzerland (*WHO Staff Member*)

Dr I.C. Munro, CanTox Health Sciences International, Mississauga, Ontario, Canada (*WHO Temporary Adviser*)

Dr A. Nishikawa, Division of Pathology, National Institute of Health Sciences, Tokyo, Japan (*WHO Temporary Adviser*)

Dr S. Page, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland (*WHO Staff Member*)

Mrs Ir M.E.J. Pronk, Center for Substances and Integrated Risk Assessment, National Institute for Public Health and the Environment, Bilthoven, The Netherlands (*WHO Temporary Adviser*)

Professor A.G. Renwick, Clinical Pharmacology Group, University of Southampton, Southampton, United Kingdom (*WHO Temporary Adviser*)

Professor I.G. Sipes, Department of Pharmacology, College of Medicine, University of Arizona, Tucson, Arizona, United States (*WHO Temporary Adviser*)

Professor L.M. Valenta Soares, Food Science Department, State University of Campinas, Campinas, Brazil (*FAO Consultant*)

Professor I. Stankovic, Institute of Bromatology, Faculty of Pharmacy, Belgrade, Serbia and Montenegro (*FAO Consultant*)

Dr A. Tritscher, International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland (*WHO Joint Secretary*)

Dr L.G. Valerio, Jr, Center for Food Safety and Applied Nutrition, US Food and Drug Administration, College Park, Maryland, United States (*WHO Temporary Adviser*)

Professor G.M. Williams, Environmental Pathology and Toxicology, New York Medical College, Valhalla, New York, United States (*WHO Temporary Adviser*)

ANNEX 4

ACCEPTABLE DAILY INTAKES, OTHER TOXICOLOGICAL INFORMATION AND INFORMATION ON SPECIFICATIONS

1. Food additives and ingredients evaluated toxicologically or assessed for dietary exposure

Food additive	Specifications[a]	Acceptable daily intake (ADI) and other toxicological recommendations
Beeswax	R	No safety concern at predicted dietary intake(< 650 mg per person per day), based on long history of use and lack of toxicity observed with major components
Candelilla wax	R	No safety concern at predicted dietary intake (< 650 mg per person per day)
L-5-Methyltetrahydrofolate	N	No safety concern for proposed use in dry crystalline or micro-encapsulated form as alternative to folic acid used in dietary supplements, foods for special dietary uses and other foods. Safety of folate fortification and supplementation as such not evaluated.
Phospholipase A1 from *Fusarium venenatum* expressed in *Aspergillus oryzae*	N	Information provided too limited to assess safety
Pullulan	N	ADI 'not specified'[b]
Quillaia extract type 1	S	Previous ADI converted to an ADI based on saponin content from the lower end of specified saponin range and established as group ADI for quillaia extract type 1 and quillaia extract type 2. Assessment of dietary exposure included additional use of quillaia extract type 1 in semi-frozen carbonated and non-carbonated beverages (≤ 500 mg/kg product).

Food additive	Specifications[a]	Acceptable daily intake (ADI) and other toxicological recommendations
Quillaia extract type 1 (contd)		In a model diet approach, high percentile consumption estimated to lead to intake of 44–157% of ADI, assuming presence of quillaia extract type 1 at 295 mg/l in all water-based flavoured drinks. In a probabilistic exposure assessment and assuming that the frequency and amount per eating occasion are independent variables, the estimated dietary intake was below the ADI at the 90th percentile. Assuming 100% dependence between frequency and amount consumed, estimated that 100–700 individuals per million in the entire population could exceed the ADI .
Quillaia extract type 2	R	Previous ADI established for quillaia extract type 1 converted to an ADI based on saponin content from the lower end of the specified saponin range and established as a group ADI for quillaia extract type 1 and type 2.

[a] N: new specifications prepared; R: existing specifications revised; S: existing specifications maintained.

[b] ADI 'not specified' is used to refer to a food substance of very low toxicity which, on the basis of the available data (chemical, biochemical, toxicological and other) and the total dietary intake of the substance arising from its use at the levels necessary to achieve the desired effects and from its acceptable background levels in food, does not, in the opinion of the Committee, represent a hazard to health. For that reason, and for the reasons stated in the individual evaluations, the establishment of an ADI expressed in numerical form is not deemed necessary. An additive meeting this criterion must be used within the bounds of good manufacturing practice, i.e. it should be technologically efficacious and should be used at the lowest level necessary to achieve this effect, it should not conceal food of inferior quality or adulterated food, and it should not create a nutritional imbalance.

2. Food additives considered for specifications only

Food additive	Specifications[a]
Aspartame acesulfame salt	R
Hexanes	See below
Laccase from *Myceliophthora thermophila* expressed in *Aspergillus oryzae*	R
Monomagnesium phosphate and trisodium diphosphate	W[b]
Sucrose esters of fatty acids	R, T

[a] R: existing specifications revised; T: tentative specifications; W: existing specifications withdrawn.
[b] As no information was received on these substances, the existing tentative specifications were withdrawn.

