国際連合 ST/SG/AC.10/C.4/80

事務局

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英語版の邦訳
（訳者　中村）

危険物輸送および化学品の分類および表示に
関する世界調和システムに関する専門家委員会

化学品の分類および表示に関する世界調和システム専門家小委員会

第40回化学品の分類および表示に関する世界調和システム（GHS）専門家小委員会報告

2021年7月5日～9日ジュネーブにおいて開催

項目

I. 参加者

1. 第40回化学品の分類および表示の世界調和システムに関する専門家小委員会は、Ms. Maureen Ruskin (United States of America)を議長として、Ms. Nina John (Austria)を副議長として、2021年7月5日から9日に開催された。

2. 以下の国々からの専門家が会議に出席した: Argentina、Australia、Austria、Belgium、Canada、China、Finland、France、Germany、Italy、Japan、Netherlands、 New Zealand、Norway、Poland、Republic of Korea、Russian Federation、South Africa、Spain、Sweden、United KingdomそしてUnited States of America。

3. 経済社会理事会の手続き規則72に基づき、Chile、the Philippines、Switzerlandからのオブザーバーも出席した。

4. また、国際労働機関（ILO）と国連訓練調査研究所（UNITAR）の代表者も参加した。

5. 以下の政府間組織からも参加した：欧州連合と経済協力開発機構（OECD）。

6. 以下の非政府組織の代表がそれぞれの関連する事項について議論に加わるために参加した：Australasian Explosives Industry Safety Group Incorporated (AEISG); Compressed Gas Association (CGA); Croplife International; Dangerous Goods Advisory Council (DGAC); European Chemical Industry Council (Cefic); European Industrial Gases Association (EIGA); Federation of European Aerosol Associations (FEA); Fertilizers Europe (FE); Industrial Federation Paints and Coats of Mercosul (IFPCM); International Association for Soaps, Detergents and Maintenance Products (A.I.S.E); International Council on Mining and Metals (ICMM); International Organization of Motor Vehicle Manufacturers (OICA); International Petroleum Industry Environmental Conservation Association (IPIECA); Institute of Makers of Explosives (IME); Responsible Packaging Management Association of Southern Africa (RPMASA); そしてSporting Arms and Ammunition Manufacturers' Institute (SAAMI)。

II. 議事次第の採択（議題 1）

文書: ST/SG/AC.10/C.4/79 及び ST/SG/AC.10/C.4/79/Add.1 (secretariat)

非公式文書: INF.1, INF.2., INF.8 及び INF.13 (secretariat)

7. 小委員会は、非公式文書 INF.1 から INF.25を考慮し、修正した後、事務局が用意した暫定議題を採択した。

8. 小委員会は、経済社会理事会が2021年6月8日に決議2021/13を採択したことに留意した。この決議は、2020年12月に委員会が提出した決議案（ST/SG/AC.10/48, annex IV）に基づき、変更を加えずに採択された。

9. 出版物の状況について、事務局から小委員会に、GHSの改訂9版の英語版とフランス語版が既に入手可能であり、残りの言語も今年後半に発行される予定であることが通知された。

III. 世界調和システム（GHS）における作業（議題 2）

A. GHS小委員会に関連する事項の危険物輸送に関する専門家小委員会（TDG小委員会）での作業

非公式文書: INF.23, paragraphs 4 and 5 (secretariat)

10. 小委員会は、非公式文書INF.23のパラグラフ4および5にある、爆発物の定義の見直しに関する事項と、急性経皮毒性の動物種に関してモデル規則をGHSと整合させる提案に関するTDG小委員会の議論の結果に留意した。

B. 物理化学的危険性クラスにおける同時分類と危険有害性の優先順位

11. ドイツの専門家は、前回までの2年の間に第2.1章の見直し作業を行ったことで、物理化学的な危険性に関する専門家がこの危険有害性の同時分類と優先順位について並行して作業を行うことができず、その結果、これまでのところこの課題はほとんど進展がなかったと報告した。

12. 彼女は、TDG小委員会の火薬類作業部会長と、試験方法と分類基準のマニュアルの中で試験者の安全性がどのように扱われているかについて、既に議論を始めていることを示した。また、物理化学的危険性クラスにおける同時分類と危険有害性の優先順位に関する作業に関心のある専門家で、まだグループの配布リストに載っていない人は、できるだけ早く彼女（Ms.Cordula Wilrich）に連絡するよう呼びかけた。

C. 健康有害性分類に対する非動物試験法の使用

文書: ST/SG/AC.10/C.4/2021/4 (United Kingdom, Netherlands)

ST/SG/AC.10/C.4/2021/5 (United Kingdom, Netherlands)

非公式文書: INF.3, INF.4, INF.22 及び INF.18 (United Kingdom, Netherlands)

13. 小委員会は、非公式作業グループの作業に感謝の意を表した。

14. 3.3.2.7、3.3.3.1.3及び3.3.5.3.7で言及されているように、何が「重要な」酸/アルカリ予備と考えられうるのかを決定するための基準がないことに関する中国の専門家からの質問に対し、国際的に合意された単一の試験方法がない場合、GHSには特定の基準が提案されていないことが指摘された。いくつかの利用可能な方法（OECDテストガイドライン122やYoungらに記載されているものなど）があり、それらの間の違いを認めた上で、最も適切な方法や結果の評価は、所管官庁の裁量に委ねられた。

15. 3.2.2.3.2を更新する非公式文書INF.22の修正は、第3.3章の提案に関して、より一貫性のある変更を提供すると同時に、GHSが試験方法に対して中立であるという原則を再確認するものであることが指摘された。

16. 小委員会は、非公式文書INF.22（付属書I参照）で修正された、文書ST/SG/AC.10/C.4/2021/4の付属書の第3.3章の修正およびその結果生じるST/SG/AC.10/C.4/2021/5の第1.2章と第3.2章の修正を採択した。

17. 小委員会は、非公式文書INF.18の非公式作業グループの作業報告に留意し、特にGHSの第3.4章に皮膚感作性物質の非動物試験法を含めることに関連した現在進行中の活動に留意した。

D. OECD TG442Bに準拠した局所リンパ節アッセイ (LLNA)試験法の結果を用いた皮膚感作性物質の分類

非公式文書: INF.10 (Japan)

18. 小委員会は、皮膚感作性物質を区分1に分類するためのOECDガイドライン442B及び429のLLNA代替法の適用性を確認した日本の研究結果に留意した。また、皮膚感作性の代替法に関するOECD専門家グループが、非公式文書INF.10のパラグラフ10と表2に記載されている範囲、作業計画、タイムテーブルに従って、日本が提案した基準のデータ及び全体的な堅牢性をレビューすることに合意したことにも留意した。

19. 日本の専門家は、第41回小委員会で中間レビューの結果を報告し、第42回小委員会での審議に向けた提案の提出に間に合うように作業を終了させることが期待されると述べた。

E. 生殖細胞変異原性の分類基準（細区分1B）

文書: ST/SG/AC.10/C.4/2021/3 (European Union)

非公式文書: INF.24 (United States of America)

20. 文書 ST/SG/AC.10/C.4/2021/3 に記載されているように、生殖細胞変異原性の分類基準の明確化に関する作業について、拡張された範囲と追加項目について全般的な支持が得られた。しかし、提案された付託事項の中で、分類基準の変更のレビューに関するOECDの役割と関与をさらに明確にする必要があると考えられた。以上の理由により、小委員会は非公式文書INF.24で修正された付託事項を検討し、採択した。

21. OECDの代表は、この作業に対するOECDの支援を確認した。小委員会は、非公式作業グループで合意された分類基準の変更点は、最終的な採択を検討する前に、OECD遺伝毒性専門家グループに送られて検討されることに留意した。

22. また、この作業をOECDレベルでどのように進めていくか、OECDの会議日程や作業計画などの詳細については、2021年7月8日(木)に開催される生殖細胞変異原性の分類基準の明確化に関する非公式作業グループで議論されるであろう。非公式作業グループのリーダーは、この議論の結果について小委員会に情報を提供することを示唆した。

F. 実際の分類に関する問題（GHSへの改定提案）

23. 実際の分類に関する問題の非公式グループからGHSの改定案が提出されていないため、この議題については議論が行われなかった。小委員会は議題項目4（b）のグループの作業状況報告を検討した（パラグラフ68～70参照）。

G. ナノマテリアル

24. この議題では文書が提出されず、本議題は検討されなかった。

H. 附属書1から3および注意書きのさらなる合理化

1. 附属書3の第1、第2及び第3節の組合せ記述の修正

文書: ST/SG/AC.10/C.4/2021/1 (United Kingdom)

25. GHSの第1節、第2節、第3節への改正案については、原則として全般的な支持が得られた。しかし、小委員会は現在の案では合意に達することができなかった。一部の専門家は、現行のテキストに対する変更点を示す非公式の文書が添付されていないと、改正案を理解することが難しいと指摘した。

26. 現行のH315+H320の修正について、何人かの専門家は、文書ST/SG/AC.10/C.4/2021/1のパラグラフ17に概説されている代替案、すなわち、皮膚腐食性/刺激性区分2および眼に対する重篤な損傷性/眼刺激2Bについては、既存の組合せの注意書きH315+H320を維持し、皮膚腐食性/刺激性区分2および眼に対する重篤な損傷性/眼刺激区分2/2Aについては、H315+H319を別に新規項目として挿入することを希望すると表明した。また、所管官庁が導入した区分（2/2Aまたは2A/2B）に応じて、適用される記述を選択するべきであることを示す注記を含めることが支持された。

27. A3.1.2.5の文章案について、一部の専門家は、より明確にして読みやすさを向上させるために、すべての危険有害性が伝えられている限り、必要に応じて危険有害性情報を組み合わせることができることを明確にするために、文章を修正することを提案した。

28. 最後に、新たなP374に関する提案と、タイプAの自己反応性物質および混合物と、タイプAの有機過酸化物へのP373の適用性について、第2.1章の意味での爆発物ではないが、爆発性を有していることが指摘された。炎が、タイプAの物質/混合物に達するまでの消火活動の妥当性について、爆発物についても同様に議論された。また、タイプAの物質/混合物は、国連モデル規制では輸送が認められていないため、市場に出回ることはほとんどないだろうと指摘された。意見交換の後、小委員会は、この問題はさらに検討する必要があると結論づけ、非公式作業部会に、提出されたコメントを踏まえて提案をさらに進展させるよう求めた。

29. 英国の専門家は、非公式作業グループにおいて、提出されたすべてのコメントを考慮した修正案を第41回会合に提出することを目指して議論を続けることを伝えた。

2. 附属書3の第2及び第3節の修正

文書: ST/SG/AC.10/C.4/2021/2 (United Kingdom)

非公式文書: INF.19 (Germany)

30. 小委員会は、文書ST/SG/AC.10/C.4/2021/2のパラグラフ6～9（P232、P264、P270の修正）および31～34（GHSの附属書3の呼吸器感作性および皮膚感作性の修正）の修正を採択した（付属書I参照）。