Hexanes

As used in the food industry, 'hexane' is a mixture of hydrocarbons. Recent changes in environmental regulations have led to a change in composition of hexanes since the original specifications were established. In addition, the composition of hexanes depends on the region of production, the source of the raw material and the site of production. Therefore, the Committee concluded that the present articles of commerce differ from those previously evaluated by the Committee and that the composition of the residues and their levels in foods may not be the same as those evaluated in the original safety assessment. The Committee also concluded that there was insufficient information available to change the current specifications, and therefore recommended a re-evaluation of hexanes.

3. Flavouring agents evaluated with the Procedure for the Safety Evaluation of Flavouring Agents

See also the discussion on the safety evaluation of flavouring agents in Annex 7.

A. Maltol and related substances

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
Maltol	1480	N[b]	See footnote c
Ethyl maltol	1481	N[b]	See footnote d
Maltyl isobutyrate	1482	N, T	No safety concern

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
2-Methyl-3-(1-oxopropoxy)-4*H*-pyran-4-one	1483	N	No safety concern (conditional)[e]
2-Butyl-5- or 6-keto-1,4-dioxane	1484	N	No safety concern
2-Amyl-5- or -6-keto-1,4-dioxane	1485	N	No safety concern
2-Hexyl-5- or -6-keto-1,4-dioxane	1486	N	No safety concern

[a] N: new specifications prepared; T: tentative specifications.
[b] Revised specifications for these substances in the standard additive format were also prepared.
[c] The ADI of 0–1 mg/kg bw established at the twenty-fifth meeting was maintained.
[d] The ADI of 0–2 mg/kg bw established at the eighteenth meeting. was maintained.
[e] Evaluation conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of this substance will be revoked if use levels or poundage data are not provided before the end of 2007.

B. Furan-substituted aliphatic hydrocarbons, alcohols, aldehydes, ketones, carboxylic acids and related esters, sulfides, disulfides and ethers

The Committee took note of the extensive positive genotoxicity data for several members of this group of flavouring agents related to furan. Furan, which is carcinogenic, is known to undergo epoxidation and ring opening to form a reactive 2-ene-1,4-dicarbonyl intermediate. Accordingly, concern arises that the observed genotoxicity may be due to formation of a reactive metabolite. Data on the potential of members of this group to form a reactive metabolite were not available and the role of metabolism in the observed genotoxicity has not been identified. Moreover, there was a paucity of in vivo genotoxicity data to allay concern. Also, specific in vivo assays to address potential carcinogenicity were lacking. Because of these concerns, the Committee concluded that the Procedure could not be applied to this group.

Flavouring agent	No.	Specifications[a]
2-Methylfuran	1487	N
2,5-Dimethylfuran	1488	N
2-Ethylfuran	1489	N
2-Butylfuran	1490	N
2-Pentylfuran	1491	N
2-Heptylfuran	1492	N
2-Decylfuran	1493	N

Flavouring agent	No.	Specifications[a]
3-Methyl-2-(3-methylbut-2-enyl)-furan	1494	N
2,3-Dimethylbenzofuran	1495	N
2,4-Difurfurylfuran	1496	N
3-(2-Furyl)acrolein	1497	N
2-Methyl-3(2-furyl)acrolein	1498	N
3-(5-Methyl-2-furyl)prop-2-enal	1499	N
3-(5-Methyl-2-furyl)-butanal	1500	N
2-Furfurylidenebutyraldehyde	1501	N
2-Phenyl-3-(2-furyl)prop-2-enal	1502	N
2-Furyl methyl ketone	1503	N
2-Acetyl-5-methylfuran	1504	N
2-Acetyl-3,5-dimethylfuran	1505	N
3-Acetyl-2,5-dimethylfuran	1506	N,T
2-Butyrylfuran	1507	N
(2-Furyl)-2-propanone	1508	N
2-Pentanoylfuran	1509	N
1-(2-Furyl)butan-3-one	1510	N
4-(2-Furyl)-3-buten-2-one	1511	N
Pentyl 2-furyl ketone	1512	N
Ethyl 3-(2-furyl)propanoate	1513	N
Isobutyl 3-(2-furan)propionate	1514	N
Isoamyl 3-(2-furan)propionate	1515	N
Isoamyl 4-(2-furan)butyrate	1516	N
Phenethyl 2-furoate	1517	N
Propyl 2-furanacrylate	1518	N
2,5-Dimethyl-3-oxo-(2*H*)-fur-4-yl butyrate	1519	N
Furfuryl methyl ether	1520	N
Ethyl furfuryl ether	1521	N
Difurfuryl ether	1522	N
2,5-Dimethyl-3-furanthiol acetate	1523	N
Furfuryl 2-methyl-3-furyl disulfide	1524	N
3-[(2-Methyl-3-furyl)thio]-2-butanone	1525	N
O-Ethyl *S*-(2-furylmethyl)thiocarbonate	1526	N

[a] N: new specifications prepared; T: tentative specifications

C. Eugenol and related hydroxyallylbenzene derivatives

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
4-Allylphenol	1527	N	No safety concern (conditional)[b]
2-Methoxy-6-(2-propenyl)phenol	1528	N	No safety concern (conditional)[b]

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
Eugenol	1529	R[c]	See footnote d
Eugenyl formate	1530	N	No safety concern
Eugenyl acetate	1531	N	No safety concern
Eugenyl isovalerate	1532	N	No safety concern (conditional)[b]
Eugenyl benzoate	1533	N	No safety concern

[a] N: new specifications prepared; R: existing specifications revised.
[b] Evaluation conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of this substance will be revoked if use levels or poundage data are not provided before the end of 2007.
[c] As this substance is used only as a flavouring agent, the Committee considered that the existing specifications in the standard food additive format should be deleted.
[d] The ADI of 0-2.5 mg/kg bw established at the twenty-sixth meeting was maintained.

D. Anthranilate derivatives

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
Methyl anthranilate	1534	R[b]	See footnote c
Ethyl anthranilate	1535	N	No safety concern
Butyl anthranilate	1536	N	No safety concern
Isobutyl anthranilate	1537	N	No safety concern
cis-3-Hexenyl anthranilate	1538	N	No safety concern (conditional)[d]
Citronellyl anthranilate	1539	N	No safety concern (conditional)[d]
Linalyl anthranilate	1540	N	No safety concern
Cyclohexyl anthranilate	1541	N	No safety concern
β-Terpinyl anthranilate	1542	N	No safety concern
Phenylethyl anthranilate	1543	N	No safety concern
β-Naphthyl anthranilate	1544	N	No safety concern
Methyl *N*-methylanthranilate	1545	R[b]	See footnote e
Ethyl *N*-methylanthranilate	1546	N	No safety concern (conditional)[d]
Ethyl *N*-ethylanthranilate	1547	N	No safety concern (conditional)[d]

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
Isobutyl *N*-methylanthranilate	1548	N	No safety concern (conditional)[d]
Methyl *N*-formylanthranilate	1549	N	No safety concern (conditional)[d]
Methyl *N*-acetylanthranilate	1550	N	No safety concern (conditional)[d]
Methyl *N*,*N*-dimethylanthranilate	1551	N	No safety concern (conditional)[d]
N-Benzoylanthranilic acid	1552	N	No safety concern (conditional)[d]

[a] N: new specifications prepared; R: existing specifications revised.
[b] As this substance is used only as a flavouring agent, the Committee decided that the existing specifications in the standard food additive format should be deleted.
[c] The ADI of 0–1.5 mg/kg bw established at the twenty-third meeting was maintained.
[d] Evaluation conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of this substance will be revoked if use levels or poundage data are not provided before the end of 2007.
[e] The ADI of 0–0.2 mg/kg bw established at the twenty-third meeting was maintained.

E. Miscellaneous nitrogen-containing substances

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
Trimethyloxazole	1553	N	No safety concern (conditional)[b]
2,5-Dimethyl-4-ethyloxazole	1554	N	No safety concern (conditional)[b]
2-Ethyl-4,5-dimethyloxazole	1555	N	No safety concern (conditional)[b]
2-Isobutyl-4,5-dimethyloxazole	1556	N	No safety concern (conditional)[b]
2-Methyl-4,5-benzo-oxazole	1557	N	No safety concern (conditional)[b]
2,4-Dimethyl-3-oxazoline	1558	N	No safety concern (conditional)[b]

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
2,4,5-Trimethyl-Δ3-oxazoline	1559	N,T	No safety concern
Allyl isothiocyanate	1560	N	No safety concern
Butyl isothiocyanate	1561	N	No safety concern (conditional)[b]
Benzyl isothiocyanate	1562	N	No safety concern (conditional)[b]
Phenethyl isothiocyanate	1563	N	No safety concern (conditional)[b]
3-Methylthiopropyl isothiocyanate	1564	N	No safety concern
4-Acetyl-2-methylpyrimidine	1565	N	No safety concern
5,7-Dihydro-2-methylthieno(3,4-*d*) pyrimidine	1566	N	No safety concern
1-Phenyl-3- or -5-propylpyrazole	1568	N	No safety concern
4,5-Dimethyl-2-propyloxazole	1569	N	No safety concern (conditional)[b]

[a] N: new specifications prepared; T: tentative specifications.
[b] Evaluation conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of this substance will be revoked if use levels or poundage data are not provided before the end of 2007.