31. 可燃性ガスのマトリックス表の修正案（文書ST/SG/AC.10/C.4/2021/2のパラグラフ25～27）について意見交換を行った後、小委員会は、非公式文書INF.19でドイツが表明した見解に同意し、GHSの附属書3（付属書I参照）において、自然発火性ガスおよび化学的に不安定なガスのマトリックス表の注釈を削除し、可燃性ガスのマトリックス表に注釈を導入しないという提案を採択した。

32. 皮膚腐食性の組合せの注意書きP302+P361+P354（「皮膚に付着した場合：直ちに汚染された衣類をすべて脱ぐこと。すぐに水で数分間洗うこと」）の曖昧さを解消するためにP354を修正するという提案については、何人かの専門家は、その組合せの記述をさらに検討する必要があると考えた。専門家からは、特に、対応措置の優先順位（例：衣類を脱いですぐにすすぐのではなく、衣類を脱ぎながらすすぐ）や、組合せの記述を見直すための全体的なアプローチの必要性などについてのコメントが寄せられた。小委員会は、非公式作業グループに対して、出されたコメントを考慮して提案を修正するよう求めた。

3. 非公式作業グループの作業進捗について

非公式文書: INF.17 (United Kingdom)

33. 小委員会は、非公式作業グループが危険有害性および注意書きの分かりやすさをさらに向上させるために行った作業に感謝の意を表し、非公式文書INF.17に記載された作業の進捗報告に留意した。

I. その他

1. 2.17章と2.1章の整合性：GHS改訂9版への修正

文書: ST/SG/AC.10/C.4/2021/6 (Sweden)

非公式文書: INF.23 paragraph 6 (Secretariat)

34. 小委員会は、TDG小委員会の火薬類作業部会がスウェーデンの専門家による文書を検討し、この提案に 対して好意的な意見を出したことに留意した。小委員会は、文書ST/SG/AC.10/C.4/2021/6（附属書II参照）で提案されたパラグラフ2.17.1.1および判定論理理2.17.1の修正を採択した。 これらの修正は GHS 改訂9 版の正誤表に記載されることが指摘された。

2. 2.17.2.1への修正

非公式文書: INF.6 (Germany)

35. 何人かの専門家は、この修正案が鈍性化爆発物（工業用ニトロセルロースを含む）の分類と試験に予期せぬ影響を与える可能性があることに懸念を示し、この問題はさらなる検討が必要であると考えた。議論の結果、小委員会はコメントした人々に対し、ドイツの専門家と協力して修正案を作成するよう要請した。修正案の範囲は、第2.17章を全面的に見直すのではなく、ドイツが非公式文書INF.6で最初に提起した問題と、工業用ニトロセルロースに関する議論の中で出されたコメントに限定すべきであると指摘された。

36. 小委員会は、改訂提案が確定したら、2022年6月に開催されるTDG小委員会の火薬類作業部会の次回会合でレビューを受け、その後、GHS小委員会での最終的な採択に向けて提出されることに合意した。

3. GHSにおける「眼刺激性」の定義のフランス語訳

非公式文書: INF.7 (Canada)

37. 「眼刺激性」に対する定義の仏語訳を見直す必要性について、フランス語圏の代表団の間で意見が一致しなかった。フランスの専門家とCeficの代表は、彼らの意見として、この提案は技術的な観点から正当化されないと指摘した。彼らは代わりに、英語版と仏語版の整合性を高めることを提案したが、この見解は小委員会では共有されなかった。現行の定義は比較的最近、実際の分類に関する問題の非公式作業グループで検討されたものであり、実施上の問題が報告されない限り、再度検討することは適切ではないのではないかと指摘された。

38. コメントを受けて、カナダの専門家は提案を取り下げた。

4. 「毒性」の定義に対する提案

非公式文書: INF.12 (RPMASA)

INF.23, paragraph 7 (secretariat)

39. 小委員会は、TDG小委員会が非公式文書INF.23で示したこの課題に関する見解と結論に同意した。

40. RPMASAの代表は、提案の意図をさらに明確にし、GHSの枠組みの中でこの概念を理解するために途上国が直面している困難に対処する方法を探るために、提案に意見を表明した人々に連絡するつもりであることを示した。

IV. GHSの実施（議題 3）

A. GHSに基づいて分類された化学品のリストの開発の可能性

非公式文書: INF.15 and INF.15/Add.1 (Canada and United States of America)

41. 小委員会は、スウェーデンが実施した「GHSの実施における国の物質分類リストの役割」に関する調査結果に留意した。

42. GHSに基づいて分類された化学品のリストの開発の可能性に関する非公式作業グループの活動について、米国の専門家は、2021年7月あるいは8月に開始される予定の調査について小委員会に報告した。この調査は、GHSに従った既存の国や地域、第三者機関の分類リストに関する知識のギャップを埋めることを目的とし、2020年に非公式作業グループで作成した指針となる質問との比較を示すものである（ST/SG/AC.10/C.4/2020/17 のパラグラフ4参照）。調査の結果は、第41回小委員会で発表される。

43. 小委員会は、非公式文書INF.15の付属書に記載された情報を確認し、検討に値する他のリストや、調査への参加に関心を持つそれらリストを管理する連絡窓口について、米国とカナダの専門家にフィードバックを提供するよう求められた。

B. 実施状況に関する報告

1. 南アフリカ

非公式文書: INF.5 (South Africa)

44. 小委員会は、南アフリカの専門家から提供された、労働安全衛生法に基づく「危険化学剤に関する規則」が2021年3月29日に法制化されたという情報に留意した。この規則は、GHS改訂8版に基づいており、職場における危険化学品について、GHS分類、安全データシート、ラベル表示を義務化し、公布日から18カ月間の移行期間を認めている。

2. チリ及びコロンビア

45. 小委員会は、チリ政府が2021年2月9日に「危険有害性物質および混合物の分類、表示、通知に関する規則」を発出したことを知らされた。この規則は、GHS改訂7版を実施するもので、官報に掲載された後、以下のような移行期間が認められている。

- 工業的使用を意図した化学品の場合：物質は1年、混合物は4年
- 規制の対象となるその他のすべての化学品：物質は2年、混合物は6年

46. 小委員会はまたコロンビアで労働省と健康・社会保護省が2021年4月7日に「2021年決議No.0733」を発行し、職場でGHS改訂6版の規定を実施しているとの情報も得た。この決議は発行日に発効し、物質については2年、混合物については3年の移行期間が設けられている。

47. 両国の実施状況に関する情報は、すでにGHS実施状況のウェブページ[1]で適宜更新されていることが言及された（両規則へのリンクを含む）。

3. アルゼンチン

48. 小委員会は、アルゼンチンの専門家が提供した、国家レベルでのGHSの実施に関連する過去および現在の活動に関する情報に留意した。化学品のリスク管理に関する法律の草案が完成し、GHSの実施に関する章を含める提案が検討されていることが言及された。

49. 南部共同市場（MERCOSUR）のレベルでは、小委員会は、2021～2024年の間に実施されるGHS関連活動に対応する有害化学品に関する作業計画が承認されたことに留意した。この計画には、GHSを実施するための技術的な規則の制定可能性についての評価も含まれている。

50. さらに、GHSに関連した活動がラテンアメリカ・カリブ地域の2021～2024年までの「化学品と廃棄物に関する政府間ネットワーク」の最新作業計画に含まれていることにも言及された。

51. 最後に、国際化学工業協会協議会（ICCA）が推進する地域バーチャル作業グループが設立され、この地域での化学品規制の枠組みづくりに関する官民の交流が図られていることが指摘された。

4. ニュージーランド

非公式文書: INF.25 (New Zealand)

[1] https://unece.org/transport/documents/2021/01/ghs-implementation-implementation-country

52. 小委員会は、ニュージーランドが、GHSの事前公開版に基づき2001年に実施された、危険有害性物質分類の枠組みの更新を完了したことに留意した。2020年10月15日には、GHS改訂7版を参照引用して適用している新たな立法文書（危険有害性物質(危険有害性分類)通知2020）が発行された。危険有害性分類告示は2021年4月30日に発効した。

53. また、新しい危険有害性分類通知により、危険有害性物質（ラベル表示）通知2017及び危険有害性物質（安全データシート）通知2017を、GHSの改訂5版から改訂7版へと整合させ、更新することができたことも言及された。危険有害性物質・新生物（Hazardous Substances and New Organisms Act：HSNO）法に基づくかなりの数の危険有害性物質の承認も、GHS改訂7版の分類基準に合わせて更新された。

54. 環境保護局（EPA）の危険有害性物質データベースの既存データは、国際統一化学情報データベース（IUCLID）に移行中で、2021年の最終四半期中にそのプロセスが完了する見込みであることが指摘された。

5. 持続可能なEUの化学品戦略

非公式文書: INF.21 (European Union)

55. 小委員会は、2020年10月14日[2]に発表された持続可能なEU化学品戦略の採択を受けたEUの今後の動きに関する情報に関心を持って留意した。

56. CLP（分類、ラベル表示および包装）規則（欧州連合規則1272/2008）をGHS改訂7版から8版、9版に改訂する作業が間もなく開始される予定であることが言及された。さらに、持続可能な化学品戦略に関連する広範な活動の一環として、CLP改訂は以下を目的としている：

(a) 内分泌かく乱物質；難分解性・生物蓄積性・毒性物質（PBTs）、難分解性・移動性・毒性物質（PMTs）に関する既存の基準を強化すること；

(b) 免疫毒性、神経毒性、陸生生物への毒性に関する特定の基準の必要性を評価すること。

57. 上記(a)および(b)の目的を達成するため、以下のようなアプローチで新たな危険有害性クラスを開発し、CLPに含める必要がある：

(a) 免疫毒性、神経毒性、陸生生物への有害性については、特定の基準の必要性を評価する提案が、2023～2024年の2年間に小委員会で検討されるために提出される。

(b) 内分泌かく乱物質、PBTs（非常に残留性が高く、非常に生物蓄積性の高い物質（vPvB）を含む）、PMTs（非常に残留性が高く、非常に移動性の高い物質（vPvM）を含む）については、既存の国際基準に基づく提案が欧州レベルですでに作成されており、まずは2022年末までにCLP規則を通じて実施される予定である。CLPを通じて欧州レベルで実施するための基準が採択された後、これらのエンドポイントをGHSに含めることを検討するための提案が、2023～2024年の期間に小委員会に提出されることになる。

58. 小委員会は、CLPで既に扱われている危険有害性クラスが、後にGHSに組み込まれ、異なる形で扱われるようになった場合には、GHSに準拠するように規制の改訂を検討するというEUの約束（コミットメント）に留意した。

59. 上記パラグラフ57に記載された提案の全体的な影響は、調査と影響評価を通じて評価されることにも留意した。また、利害関係者（EU域内外）との公開協議も行われることになった。小委員会のメンバーは、2021年7月から10月にかけて欧州委

[2] https://ec.europa.eu/environment/strategy/chemicals-strategy_en

員会のウェブサイト[3]を通じて実施される予定のCLP公開オンライン協議に参加するよう招かれた。

60. 小委員会は、持続可能なEU化学品戦略の実施に関する進捗状況について、引き続き報告を受ける。

6. GHSの実施における国際貿易協定の役割に関する調査

非公式文書: INF.14 (Sweden)