F. Epoxides

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
4,5-Epoxy-(E)-2-decenal	1570	N	No safety concern (conditional)[b]
β-Ionone epoxide	1571	N	No safety concern (conditional)[b]
trans-Carvone-5,6-oxide	1572	N	No safety concern
Epoxyoxophorone	1573	N	No safety concern (conditional)[b]
Piperitenone oxide	1574	N	No safety concern
β-Caryophyllene oxide	1575	N	No safety concern
Ethyl 3-phenylglycidate	1576	Rc	No safety concern
Ethyl methylphenylglycidate	1577	Rc	See footnote d
Ethyl methyl-*para*-tolylglycidate	1578	N	No safety concern

[a] N: new specifications prepared; R: existing specifications revised.

[b] Evaluation conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of this substance will be revoked if use levels or poundage data are not provided before the end of 2007.
[c] As this substance is used only as a flavouring agent, the Committee decided that the existing specifications in the standard food additive format should be deleted.
[d] The ADI of 0–0.5 mg/kg bw established at the 28th meeting. was maintained.

G. Aliphatic and aromatic amines and amides

Acetamide (No. 1592)

The Committee noted that the available data on the toxicity of this substance indicate that it is clearly carcinogenic in both mice and rats, and, although the mechanism of tumour formation is unknown, the possibility of a genotoxic mechanism cannot be discounted. The Committee considered it inappropriate for such a compound to be used as a flavouring agent or for any other food additive purpose and agreed that acetamide would not be evaluated according to the Procedure. No specifications were prepared.

Other substances in this group

Flavouring agent	No.	Specifi-cations[a]	Conclusions based on current intake
Ethylamine	1579	N	No safety concern (conditional)[b]
Propylamine	1580	N	No safety concern (conditional)[b]
Isopropylamine	1581	N	No safety concern (conditional)[b]
Butylamine	1582	N	No safety concern
Isobutylamine	1583	N	No safety concern (conditional)[b]
sec-Butylamine	1584	N	No safety concern (conditional)[b]
Pentylamine	1585	N	No safety concern (conditional)[b]
2-Methylbutylamine	1586	N	No safety concern (conditional)[b]
Isopentylamine	1587	N	No safety concern
Hexylamine	1588	N	No safety concern (conditional)[b]
Phenethylamine	1589	N	No safety concern

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
2-(4-Hydroxyphenyl)ethylamine	1590	N	No safety concern (conditional)[b]
1-Amino-2-propanol	1591	N	No safety concern (conditional)[b]
Butyramide	1593	N	No safety concern (conditional)[b]
1,6-Hexalactam	1594	N	No safety concern (conditional)[b]
2-Isopropyl-*N*,2,3-trimethylbutyramide	1595	N	No safety concern (conditional)[b]
N-Ethyl (E)-2,(Z)-6-nonadienamide	1596	N	No safety concern (conditional)[b]
N-Cyclopropyl (E)-2,(Z)-6-nonadienamide	1597	N	No safety concern (conditional)[b]
N-Isobutyl (E,E)-2,4-decadienamide	1598	N	No safety concern (conditional)[b]
Nonanoyl 4-hydroxy-3-methoxybenzylamide	1599	N	No safety concern
Piperine	1600	N	No safety concern
N-Ethyl-2-isopropyl-5-methylcyclohexane carboxamide	1601	N	No safety concern
(+/–)-*N*,*N*-Dimethyl menthyl succinamide	1602	N	No safety concern (conditional)[b]
1-Pyrroline	1603	N	No safety concern (conditional)[b]
2-Acetyl-1-pyrroline	1604	N	No safety concern (conditional)[b]
2-Propionylpyrroline	1605	N	No safety concern (conditional)[b]
Isopentylidene isopentylamine	1606	N	No safety concern (conditional)[b]
Piperidine	1607	N	No safety concern
2-Methylpiperidine	1608	N	No safety concern (conditional)[b]
Pyrrolidine	1609	N	No safety concern
Trimethylamine	1610	N	No safety concern
Triethylamine	1611	N	No safety concern (conditional)[b]
Tripropylamine	1612	N	No safety concern (conditional)[b]
N,*N*-Dimethylphenethylamine	1613	N	No safety concern (conditional)[b]

Flavouring agent	No.	Specifications[a]	Conclusions based on current intake
Trimethylamine oxide	1614	N	No safety concern (conditional)[b]
Piperazine	1615	N	No safety concern (conditional)[b]

[a] N: new specifications prepared.

[b] Evaluation conditional because the estimated daily intake is based on the anticipated annual volume of production. The conclusion of the safety evaluation of this substance will be revoked if use levels or poundage data are not provided before the end of 2007.

4. Flavouring agents considered for specifications only

Flavouring agent	No.	Specifications[a]
Sodium salt of 3-methyl-2-oxobutanoic acid	631.2	R,T
Sodium salt of 3-methyl-2-oxopentanoic acid	632.2	R,T
Sodium salt of 4-methyl-2-oxopentanoic acid	633.2	R,T
Sodium 2-oxo-3-phenylpropionate	1479	R,T

[a] R: existing specifications revised; T: tentative specifications

ANNEX 5

SUMMARY OF SAFETY EVALUATIONS OF SECONDARY COMPONENTS OF FLAVOURING AGENTS WITH MINIMUM ASSAY VALUES OF LESS THAN 95%

Annex 4

Summary of safety evaluations of secondary components of flavouring agents with minimum assay values of less than 95%

No.	Name	Minimum assay value (%)	Other requirements	Comments on secondary components
Eugenol and related hydroxyallylbenzene derivatives				
1530	Eugenyl formate	94	2–3% eugenol	Eugenol (No. 1529) was evaluated at the current meeting (see monograph). It has been examined for toxicity in studies lasting from 30 days to 2 years. The NOELs in most of these studies were > 400 mg/kg bw per day (Trubek, 1958; Hagan et al., 1965; Bar & Griepentrog, 1967; Hagan et al., 1967; Miller et al., 1983; National Toxicology Program, 1983; Hirose et al., 1987). In a 2-year study, the NOEL was > 450 mg/kg per day in mice and 300 mg/kg per day in rats (National Toxicology Program, 1983).
Miscellaneous nitrogen-containing substances				
1559	2,4,5-Trimethyl-Δ-3-oxazoline	94	2–3% trimethyloxazole	Trimethyloxazole (No. 1553) was evaluated at the current meeting. It is expected to have a similar metabolic fate and similar toxicity as the primary material, 2,4,5-trimethyl-Δ-3-oxazoline, and the other oxazoles and oxazolines in this group. In a 90-day study with the primary material, the NOEL was > 41 mg/kg per day (Morgareidge, 1972).

Annex 5 (contd)

No.	Name	Minimum assay value (%)	Other requirements	Comments on secondary components
Epoxides				
1570	4,5-Epoxy-(E)-2-decenal	87	8–10% Z isomer	4,5-Epoxy-(Z)-2-decenal is expected to have the same metabolic fate as the E isomer and the other epoxides in this group. Epoxide hydrolase present in the cytosol (Gill et al., 1974), endoplasmic reticulum (Oesch et al., 1970) and nucleus (Bresnick et al., 1977) catalyses epoxide ring cleavage by water to yield vicinal *trans*-diols. Alternatively, glutathione transferase present in the cytosol catalyses ring cleavage by glutathione to yield *trans*-thioalcohol conjugates (Jakoby, 1978). In a 28-day study, the NOEL for the structurally related compound cyclohexane oxide was 100 mg/kg bw per day (Sauer et al., 1997).
Aliphatic and aromatic amines and amides				
1606	Isopentylidene isopentylamine	93	2–3% diisopentylamine; 1-2% 3-methylbutyraldehyde	Diisopentylamine is expected to have the same metabolic fate as the other primary, secondary and tertiary amines in this group. They are mainly oxidized to imines by flavin-containing monooxygenases, monoamine oxidases or amine oxidases. The resulting imine can be further oxidized to the corresponding aldehyde and ammonia (Kearney et al., 1971). In 90-day studies with structurally related materials, the NOELs were 80 mg/kg bw per day for piperidine and 160 mg/kg bw per day for trimethylamine (Amoore et al., 1978). 3-Methylbutyraldehyde (No. 258) was evaluated by the Committee at its forty-sixth meeting and found to be of no safety concern at current levels of exposure.

References for ***Annex 6***

Amoore, J.E., Gumbmann, M.R., Booth, A.N. & Gould, D.H. (1978) Synthetic flavors: Efficiency and safety factors for sweaty and fishy odorants. *Chem. Senses Flavour*, **3**, 307.

Bär, V.F. & Griepentrog, F. (1967) [Where we stand concerning the evaluation of flavouring substances from the viewpoint of health]. *Med. Ernahr.*, **8**, 244–251.

Bresnick, E., Stoming, T.A., Vaught, J.B., Thakker, D.K. & Jerina, D.M. (1977) Nuclear metabolism of benzo(a)pyrene and of (±)-trans-7,8-dihydroxy-7,8-dihydrobenzo[a]pyrene—Comparative chromatographic analysis of alkylated DNA. *Arch. Biochem. Biophys.*, **183**, 31–37.

Gill, S.S., Hammock, B.D. & Casida, J.E. (1974) Mammalian metabolism and environmental degradation of juvenoid 1-(4′-ethylphenoxy)-3,7-dimethyl-6,7-epoxy-*trans*-2-octene and related compounds. *J. Agric. Food Chem.*, **22**, 386–395.

Hagan, E.C., Jenner, P.M., Jones, W.I., Fitzhugh, O.G., Long, E.L., Brouwer, J.G. & Webb, W.K. (1965) Toxic properties of compounds related to safrole. *Toxicol. Appl. Pharmacol.*, **7**, 18–24.