61. 小委員会は、非公式文書INF.14のパラグラフ7～10に反映されているように、地域貿易協定の環境条項がGHSの実施を促進するために利用されているかどうかを調査するために、スウェーデン化学品庁（KemI）が委託した研究結果に留意した。

62. 小委員会は、GHSに基づく分類及び表示に必要な情報が、化学品を輸入する国でどの程度利用可能かを調査するためのパイロット研究が進行中であることを知らされた。スウェーデンの専門家は、2021年末までにいくつかの予備的な結果が得られる可能性があり、その場合、それらは第41回小委員会会合で報告されるとした。

7. GHSの実施を支援するためのUNITARの活動

63. UNITARの代表は、GHSを実施するためのグローバルパートナーシップと連携して、GHS実施に関する各国の経験の背景調査が行われていることを示した。2021年に発表される予定の追加結果には、実施のための教訓に関する研究と、GHSに関連する法律の策定に関するガイダンスが含まれる。これらの情報は、グローバルパートナーシップのウェブサイト[4]で公開される予定である。

64. 小委員会は、ILOが作成したILOの方策とGHSに関する文書も利用可能であることに留意した。

C. 他の機関あるいは国際機関との共同作業

65. この議題では文書が提出されず、本課題は検討されなかった。

D. その他

66. この議題では文書が提出されず、本課題は検討されなかった。

V. GHS基準の適用に関するガイダンスの開発（議題 4）

A. 附属書9（セクションA9.7）及び附属書10と第4.1章との基準との整合

67. ICMMの代表は、第39回会合以降の非公式作業グループの活動について小委員会に報告した。同代表は、2回の書面による意見出しが完了し、非公式文書INF.9/Rev.1（第39回会合）で特定された未解決問題のうち2つについては、非公式作業グループで既に詳細に検討しており、他の2つの問題についてはまだ検討していないことを述べた。小委員会は、非公式作業グループが、第41回小委員会会合での検討に向けて文書を提出することを目指して作業を進めていることに留意した。

[3] https://ec.europa.eu/info/law/better-regulation/have-your-say_en
[4] https://unitar.org/global-partnership-implement-ghs

B. 実際の分類に関する問題

非公式文書: INF.20 (United States of America)

68. 小委員会は、非公式作業グループが、項目(c)と(d)の作業が完了するまで作業プログラムの項目(f)の検討を延期することを決定したことに留意した。

69. 項目(c)（暴露時間が1時間以外の試験データに対する吸入毒性値の変換に関するガイダンス）について、小委員会は、グループがガイダンスのいくつかの重要な原則について合意に達したことを知らされ、第41回会合での検討のために提案を提出する予定であることに留意した。

70. 項目(d)（加成方式）について、小委員会は、検討開始事項の議論が終了した後、欧州化学品庁が第1.3章の文章を提案するための最善の道筋と追加のガイダンスを作成する必要性を検討していることを通知された。

C. 実際の表示に関する問題

非公式文書: INF.9 (Cefic)

71. 小委員会は、非公式文書 INF.9 のパラグラフ 5 の質問に留意した。ある専門家は、職場でのデジタル化の適用の難しさも考慮すべきだと提案した。

72. Ceficの代表者は、危険有害性情報のデジタル化に関する経験を非公式作業グループと共有するよう専門家に呼びかけた。

D. その他

73. この議題では文書が提出されず、本課題は検討されなかった。

VI. 能力開発（議題 5）

74. UNITARの代表は、ガーナとキリバスがGHS実施法を策定することを支援する作業が進行中であり、スペイン語圏の利害関係者を対象とした安全データシート、ラベル表示、データ検索に関する技術ウェビナーが2021年6月に実施されたことを示した。小委員会は、次回のUNITARのGHS e-ラーニングコースが、2021年9月20日から11月29日まで（英語コース）、2021年9月27日から12月6日まで（スペイン語コース）開催されることに留意した。

75. アルゼンチンの専門家は、GHSの実施を支援するために自国で行われた活動の概要を提供した。例えば、GHSに準拠した安全データシート、分類、ラベル表示や試験の開発のための産業界への技術支援や、地球環境ファシリティ（GEF）プロジェクトのフレームワーク内で実施される活動が含まれる。

非公式文書: INF.11 (RPMASA)

76. 小委員会は、RPMASAによる南アフリカでの能力開発活動に関する情報に留意した。

VII. その他（議題 6）

A. 2020年のベイルート港での爆発事故をフォローアップするセミナー

非公式文書: INF.16 (secretariat to the UNECE Convention on the transboundary effects of Industrial accidents)

77. 小委員会は、2020年8月4日にベイルート港で発生した大量の硝酸アンモニウムの爆発事故を受けて、経験、優れた取り組み、教訓に関するオンラインセミナーの開催に関する情報に留意した。諮問グループのメンバーとして、既存のガイダンスや優れた取り組みに関する調査に回答したり、あるいは専門知識を共有することにより、セミナーに参加することに関心がある専門家は、事務局に連絡するよう求められた。なお、その調査は現在作成中であり、近日中に利用可能になることが指摘された。

78. アメリカの専門家は、セミナーへの参加と貢献の方法を検討することに関心を示した。

B. 第41回会合の開催日と提出期限

79. 事務局から、2021年の会議カレンダー計画は、会議管理部門の会議管理セクションが四半期ごとに評価しており、最終四半期の計画はまだ検討中であることが小委員会に伝えられた。可能性は低いものの、小委員会の第41回会合の会議準備の変更も完全には排除できないことが指摘された。ECEレベルでの計画に関する議論の結果が出るまで、小委員会は第41回会合の会議日程と文書提出期限を以下のように決めた：

- 会議日程：2021年12月8日～10日
- 公式文書の提出期限 : 2021年9月15日（GHS小委員会のみで検討するために提出された文書の場合）及び2021年9月6日（両小委員会、すなわちTDGとGHSによって検討するために提出された文書の場合）

C. Leroy氏 (Cefic)への賛辞

80. 小委員会は、2003年から小委員会の作業に参加してきたMs. Marie-Hélène Leroyが最後の出席となることを知らされた。小委員会は、Cefic代表団の団長として、また実際の表示の問題に関する非公式作業グループのリーダーとしての彼女の働きに感謝の意を表し、引退後の活躍を祈った。

VIII. 報告書の採択（議題 7）

81. 小委員会は、事務局により準備された草案に基づいて第 40 回会合の報告書（及びその付属書）を採択した。

付属書 I

[オリジナル: 英語と仏語]

化学品の分類および表示に関する世界調和システム改訂9版（ST/SG/AC.10/30/Rev.9）の修正案（実際の翻訳物と齟齬が出るとよろしくないため、和訳はしない）

第3.2章

3.2.1.2 Replace the second sentence with the following:

"Classification should be based on mutually acceptable data generated using methods that are validated according to international procedures. These include both OECD guidelines and equivalent methods (see 1.3.2.4.3).".

In the last sentence, replace "3.2.2.6" with "3.2.2.7".

3.2.1.3 In the first sentence, replace "3.2.2.7" with "3.2.2.8".

In the last sentence, replace "3.2.2.7.3" with "3.2.2.8.3"; "weight of evidence approach" with "weight of evidence assessment" and insert ", 3.2.2.7" after "1.3.2.4.9" in the references between brackets at the end of the paragraph.

3.2.2.1 Add ***"(Tier 1 in Figure 3.2.1)***" at the end of the heading.

3.2.2.2 In the heading: delete "test" and add ***"(Tier 1 in Figure 3.2.1)"*** at the end.

Amend the beginning of the first sentence to read: "OECD Test Guideline 404 is the currently available and internationally accepted animal test method…".

3.2.2.3 In the heading, add ***"(Tier 2 in Figure 3.2.1)"*** at the end.

3.2.2.3.2 Replace the first sentence (Wherever possible … to be applied") with the following:

"The classification criteria for the currently available in vitro/ex vivo test methods adopted by the OECD in test guidelines 430, 431, 435, and 439 are described in Tables 3.2.6 and 3.2.7 (see 3.2.5.3.4). Other validated in vitro/ex vivo test methods accepted by some competent authorities may also be considered. A competent authority may decide which classification criteria, if any, should be applied for other test methods to conclude on classification, including that a substance is not classified for effects on the skin.".

3.2.2.3.3 (new) Place the two last sentences of current paragraph 3.2.2.3.2 ("In vitro/ex vivo…into consideration") under a new paragraph 3.2.2.3.3 and replace "test method used" with "test method(s) used".

Renumber current paragraphs 3.2.2.2.3 to 3.2.2.3.3.3 as 3.2.2.3.4 to 3.2.2.3.4.3.

3.2.2.3.4.1 (new, former 3.2.2.3.3.1) Add "(see 3.2.5.3.4)" at the end of the paragraph after "Table 3.2.6".

Renumber current paragraphs 3.2.2.3.4 to 3.2.2.3.4.2 as 3.2.2.3.5 to 3.2.2.3.5.2

3.2.2.3.5.1 (new, former 3.2.2.3.4.1) Add "(see 3.2.5.3.4)" at the end of the paragraph after "Table 3.2.7".

3.2.2.3.5.2 (new, former 3.2.2.3.4.2) Delete the last sentence.

3.2.2.3.6 (new) Insert a new heading to read as follows:

"3.2.2.3.6 *No classification for effect on the skin*"

3.2.2.3.6.1 (new, former 3.2.2.3.4.3) Amend to read as follows:

"3.2.2.3.6.1 Where competent authorities do not adopt Category 3, a negative result in an *in vitro/ex vivo* test method for skin irritation that is validated according to international procedures, e.g. OECD Test Guideline 439, can be

used to conclude as not classified for skin irritation. Where competent authorities adopt Category 3, additional information is required to differentiate between Category 3 and no classification.

3.2.2.4 Amend the heading to read as follows:

*"***3.2.2.4** ***Classification based on other existing animal skin data (Tier 3 in Figure 3.2.1)****"*

3.2.2.5 Amend to read as follows:

*"***3.2.2.5** ***Classification based on extreme pH (pH ≤ 2 or ≥ 11.5) and acid/alkaline reserve (Tier 4 in Figure 3.2.1)***

In general, substances with an extreme pH (pH ≤ 2 or ≥ 11.5) are expected to cause significant skin effects, especially when associated with significant acid/alkaline reserve. A substance with pH ≤ 2 or ≥ 11.5 is therefore considered to cause skin corrosion (Category 1) in this tier if it has a significant acid/alkaline reserve or if no data for acid/alkaline reserve are available. However, if consideration of acid/alkaline reserve suggests the substance may not be corrosive despite the extreme pH value, the result is considered inconclusive within this tier (see Figure 3.2.1). A pH > 2 and < 11.5 is considered inconclusive and cannot be used for classification purposes. Acid/alkaline reserve and pH can be determined by different methods including those described in OECD Test Guideline 122 and Young et al. (1988), acknowledging that there are some differences between these methods (see 3.2.5.3.6). A competent authority may decide which criteria for significant acid/alkaline reserve can be applied."