Hagan, E.C., Hansen, W.H., Fitzhugh, O.G., Jenner, P.M., Jones, W.I., Taylor, J.M., Long, E.L., Nelson, A.A. & Brouwer, J.B. (1967) Food flavourings and compounds of related structure. II. Subacute and chronic toxicity. *Food Cosmet. Toxicol.*, **5**, 141–157.

Hirose, M., Masuda, A., Imaida, K., Kagawa, M., Tsuda, H. & Ito, N. (1987) Induction of forestomach lesions in rats by oral administrations of naturally occurring antioxidants for 4 weeks. *Jpn. J. Cancer Res. (Gann)*, **78**, 317–321.

Kearney, E.B., Salach, J.I., Walker, W.H., Seng, R. & Singer, T.P. (1971) Structure of the covalently bound flavin of monoamine oxidase. *Biochem. Biophys. Res Commun.*, **42**, 490–496.

Miller, E.C., Swanson, A.B., Phillips, D., Fletcher, L.T., Liem, A. & Miller, J.A. (1983) Structure–activity studies of the carcinogenicities in the mouse and rat of some naturally occurring and synthetic alkenylbenzene derivatives related to safrole and estragole. *Cancer Res.*, **43**, 1124–1134.

Morgareidge, K. (1972) 90-day feeding studies in rats with 2,4,5-trimethyl-Δ3-oxazoline (31202). Food and Drug Research Laboratories. Unpublished report submitted to WHO by the Food and Extract Manufacturers Association of the United States, Washington DC, USA.

National Toxicology Program (1983) *Carcinogenesis Studies of Eugenol (CAS No. 97-53-0) in F344/N Rats and B6C3F1 Mice (Feed Studies)* (NTP TR 223. NTP 84-1779), Research Triangle Park, North Carolina, USA, National Toxicology Program.

Oesch, F., Jerina, D.M. & Daly, J. (1970) A radiometric assay for hepatic epoxide hydrase activity with 7-^{3}H-styrene oxide. *Biochim. Biophys. Acta*, **227**, 685–691.

Sauer, J.-M., Bao, J., Smith, R.L., McClure, T.D., Mayersohn, M., Pillai, U., Cunningham, M.L. & Sipes, I.G. (1997) Absorption, disposition kinetics, and metabolic pathways of cyclohexane oxide in the male Fischer 244 rat and female B6C3F1 mouse. *Drug Metab. Disposition*, **25**, 371–378.

Trubek Laboratories, Inc. (1958) Toxicolgical screening of eugenol, p-methoxybenzaldehyde and piperonal in rats. Class IX. Aromatic aldehydes. Unpublished report submitted to WHO by the Flavor and Extract Manufacturers Association of the United States, Washington DC, USA.

ANNEX 6

FLAVOURING AGENTS FOR WHICH USE LEVEL OR REPORTED POUNDAGE DATA ARE REQUIRED

The safety assessments of these flavouring agents will be revoked if data on levels of use or reported poundage data are not provided before the end of 2007 (see Annex 4).

1. Flavouring agents evaluated at the present meeting that were assessed as of 'no safety concern' on a conditional basis

No.	Flavouring agent
1483	2-Methyl-3-(1-oxopropoxy)-4*H*-pyran-4-one
1527	4-Allylphenol
1528	2-Methoxy-6-(2-propenyl)phenol
1532	Eugenyl isovalerate
1538	*cis*-3-Hexenyl anthranilate
1539	Citronellyl anthranilate
1546	Ethyl *N*-methylanthranilate
1547	Ethyl *N*-ethylanthranilate
1548	Isobutyl *N*-methylanthranilate
1549	Methyl *N*-formylanthranilate
1550	Methyl *N*-acetylanthranilate
1551	Methyl *N,N*-dimethylanthranilate
1552	*N*-Benzoylanthranilic acid
1553	Trimethyloxazole
1554	2,5-Dimethyl-4-ethyloxazole
1555	2-Ethyl-4,5-dimethyloxazole
1556	2-Isobutyl-4,5-dimethyloxazole
1557	2-Methyl-4,5-benzo-oxazole
1558	2,4-Dimethyl-3-oxazoline
1561	Butyl isothiocyanate
1562	Benzyl isothiocyanate
1563	Phenethyl isothiocyanate
1569	4,5-Dimethyl-2-propyloxazole
1570	4,5-Epoxy(E)-2-decenal
1571	β-Ionone epoxide
1573	Epoxyoxophorone
1579	Ethylamine
1580	Propylamine
1581	Isopropylamine
1583	Isobutylamine
1584	*sec*-Butylamine
1585	Pentylamine
1586	2-Methylbutylamine
1588	Hexylamine
1590	2-(4-Hydroxyphenyl)ethylamine
1591	1-Amino-2-propanol
1593	Butyramide

No.	Flavouring agent
1594	1,6-Hexalactam
1595	2-Isopropyl-*N*,2,3-trimethylbutyramide
1596	*N*-Ethyl (E)-2(Z)-6-nonadienamide
1597	*N*-Cyclopropyl (E)-2(Z)-6-nonadienamide
1598	*N*-Isobutyl (E,E)-2,4-decadienamide
1602	(±)-*N*,*N*-Dimethyl menthyl succinamide
1603	1-Pyrroline
1604	2-Acetyl-1-pyrroline
1605	2-Propionylpyrroline
1606	Isopentylidene isopentylamine
1608	2-Methylpiperidine
1611	Triethylamine
1612	Tripropylamine
1613	*N*,*N*-Dimethylphenethylamine
1614	Trimethylamine oxide
1615	Piperazine

2. Flavouring agents evaluated at the fifty-ninth (2002), sixty-first (2003) and sixty-third (2004) meetings of JECFA, for which only anticipated poundage data were available or for which the MSDI derived from anticipated poundage data from one region (European Union or USA) was greater than the MSDI derived from recorded poundage data for the other region

No.	Flavouring agent	Year	Note
963	Ethyl cyclohexanecarboxylate	2002	a
986	10-Hydroxymethylene-2-pinene	2002	a
1063	2,5-Dimethyl-3-furanthiol	2002	b
1065	Propyl 2-methyl-3-furyl disulfide	2002	a
1066	Bis(2-methyl-3-furyl) disulfide	2002	b
1067	Bis(2,5-dimethyl-3-furyl) disulfide	2002	b
1068	Bis(2-methyl-3-furyl) tetrasulfide	2002	a
1070	2,5-Dimethyl-3-furan thioisovalerate	2002	a
1077	Furfuryl isopropyl sulfide	2002	b
1082	2-Methyl-3,5- or -6-(furfurylthio)pyrazine	2002	b
1085	3-[(2-Methyl-3-furyl)thio]-4-heptanone	2002	a
1086	2,6-Dimethyl-3-[(2-methyl-3-furyl)thio]-4-heptanone	2002	a
1087	4-[(2-Methyl-3-furyl)thio]-5-nonanone	2002	a
1089	2-Methyl-3-thioacetoxy-4,5-dihydrofuran	2002	a
1157	4-Hydroxy-4-methyl-5-hexenoic acid γ-lactone	2003	a
1158	(±) 3-Methyl-γ-decalactone	2003	a
1159	4-Hydroxy-4-methyl-7-*cis*-decenoic acid γ-lactone	2003	a
1160	Tuberose lactone	2003	a
1161	Dihydromintlactone	2003	a
1162	Mintlactone	2003	b

No.	Flavouring agent	Year	Not
1163	Dehydromenthofurolactone	2003	b
1164	(±)-(2,6,6-Trimethyl-2-hydroxycyclohexylidene)acetic acid γ-lactone	2003	a
1167	2-(4-Methyl-2-hydroxyphenyl)propionic acid γ-lactone	2003	a
1174	2,4-Hexadien-1-ol	2003	a
1176	(E,E)-2,4-Hexadienoic acid	2003	a
1180	(E,E)-2,4-Octadien-1-ol	2003	a
1183	2,4-Nonadien-1-ol	2003	a
1188	(E,Z)-2,6-Nonadien-1-ol acetate	2003	a
1189	(E,E)-2,4-Decadien-1-ol	2003	a
1191	Methyl (E)-2-(Z)-4-decadienoate	2003	a
1193	Ethyl 2,4,7-decatrienoate	2003	a
1199	(±)-2-Methyl-1-butanol	2003	a
1217	2-Methyl-2-octenal	2003	a
1218	4-Ethyloctanoic acid	2003	a
1226	8-Ocimenyl acetate	2003	a
1228	3,7,11-Trimethyl-2,6,10-dodecatrienal	2003	a
1229	12-Methyltridecanal	2003	a
1232	1-Ethoxy-3-methyl-2-butene	2003	b
1236	2,2,6-Trimethyl-6-vinyltetrahydropyran	2003	b
1239	Cycloionone	2003	a
1245	2,4-Dimethylanisole	2003	a
1248	1,2-Dimethoxybenzene	2003	a
1265	4-Propenyl-2,6-dimethoxyphenol	2003	a
1289	Erythro- and threo-3-mercapto-2-methylbutan-1-ol	2003	b
1290	(±)-2-Mercaptomethylpentan-1-ol	2003	b
1292	3-Mercapto-2-methylpentanal	2003	b
1293	4-Mercapto-4-methyl-2-pentanone	2003	b
1296	*spiro*[2,4-Dithia-1-methyl-8-oxabicyclo(3.3.0)octane-3,3´-(1´-oxa-2´-methyl)cyclopentane]	2003	a
1299	2,3,5-Trithiahexane	2003	b
1300	Diisopropyl trisulfide	2003	b
1311	2-(2-Methylpropyl)pyridine	2004	a
1319	2-Propionylpyrrole	2004	b
1322	2-Propylpyridine	2004	a
1334	4-Methylbiphenyl	2004	b
1342	δ-3-Carene	2004	a
1343	α-Farnesene	2004	a
1344	1-Methyl-1,3-cyclohexadiene	2004	a
1367	*trans*-2-Octen-1-yl acetate	2004	b
1368	*trans*-2-Octen-1-yl butanoate	2004	b
1369	*cis*-2-Nonen-1-ol	2004	b
1370	(E)-2-Octen-1-ol	2004	a
1371	(E)-2-Butenoic acid	2004	a
1372	(E)-2-Decenoic acid	2004	a
1373	(E)-2-Heptenoic acid	2004	a
1374	(Z)-2-Hexen-1-ol	2004	a
1375	*trans*-2-Hexenyl butyrate	2004	a