3.2.2.6 Add ***"(Tier 5 in Figure 3.2.1)"*** at the end of the heading.

3.2.2.6.1 In the last sentence, replace "(structural alerts, SAR); quantitative structure-activity relationships (QSARs); computer experts systems; and" with "(structural alerts, SAR) or quantitative structure-activity relationships (QSARs), computer experts systems, and".

3.2.2.7 (new) Insert a new section 3.2.2.7 to read as follows:

"**3.2.2.7** ***Classification based on an overall weight of evidence assessment (Tier 6 in Figure 3.2.1)***

3.2.2.7.1 An overall weight of evidence assessment is indicated where none of the previous tiers resulted in a definitive conclusion on classification. In some cases, where the classification decision was postponed until the overall weight of evidence, but no further data are available, a classification may still be possible.

3.2.2.7.2 A substance with an extreme pH (pH ≤ 2 or ≥ 11.5) and non-significant acid/alkaline reserve (result considered inconclusive in Tier 4; see 3.2.2.5) and for which no other information is available, should be classified as skin corrosion Category 1 in this tier. If inconclusive information is also available from other tiers but the overall weight of evidence assessment remains inconclusive, the extreme pH (pH ≤ 2 or ≥ 11.5) result should take precedence and the substance should be classified as skin corrosion Category 1 in this tier independently of its acid/alkaline reserve. For mixtures, the approach is different and is detailed in 3.2.3.1.3.".

Renumber current section 3.2.2.7 as 3.3.2.8, and paragraphs 3.2.2.7.1, 3.2.2.7.2 and 3.2.2.7.3 as 3.2.2.8.1, 3.2.2.8.2 and 3.2.2.8.3.

3.2.2.8 (new, former 3.2.2.7) Add "***"(Figure 3.2.1)"*** at the end of the heading.

3.2.2.8.2 (new, former 3.2.2.7.2) Amend the first sentence to read as follows:

"In the tiered approach (Figure 3.2.1), existing human and standard animal data form the highest tier, followed by *in vitro/ex vivo* data, other existing animal

skin data, extreme pH and acid/alkaline reserve, and finally non-test methods.”.

In the second sentence, replace “weight of evidence approach” with “weight of evidence assessment”.

3.2.2.8.3 (new, former 3.2.2.7.3) Replace (twice) “weight of evidence approach” with “weight of evidence assessment”.

In the last sentence, replace “irritation” with “skin irritation” and add “are also available” at the end of the paragraph.

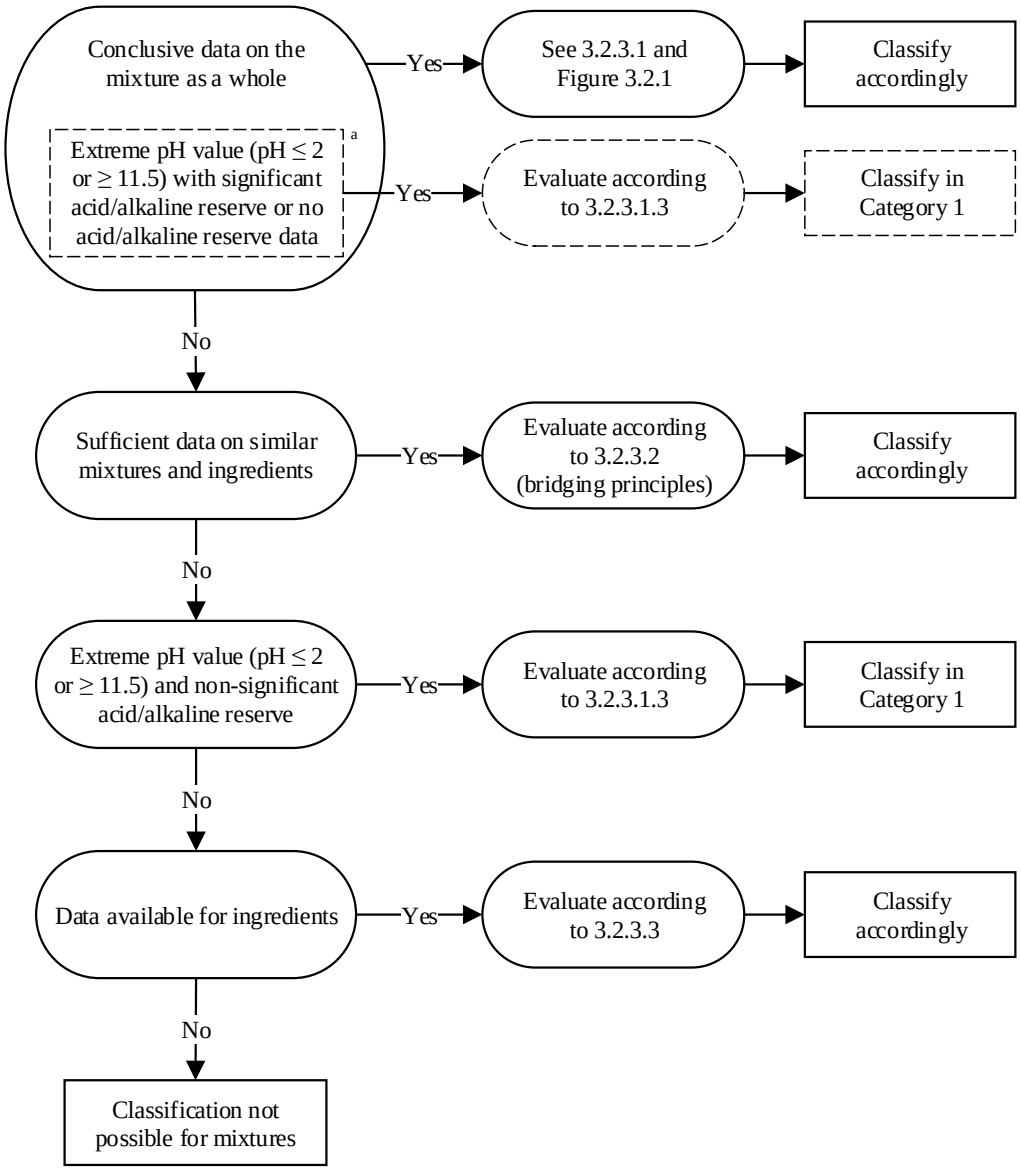
Figure 3.2.1 Amend as follows:

- Text between tier 3 and tier 4 boxes: Replace “No data or inconclusive[b]” with “No data, not classified for skin corrosion/irritation or inconclusive[b]”.
- Text between tier 4 and tier 5 boxes: Replace “data showing significant acid/alkaline reserve” with “data showing non-significant acid/alkaline reserve”.
- Text box for tier 6: add “(see 3.2.2.7)” at the end, after “assessment”.
- Exit box “Classification not possible”: amend the text to read: “Classification not possible for substances[c]”.
- In the box on the right-hand side starting with “Assess consistency with lower tiers” replace “3.2.2.7.3” with “3.2.2.8.3”.
- In note “a”, replace “3.2.2.7” with “3.2.2.8”.
- Add a new note “c” to read as follows: “[c] For mixtures, the flow chart in Figure 3.2.2 should be followed”.

3.2.3 Insert the following new text and figure under the current heading:

“The approach to classification for skin corrosion/irritation is tiered and is dependent upon the amount of information available for the mixture itself and for its ingredients. The flow chart of Figure 3.2.2 below outlines the process to be followed.

Figure 3.2.2: Tiered approach to classification of mixtures for skin corrosion/irritation



[a] *The dashed boxes represent an individual tier within conclusive data on the mixture as whole. However, in contrast to substances, mixtures having an "extreme pH value (pH ≤ 2 or ≥ 11.5) and non-significant acid/alkaline reserve" but no other conclusive data on the mixture as a whole, or no conclusive weight of evidence assessment from all available data on the mixture as whole, are not conclusive within the tiers for conclusive data on the mixture as a whole. Such mixtures should be first evaluated according to the bridging principles before the extreme pH value is considered as conclusive for classification.".*

3.2.3.1.1 In the last sentence, replace “calculation method” with “classification based on ingredients”.

3.2.3.1.2 Amend the first sentence to read as follows:

“*In vitro/ex vivo* test methods validated according to international procedures may not have been validated using mixtures; although these methods are considered broadly applicable to mixtures, they can only be used for classification of mixtures when all ingredients of the mixture fall within the applicability domain of the test method(s) used”.

3.2.3.1.3 Amend to read as follows:

"A mixture with an extreme pH (pH ≤ 2 or ≥ 11.5) is considered corrosive (Category 1) in Tier 4 if it has a significant acid/alkaline reserve or if no data for acid/alkaline reserve are available. However, if consideration of acid/alkaline reserve suggests the mixture may not be corrosive despite the extreme pH value, the result is considered inconclusive within Tier 4 (see Figure 3.2.1). If the overall weight of evidence assessment remains inconclusive or no data other than pH and acid/alkaline reserve are available, mixtures with an extreme pH (pH ≤ 2 or ≥ 11.5) and non-significant acid/alkaline reserve should be assessed using the bridging principles described in 3.2.3.2. If the bridging principles cannot be applied, mixtures with an extreme pH (pH ≤ 2 or ≥ 11.5) and non-significant acid/alkaline reserve should be classified as skin Category 1 (see Figure 3.2.2). A pH > 2 and < 11.5 is considered inconclusive and cannot be used for classification purposes. Acid/alkaline reserve and pH can be determined by different methods including those described in OECD Test Guideline 122 and Young et al. (1988), acknowledging that there are some differences between these methods (see 3.2.5.3.6). A competent authority may decide which criteria for significant acid/alkaline reserve can be applied."

3.2.3.2.5 Add "category" at the end of the current heading.

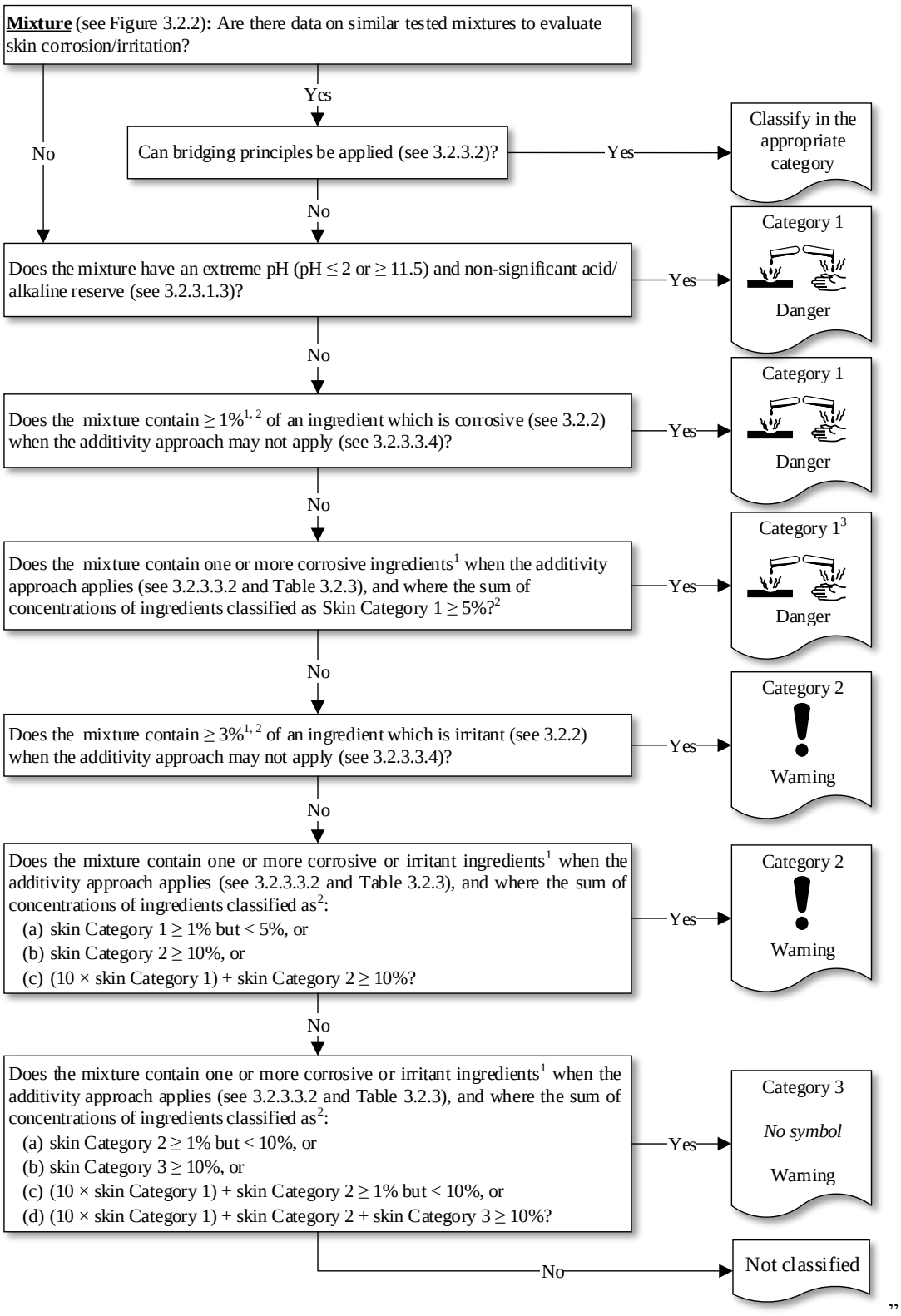
3.2.3.3.4 Amend the middle of the third sentence to read "…the pH should be used as the classification criterion (see 3.2.3.1.3) since extreme pH…".

3.2.5.1 In decision logic 3.2.1, amend the question starting with "Is the **substance or mixture**" to read as follows:

"Is the **substance or mixture corrosive**, an **irritant** or a **mild irritant** (see 3.2.2 and 3.2.3.1) in accordance with the tiered approach (see 3.2.2.8 and Figures 3.2.1 and 3.2.2?".

3.2.5.2 Replace decision logic 3.2.2 with the following:

"



"

In footnote 2, replace "*see 3.2.3.3.6*" with "*see 3.2.3.3.5 and 3.2.3.3.6"*.

3.2.5.3.1 Replace "weight of evidence approach" with "weight of evidence assessment".

3.2.5.3.4 In the heading, replace "*ex vivo* data" with "*in vitro/ex vivo* data" and in the first sentence replace "or 439" with "and/or 439".

3.2.5.3.6 Insert the following new paragraphs:

"3.2.5.3.6 *Guidance on the use of pH and acid/alkaline reserve for classification as skin corrosion/irritation*

3.2.5.3.6.1 Methods to determine the pH value such as OECD Test Guideline 122 and the method described by Young et al. (1988) differ in the concentration of the substance or mixture for which the pH is determined and include values of 1%, 10% and 100%. These methods also differ in the way the acid/alkaline reserve is determined, namely up to a pH of 7 for both acids and bases (OECD Test Guideline 122) or up to a pH of 4 for acids and a pH of 10 for bases (Young et al., 1988). Furthermore, there are differences between OECD Test Guideline 122 and Young et al. (1988) in the units used to express the acid/alkaline reserve.

3.2.5.3.6.2 Criteria to identify substances and mixtures requiring classification in Category 1 based on pH and acid/alkaline reserve have been developed for effects on the skin (Young et al., 1988). These criteria were developed using a combination of pH and acid/alkaline reserve values that were determined in a specific way (Young et al., 1988). Therefore, these criteria may not be directly applicable when other test concentrations or methods are used to measure pH and acid/alkaline reserve. Furthermore, the calibration and validation of these criteria was based on a limited dataset for effects on the skin. Thus, the predictive value of the combination of pH and acid/alkaline reserve for classification in Category 1 for effects on the skin is limited, especially for substances and mixtures with an extreme pH but a non-significant acid/alkaline reserve. The criteria developed by Young et al. (1988) for classification in Category 1 may be used as a starting point for determining whether a substance or a mixture has a significant acid/alkaline reserve or a non-significant acid/alkaline reserve. A competent authority may decide which criteria for significant acid/alkaline reserve can be applied.

_____

* *References:*

Young, J.R., M.J. How, A.P. Walker, and W.M. Worth. 1988. Classification as corrosive or irritant to skin of preparations containing acidic or alkaline substances, without testing on animals. Toxicol. In Vitro, 2(1): 19-26. doi: 10.1016/0887-2333(88)90032-x.".

(Ref. Doc: ST/SG/AC.10/C.4/2021/5 as amended by informal document INF.22)

Chapter 3.3

3.3.1.2 Replace with the following:

"3.3.1.2 To classify, all available and relevant information on serious eye damage/eye irritation is collected and its quality in terms of adequacy and reliability is assessed. Classification should be based on mutually acceptable data/results generated using methods and/or defined approaches[1] that are validated according to international procedures. These include both OECD guidelines and equivalent methods/defined approaches (see 1.3.2.4.3). Sections 3.3.2.1 to 3.3.2.8 provide classification criteria for the different types of information that may be available.".

Insert a new footnote 1 to read as follows:

"[1] According to OECD Guidance Document 255 on the reporting of defined approaches to be used within integrated approaches to testing and assessment, a defined approach to testing and assessment consists of a fixed data interpretation procedure (DIP) applied to data generated with a defined

set of information sources to derive a result that can either be used on its own, or together with other information sources within an overall weight of evidence assessment, to satisfy a specific regulatory need.".

3.3.1.3 and 3.3.1.4 Insert the following two new paragraphs:

"3.3.1.3 A *tiered approach* (see 3.3.2.10) organizes the available information into levels/tiers and provides for decision-making in a structured and sequential manner. Classification results directly when the information consistently satisfies the criteria. However, where the available information gives inconsistent and/or conflicting results within a tier, classification of a substance or a mixture is made on the basis of the weight of evidence within that tier. In some cases when information from different tiers gives inconsistent and/or conflicting results (see 3.3.2.10.3) or where data individually are insufficient to conclude on the classification, an overall weight of evidence assessment is used (see 1.3.2.4.9, 3.3.2.9 and 3.3.5.3.1).

3.3.1.4 Guidance on the interpretation of criteria and references to relevant guidance documents are provided in 3.3.5.3.".

3.3.2 Delete "(see Table 3.3.1)" in sub-paragraph (a) and "(see Table 3.3.2)" in sub-paragraph (b) and in the last sentence.

3.3.2.1 and 3.3.2.2 (new) Insert the following two new paragraphs:

"**3.3.2.1** ***Classification based on human data (Tier 1 in Figure 3.3.1)***

Existing reliable and good quality human data on serious eye damage/eye irritation should be given high weight where relevant for classification (see 3.3.5.3.2) and should be the first line of evaluation, as this gives information directly relevant to effects on the eye. Existing human data could be derived from single or repeated exposure(s), for example in occupational, consumer, transport or emergency response scenarios and epidemiological and clinical studies in well-documented case reports and observations (see 1.1.2.5 (c), 1.3.2.4.7 and 1.3.2.4.9). Although human data from accident or poison centre databases can provide evidence for classification, absence of incidents is not itself evidence for no classification, as exposures are generally unknown or uncertain.

3.3.2.2 ***Classification based on standard animal data (Tier 1 in Figure 3.3.1)***

OECD Test Guideline 405 is the currently available and internationally accepted animal test method for classification as serious eye damage or eye irritant (see Tables 3.3.1 and 3.3.2, respectively) and is the standard animal test. The current version of OECD Test Guideline 405 uses a maximum of 3 animals. Results from animal studies conducted under previous versions of OECD Test Guideline 405 that used more than 3 animals are also considered standard animal tests when interpreted in accordance with 3.3.5.3.3.".

3.3.2.1.1 to 3.3.2.1.2.3 Current paragraphs 3.3.2.1.1 to 3.3.2.1.2.3 become new paragraphs 3.3.2.2.1 to 3.3.2.2.2.3.

Table 3.3.1 Delete note "a". Current notes "b" and "c" become "a" and "b" respectively.

In note "b" replace "3.3.5.3" with "3.3.5.3.3".

3.3.2.2.2.1 (new, former 3.3.2.1.2.1) In the last sentence, replace "chemical" with "substance".

3.3.2.2.2.2 (new, former 3.3.2.1.2.2) Replace "categories 2A and 2B" with "Category 2A and Category 2B".

Table 3.3.2 Delete note "a". Current notes "b" and "c" become "a" and "b" respectively.

In note "b", replace "3.3.5.3" with "3.3.5.3.3.".

3.3.2.2 and 3.3.2.2.1 Current paragraphs 3.3.2.2 and 3.3.2.2.1 become new paragraphs 3.3.2.10 and 3.3.2.10.1.

Delete paragraphs 3.3.2.2.2; 3.3.2.2.3, 3.3.2.2.4, 3.3.2.2.5 and 3.3.2.2.6.

3.3.2.3 to 3.3.2.9 Insert the following new paragraphs (and related footnotes 2 and 3):

"3.3.2.3 *Classification based on defined approaches (Tier 2 in Figure 3.3.1)*

Defined approaches consist of a rule-based combination of data obtained from a predefined set of different information sources (e.g. *in vitro* methods, *ex vivo* methods, physico-chemical properties, non-test methods). It is recognized that most single *in vitro*/*ex vivo* methods are not able to replace *in vivo* methods fully for most regulatory endpoints. Thus, defined approaches can be useful strategies of combining data for classifying substances and mixtures. Results obtained with a defined approach validated according to international procedures, such as an OECD defined approach guideline or an equivalent approach, is conclusive for classification for serious eye damage/eye irritation if the criteria of the defined approach are fulfilled (see 3.3.5.3.4)[2]. Data from a defined approach can only be used for classification when the tested substance is within the applicability domain of the defined approach used. Additional limitations described in the published literature should also be taken into consideration.