No.	Flavouring agent	Year	Note
1376	(E)-2-Hexenyl formate	2004	a
1377	*trans*-2-Hexenyl isovalerate	2004	a
1378	*trans*-2-Hexenyl propionate	2004	a
1379	*trans*-2-Hexenyl pentanoate	2004	a
1380	(E)-2-Nonenoic acid	2004	a
1381	(E)-2-Hexenyl hexanoate	2004	a
1382	(Z)-3- and (E)-2-Hexenyl propionate	2004	a
1384	2-Undecen-1-ol	2004	a
1407	Dihydronootkatone	2004	b
1409	β-Ionyl acetate	2004	a
1410	α-Isomethylionyl acetate	2004	a
1411	3-(l-Menthoxy)-2-methylpropane-1,2-diol	2004	a
1412	Bornyl butyrate	2004	a
1413	DL-Menthol(±)propylene glycol carbonate	2004	a
1414	L-Monomenthyl glutarate	2004	a
1415	L-Menthyl methyl ether	2004	a
1416	*para*-Menthane-3,8-diol	2004	a
1435	Taurine	2004	a
1438	L-Arginine	2004	a
1439	L-Lysine	2004	a
1447	Tetrahydrofurfuryl cinnamate	2004	a
1457	(±)-2-(5-Methyl-5-vinyltetrahydrofuran-2-yl)-propionaldehyde	2004	a
1475	Ethyl 2-ethyl-3-phenylpropanoate	2004	a
1478	2-Oxo-3-phenylpropionic acid	2004	a

[a] Flavourings for which only anticipated poundage data were available

[b] Flavourings for which the MSDI derived from anticipated poundage data from the USA was greater than the MSDI derived from recorded poundage data from the European Union

ANNEX 7

DIVERGENT OPINION ON SAFETY ASSESSMENT OF FLAVOURING SUBSTANCES

Gérard Pascal and Philippe Verger

Institut National de la Recherche Agronomique, Paris, France

JECFA has adopted part of the concept of 'threshold of toxicological concern' for evaluating flavouring agents. The concept is based on the assumption that, if the level of exposure is low, risk assessment can be based on data for structurally related compounds. The data include those on absorption, distribution, metabolism, excretion and toxicity for compounds of the same structural class. The threshold of toxicological concern is defined as the level of human exposure below which it can be anticipated there are no significant risk for health even in the absence of data on the compound itself.

The quality of the estimate of dietary exposure is therefore crucial for reaching a conclusion about the safety of flavouring agents evaluated by this Procedure.

The estimated dietary intake used by the Committee is based on the amount of the flavouring agent produced per year by industry (also called poundage data) divided by the number of consumers, assumed to be 10% of the population.

During the sixty-fifth meeting, 135 flavouring substances were submitted for safety assessment. Production figures were not available for 60 of them, and industry provided the Committee with 'anticipated production data', corresponding to volumes that might be produced in the future. The Committee agreed that these data were not adequate for use in its procedure for evaluating the safety of flavouring substances. Nevertheless, the Committee came to conclusions about the safety of these substances by applying the normal procedure, although making the conclusions conditional.

The minority opinion is that the safety of the 60 flavouring substances without reported poundage data should not be evaluated by the normal procedure, even on a conditional basis.

This volume contains monograph's prepared at the sixty-fifth meeting of the joint FAO/WHO Expert Committee on Food Additives (JECFA), which met in Geneva, Switzerland, from 7 to 16 June 2005.

The toxicological monograph's in this volume summarise the safety data on a number of food additives: Beeswax, Candelilla wax Quillaia extract Type 1 and 2, Phospholipase from *fusarium venenatum* expressed in *Aspergillus oryzae*, Calcium L-5 methyltetrahydrofolate (L-5_MTHF), and Pulllulan (Pullulan P1-20).

Monograph's on seven groups of related flavouring agents evaluated by the Procedure for the Safety Evaluation of Flavouring Agents are also included.

This volume and others in the WHO Food Additives series contain information that is useful to those who produce and use food additives and veterinary drugs and those involved with controlling contaminats in food, government and food regulatory officers, industrial testing laboratories, toxicological laboratories, and universities.