3.3.2.4 *Classification based on in vitro/ex vivo data (Tier 2 in Figure 3.3.1)*

3.3.2.4.1 The classification criteria for the currently available *in vitro*/*ex vivo* test methods adopted by the OECD in test guidelines 437, 438, 460, 491, 492, 494 and 496 are described in Table 3.3.6 (see 3.3.5.3.5.1). When considered individually, these *in vitro/ex vivo* OECD test guidelines address serious eye damage and/or no classification for eye hazard, but do not address eye irritation. Therefore, data from a single *in vitro/ex vivo* OECD test guideline can only be used to conclude on either classification in Category 1 or no classification and cannot be used to conclude on classification in Category 2. When the result of a single *in vitro*/*ex vivo* method is "no stand-alone prediction can be made" (e.g. see Table 3.3.6), a conclusion cannot be drawn on the basis of that single result and further data are necessary for classification (see 3.3.5.3.4.3 and 3.3.5.3.4.4).

3.3.2.4.2 Other validated *in vitro/ex vivo* test methods accepted by some competent authorities are described in 3.3.5.3.5.2. Some of these *in vitro/ex vivo* test methods may be useful to classify in Category 2. A competent authority may decide which classification criteria, if any, should be applied for these test methods to conclude on classification, including that a substance is not classified for effects on the eye.

3.3.2.4.3 *In vitro/ex vivo* data can only be used for classification when the tested substance is within the applicability domain of the test method(s) used. Additional limitations described in the published literature should also be taken into consideration.

3.3.2.4.4 *Serious eye damage (Category 1)/Irreversible effects on the eye*

3.3.2.4.4.1 Where tests have been undertaken in accordance with OECD test guidelines 437, 438, 460, 491 and/or 496, a substance is classified for serious eye damage in Category 1 based on the criteria in Table 3.3.6 (see 3.3.5.3.5.1).

3.3.2.4.4.2 Although the currently available OECD *in vitro*/*ex vivo* test guidelines and equivalent methods have not been developed to identify substances inducing discolouration of the eye, some comparable effects may be observed in these tests. Therefore, where, after washing, discolouration of the cornea or of the tested cells compared to the control is observed in OECD Test Guideline 437, 438, 492 or 494, or in other equivalent methods,

suggesting a permanent effect, a competent authority may require classification of a substance for serious eye damage in Category 1.

3.3.2.4.5 *Eye irritation (Category 2)/Reversible effects on the eye*

3.3.2.4.5.1 A positive result in an *in vitro*/*ex vivo* test method that is validated according to international procedures for identification of substances inducing eye irritation can be used to classify for eye irritation in Category 2/2A[3].

3.3.2.4.5.2 Where competent authorities adopt Category 2A and Category 2B, it is important to note that the currently validated *in vitro/ex vivo* test methods for effects on the eye do not allow discrimination between these two categories. In this situation, if the criteria for classification in Category 2 have been considered fulfilled, and no other relevant information is available, classification in Category 2/2A should be applied.

3.3.2.4.6 *No classification for effects on the eye*

OECD test guidelines 437, 438, 491, 492, 494 and 496 (see Table 3.3.6 in 3.3.5.3.5.1) can be used to conclude that a substance is not classified for effects on the eye.

3.3.2.5 *Classification based on conclusive human data, standard animal data or in vitro/ex vivo data for skin corrosion (Tier 3 in Figure 3.3.1)*

Substances classified as corrosive to skin (skin Category 1) based on conclusive human data, standard animal data or *in vitro*/*ex vivo* data for skin corrosion according to the criteria in Chapter 3.2 are also deemed as inducing serious eye damage (eye Category 1). Skin irritation (skin Category 2), mild skin irritation (skin Category 3) and no classification for skin irritation, as well as human patch data (as described in Chapter 3.2), cannot be used alone to conclude on eye irritation or no classification for effects on the eye, but may be considered in an overall weight of evidence assessment.

3.3.2.6 *Classification based on other existing animal skin or eye data (Tier 4 in Figure 3.3.1)*

Other existing skin or eye data in animals may be used for classification, but there may be limitations regarding the conclusions that can be drawn (see 3.3.5.3.6). Substances classified as corrosive to skin (skin Category 1) based on other existing skin data according to the criteria in Chapter 3.2 are also deemed as inducing serious eye damage (eye Category 1). Other existing skin data leading to classification in skin Category 2, 3 or no classification, cannot be used alone to conclude on eye irritation or no classification for effects on the eye, but may be considered in an overall weight of evidence assessment."

3.3.2.7 *Classification based on extreme pH (pH ≤ 2 or ≥ 11.5) and acid/alkaline reserve (Tier 5 in Figure 3.3.1)*

In general, substances with an extreme pH (pH ≤ 2 or ≥ 11.5) are expected to cause significant eye effects, especially when associated with significant acid/alkaline reserve. A substance with pH ≤ 2 or ≥ 11.5 is therefore considered to cause serious eye damage (Category 1) in this tier if it has a significant acid/alkaline reserve or if no data for acid/alkaline reserve are available. However, if consideration of acid/alkaline reserve suggests the substance may not cause serious eye damage despite the extreme pH value, the result is considered inconclusive within this tier (see Figure 3.3.1). A pH > 2 and < 11.5 is considered inconclusive and cannot be used for classification purposes. Acid/alkaline reserve and pH can be determined by different methods including those described in OECD Test Guideline 122 and Young et al. (1988), acknowledging that there are some differences between these methods (see 3.3.5.3.7). A competent authority may decide which criteria for significant acid/alkaline reserve can be applied.

3.3.2.8 ***Classification based on non-test methods for serious eye damage/eye irritation or for skin corrosion (Tier 6 in Figure 3.3.1)***

3.3.2.8.1 Classification, including the conclusion not classified, can be based on non-test methods, with due consideration of reliability and applicability, on a case-by-case basis. Such methods include computer models predicting qualitative structure-activity relationships (structural alerts, SAR) or quantitative structure-activity relationships (QSARs), computer expert systems, and read-across using analogue and category approaches.

3.3.2.8.2 Read-across using analogue or category approaches requires sufficiently reliable test data on similar substance(s) and justification of the similarity of the tested substance(s) with the substance(s) to be classified. Where adequate justification of the read-across approach is provided, it has in general higher weight than (Q)SARs.

3.3.2.8.3 Classification based on (Q)SARs requires sufficient data and validation of the model. The validity of the computer models and the prediction should be assessed using internationally recognized principles for the validation of (Q)SARs. With respect to reliability, lack of alerts in a SAR or expert system is not sufficient evidence for no classification.

3.3.2.8.4 Conclusive non-test data for skin corrosion may be used for classification for effects on the eye. Thus, substances classified as corrosive to skin (skin Category 1) according to the criteria in Chapter 3.2 are also deemed as inducing serious eye damage (eye Category 1). Skin irritation (skin Category 2), mild skin irritation (skin Category 3) and no classification for skin irritation according to Chapter 3.2 cannot be used alone to conclude eye irritation or no classification for effects on the eye, but may be considered in an overall weight of evidence assessment.

3.3.2.9 ***Classification based on an overall weight of evidence assessment (Tier 7 in Figure 3.3.1)***

3.3.2.9.1 An overall weight of evidence assessment using expert judgement is indicated where none of the previous tiers resulted in a definitive conclusion on classification. In some cases, where the classification decision was postponed until the overall weight of evidence, but no further data are available, a classification may still be possible.

3.3.2.9.2 A substance with an extreme pH (pH $\leq$ 2 or $\geq$ 11.5) and non-significant acid/alkaline reserve (result considered inconclusive in Tier 5; see 3.3.2.7) and for which no other information is available, should be classified as serious eye damage Category 1 in this tier. If inconclusive information is also available from other tiers but the overall weight of evidence assessment remains inconclusive, the extreme pH (pH $\leq$ 2 or $\geq$ 11.5) result should take precedence and the substance should be classified as serious eye damage Category 1 in this tier independently of its acid/alkaline reserve. For mixtures, the approach is different and is detailed in 3.3.3.1.3.”.

Insert the following new footnotes 2 and 3 at the bottom of the page in relation to paragraphs 3.3.2.3 (for footnote 2) and 3.3.2.4.5.1 (for footnote 3):

“[2] *Some defined approaches have been proposed for serious eye damage/eye irritation (Alépée et al., 2019a, b) but no classification criteria have yet been agreed internationally.”.*

“[3] *Although no classification criteria have yet been agreed internationally for some validated and/or accepted in vitro/ex vivo test methods proposed for identifying substances inducing eye irritation, these test methods may still be accepted by some competent authorities (see 3.3.2.4.2). If a defined approach (see 3.3.2.3) is not available or is not adequate for classification, data from these methods may be considered in a weight of evidence assessment within this tier.”.*

3.3.2.10 and 3.3.2.10.1 (new, former 3.3.2.2 and 3.3.2.2.1) Amend to read as follows:

"3.3.2.10 *Classification in a tiered approach (Figure 3.3.1)"*

3.3.2.10.1 A tiered approach to the evaluation of initial information should be considered, where applicable (Figure 3.3.1), recognizing that not all elements may be relevant. However, all available and relevant information of sufficient quality needs to be examined for consistency with respect to the resulting classification.".

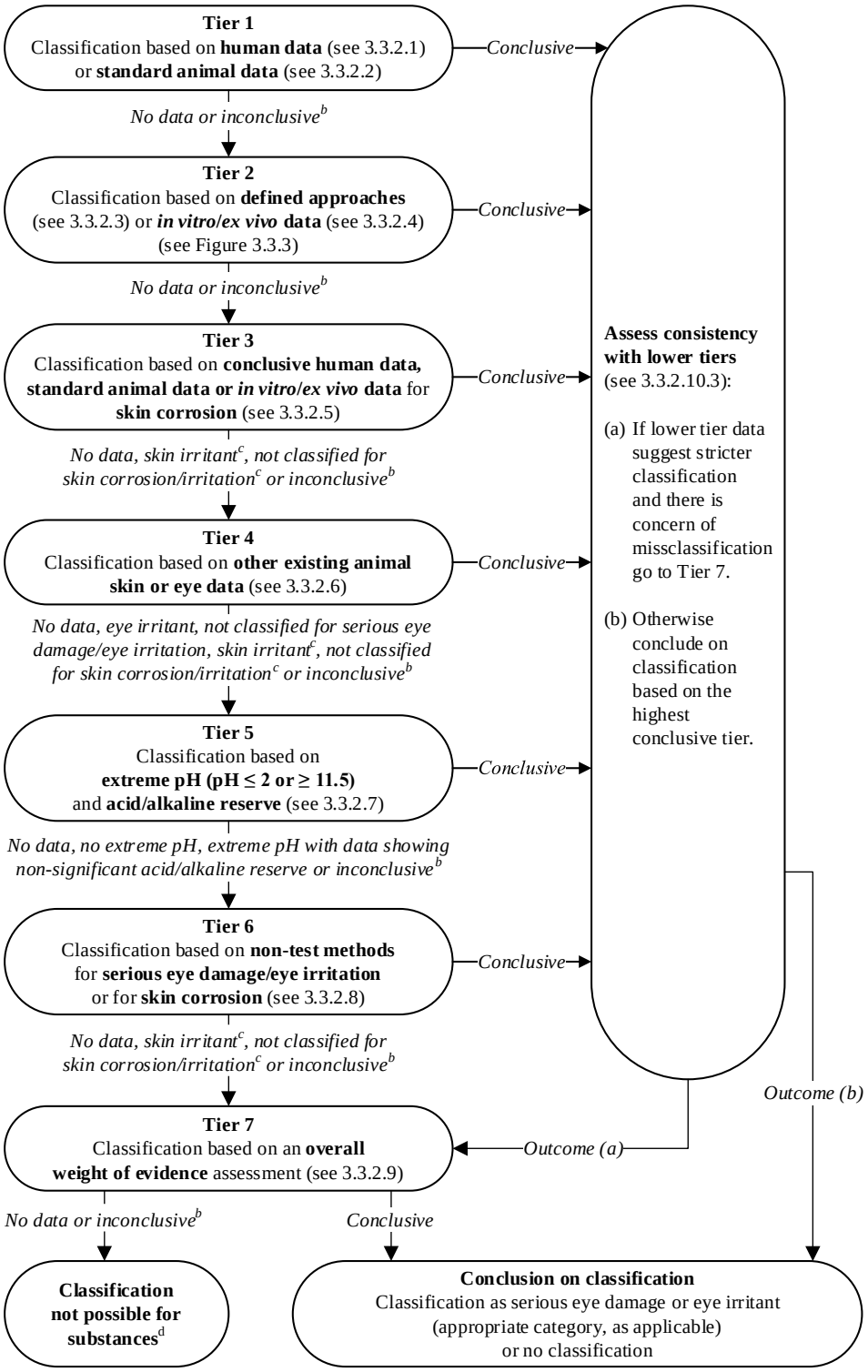
3.3.2.10.2 and 3.3.2.10.3 Insert the following two new paragraphs:

"3.3.2.10.2 In the tiered approach (Figure 3.3.1), existing human and standard animal data for eye effects form the highest tier, followed by defined approaches and *in vitro/ex vivo* data for eye effects, existing human/standard animal/*in vitro*/*ex vivo* data for skin corrosion, other existing animal skin or eye data, extreme pH and acid/alkaline reserve, and finally non-test methods. Where information from data within the same tier is inconsistent and/or conflicting, the conclusion from that tier is determined by a weight of evidence assessment.

3.3.2.10.3 Where information from several tiers is inconsistent and/or conflicting with respect to the resulting classification, information of sufficient quality from a higher tier is generally given a higher weight than information from a lower tier. However, when information from a lower tier would result in a stricter classification than information from a higher tier and there is concern for misclassification, then classification is determined by an overall weight of evidence assessment. For example, having consulted the guidance in 3.3.5.3 as appropriate, classifiers concerned with a negative result for serious eye damage in an *in vitro/ex vivo* study when there is a positive result for serious eye damage in other existing eye data in animals would utilise an overall weight of evidence assessment. The same would apply in the case where there is human data indicating eye irritation but positive results from an *in vitro/ex vivo* test for serious eye damage are also available."

Figure 3.3.1: Replace with the following:

"**Figure 3.3.1: Application of the tiered approach for serious eye damage/eye irritation[a]**"



".

Replace current notes “a”, “b”, “c” and “d” to Figure 3.3.1 with the following:

“[a] *Before applying the approach, the explanatory text in 3.3.2.10 as well as the guidance in 3.3.5.3 should be consulted. Only adequate and reliable data of sufficient quality should be included in applying the tiered approach.*

[b] *Information may be inconclusive for various reasons, e.g.:*

- *The available data may be of insufficient quality, or otherwise insufficient/inadequate for the purpose of classification, e.g. due to quality issues related to experimental design and/or reporting;*
- *The available data may be insufficient to conclude on the classification, e.g. they might be indicative for absence of serious eye damage, but inadequate to demonstrate eye irritation;*
- *Where competent authorities make use of the eye irritation categories 2A and 2B, the available data may not be capable of distinguishing between Category 2A and Category 2B.”*

[c] *It is recognized that not all skin irritants are eye irritants and that not all substances that are non-irritant to skin are non-irritant to the eye (see 3.3.2.5, 3.3.2.6, 3.3.2.8.4 and 3.3.2.9.1).”*

[d] *For mixtures, the flow chart in Figure 3.3.2 should be followed.”.*

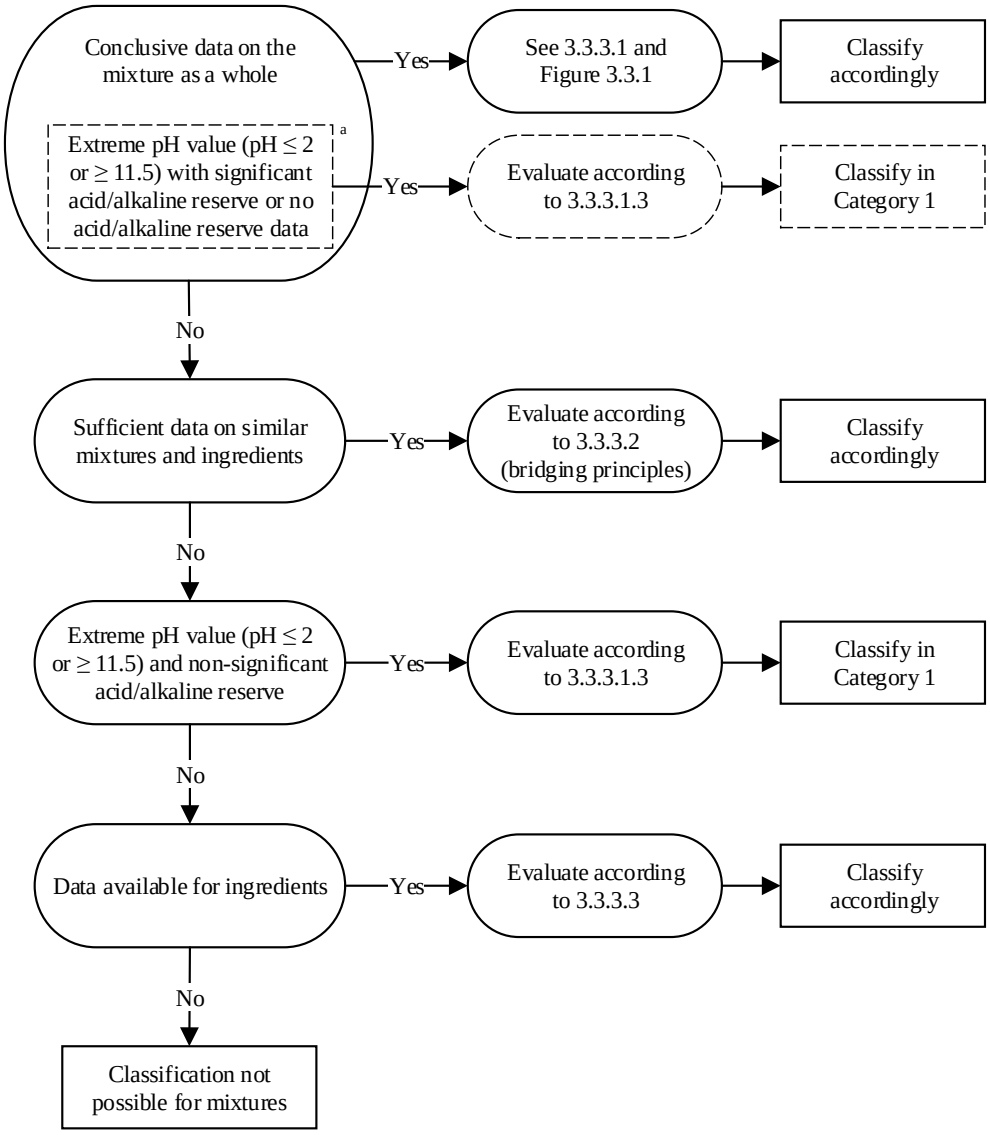
Delete current notes “e” and “f” to Figure 3.3.1.

3.3.3 Amend to read as follows:

“3.3.3 Classification criteria for mixtures

The approach to classification for serious eye damage/eye irritation is tiered and is dependent upon the amount of information available for the mixture itself and for its ingredients. The flow chart of Figure 3.3.2 below outlines the process to be followed.

Figure 3.3.2: Tiered approach to classification of mixtures for serious eye damage/eye irritation



”

[a] *The dashed boxes represent an individual tier within conclusive data on the mixture as whole. However, in contrast to substances, mixtures having an "extreme pH value (pH ≤ 2 or ≥ 11.5) and non-significant acid/alkaline reserve" but no other conclusive data on the mixture as a whole, or no conclusive weight of evidence assessment from all available data on the mixture as whole, are not conclusive within the tiers for conclusive data on the mixture as a whole. Such mixtures should be first evaluated according to the bridging principles before the extreme pH value is considered as conclusive for classification.”.*

3.3.3.1.1 and 3.3.3.1.2 Amend to read as follows:

“3.3.3.1.1 In general, the mixture should be classified using the criteria for substances, taking into account the tiered approach to evaluate data for this hazard class (as illustrated in Figure 3.3.1) and 3.3.3.1.2 and 3.3.3.1.3 below. If classification is not possible using the tiered approach, then the approach described in 3.3.3.2 (bridging principles), or, if that is not applicable, 3.3.3.3 (classification based on ingredients) should be followed.

3.3.3.1.2 Defined approaches and/or in vitro/ex vivo test methods validated according to international procedures may not have been validated using mixtures; although these approaches/methods are considered broadly applicable to mixtures, they can only be used for classification of mixtures

when all ingredients of the mixture fall within the applicability domain of the defined approach or test method(s) used. Specific limitations regarding applicability domains are described in the respective defined approaches and test methods and should be taken into consideration as well as any further information on such limitations from the published literature. Where there is reason to assume or evidence indicating that the applicability domain of a particular defined approach or test method is limited, data interpretation should be exercised with caution, or the results should be considered not applicable.".

3.3.3.1.3 Insert a new paragraph to read as follows:

"3.3.3.1.3 A mixture with an extreme pH (pH ≤ 2 or ≥ 11.5) is considered to cause serious eye damage (Category 1) in Tier 5 if it has a significant acid/alkaline reserve or if no data for acid/alkaline reserve are available. However, if consideration of acid/alkaline reserve suggests the mixture may not cause serious eye damage despite the extreme pH value, the result is considered inconclusive within Tier 5 (see Figure 3.3.1). If the overall weight of evidence assessment remains inconclusive or no data other than pH and acid/alkaline reserve are available, mixtures with an extreme pH (pH ≤ 2 or ≥ 11.5) and non-significant acid/alkaline reserve should be assessed using the bridging principles described in 3.3.3.2. If the bridging principles cannot be applied, mixtures with an extreme pH (pH ≤ 2 or ≥ 11.5) and non-significant acid/alkaline reserve should be classified as eye Category 1 (see Figure 3.3.2). A pH > 2 and < 11.5 is considered inconclusive and cannot be used for classification purposes. Acid/alkaline reserve and pH can be determined by different methods including those described in OECD Test Guideline 122 and Young et al. (1988), acknowledging that there are some differences between these methods (see 3.3.5.3.7). A competent authority may decide which criteria for significant acid/alkaline reserve can be applied.".

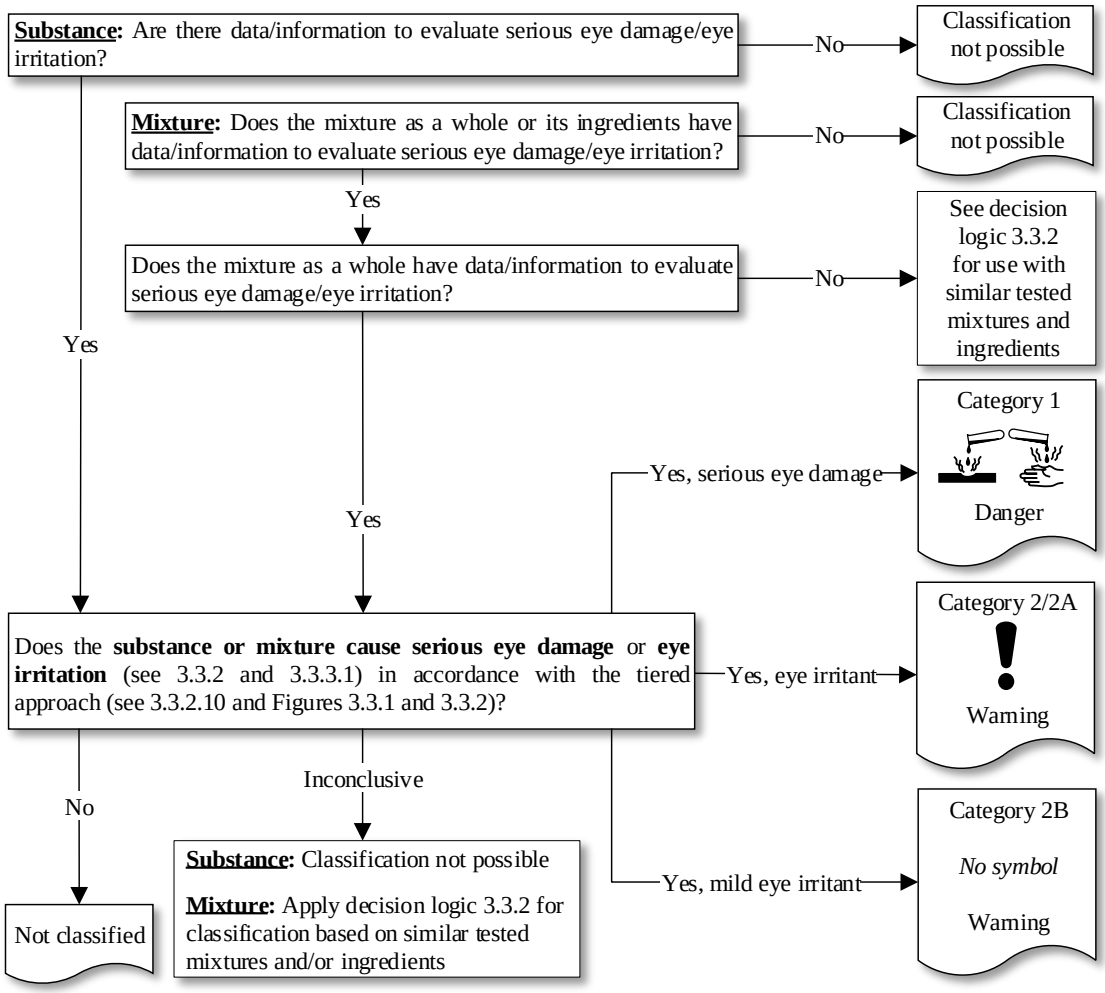
3.3.3.2.7 Replace "aerosolized form of mixture" with "aerosolized form of the mixture". Renumber footnote 3 as 4.

3.3.3.3.4 In the second sentence, replace "should be used as classification criterion (see 3.3.3.1.2) since pH" with "should be used as the classification criterion (see 3.3.3.1.3) since extreme pH" and delete "(subject to consideration of acid/alkali reserve).

Table 3.3.5, third column Replace "Category 2A" with: "Category 2/2A".

3.3.5.1 Replace decision logic 3.3.1 with the following:

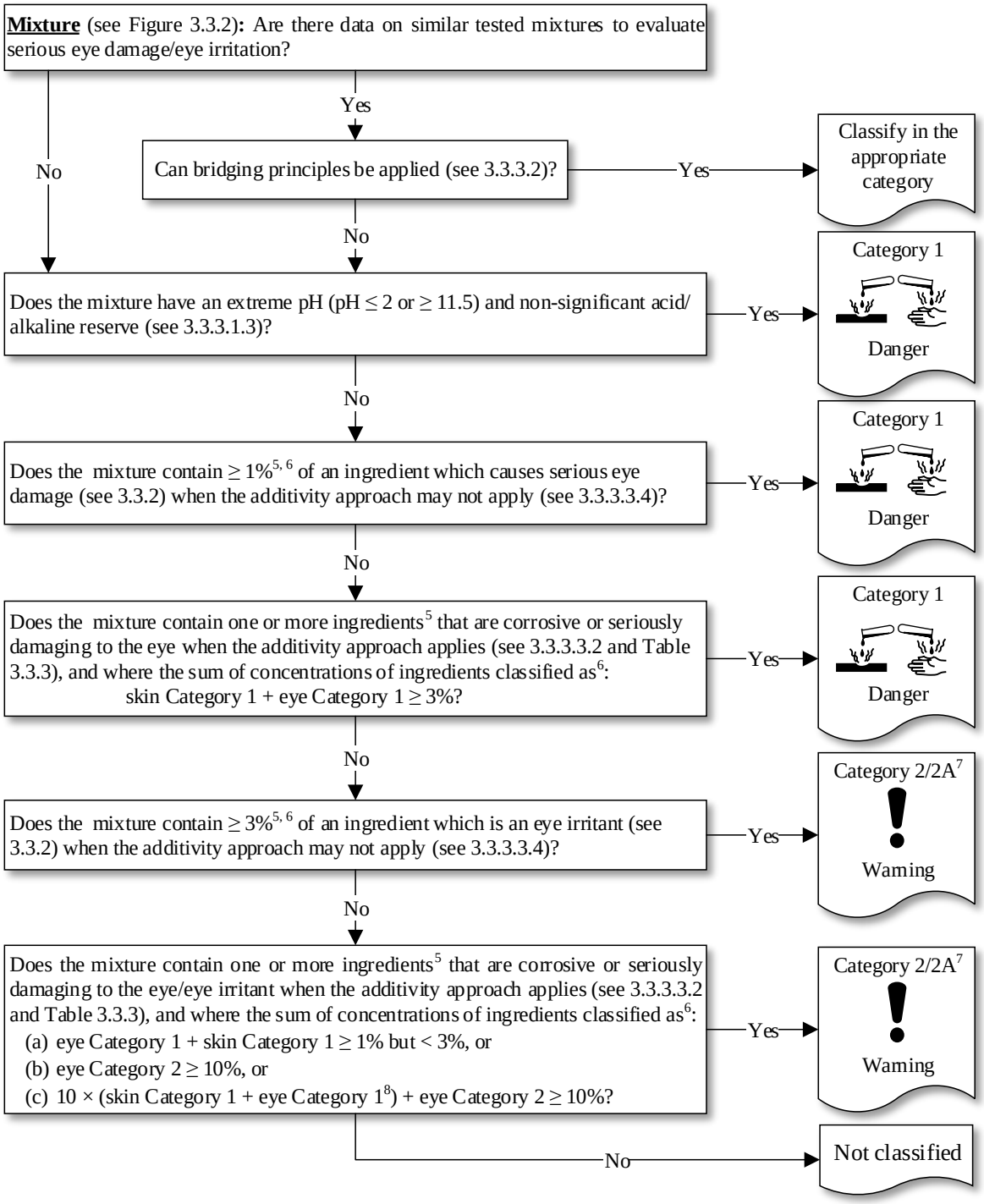
“



”

3.3.5.2 Replace decision logic 3.3.2 with the following:

"



"

Current footnotes "4", "5", "6" and "7" become "5", "6", "7" and "8".

3.3.5.3.1 to 3.3.5.3.5 Current paragraphs 3.3.5.3.1 to 3.3.5.3.5 become new paragraphs 3.3.5.3.3.1 to 3.3.5.3.3.5.

3.3.5.3.1 and 3.3.5.3.2 (new) Insert the following two new paragraphs:

"3.3.5.3.1 *Relevant guidance documents*

Helpful information on the strengths and weaknesses of the different test and non-test methods, as well as useful guidance on how to apply a weight of evidence assessment, is provided in OECD Guidance Document

263 on an integrated approach on testing and assessment (IATA) for serious eye damage and eye irritation.

3.3.5.3.2 *Guidance on the use of human data for classification as serious eye damage/eye irritation*

The availability of human data for serious eye damage/eye irritation is limited and the data available may contain some uncertainty. However, where such data exist, they should be considered based on their quality. Human data may be obtained from epidemiological studies, human experience (e.g. consumer experience), poison control centres, national and international home accident surveillance programs, case studies, or worker experience and accidents. Human case studies may have limited predictive value as often the presence of a substance or mixture in the eye will result in pain and quick washing of the eyes. Therefore, the effects observed may underestimate the intrinsic property of the substance or the mixture to affect the eye without washing. Further details on the strengths and limitations of human data for serious eye damage/eye irritation can be found in OECD Guidance Document 263 (section 4.1. Module 1: Existing human data on serious eye damage and eye irritation).".

3.3.5.3.3 Insert the following new heading:

"3.3.5.3.3 *Classification based on standard animal tests with more than 3 animals*"

3.3.5.3.3.2 (new, former 3.3.5.3.2) Replace "3.3.2.1" with "3.3.2.2", "done" with "performed".

3.3.5.3.4 to 3.3.5.3.7.2 Insert the following new sections:

"3.3.5.3.4 *Guidance on the use of defined approaches and/or in vitro/ex vivo data for classification within Tier 2 of Figure 3.3.1*

3.3.5.3.4.1 Defined approaches consist of a predefined set of different information sources (e.g. *in vitro* methods, *ex vivo* methods, physico-chemical properties, non-test methods) which, combined together through a fixed Data Interpretation Procedure (DIP) to convert input data into a prediction (or result), can provide a conclusion on the classification of a substance or mixture. A fixed DIP is defined as any fixed algorithm for interpreting data from one or typically several information sources and is rule-based in the sense that it is based, for example on a formula or an algorithm (e.g. decision criteria, rule or set of rules) that do not involve expert judgment. The output of a DIP generally is a prediction of a biological effect of interest or regulatory endpoint. Since in a defined approach the information sources are prescribed and the set of rules on how to integrate and interpret them is predetermined, the same conclusion will always be reached by different assessors on the same set of data as there is no room for subjective interpretation. In contrast, in a weight of evidence assessment, expert judgment is applied on an ad hoc basis to the available information, which may lead to different conclusions because there are no fixed rules for interpreting the data.

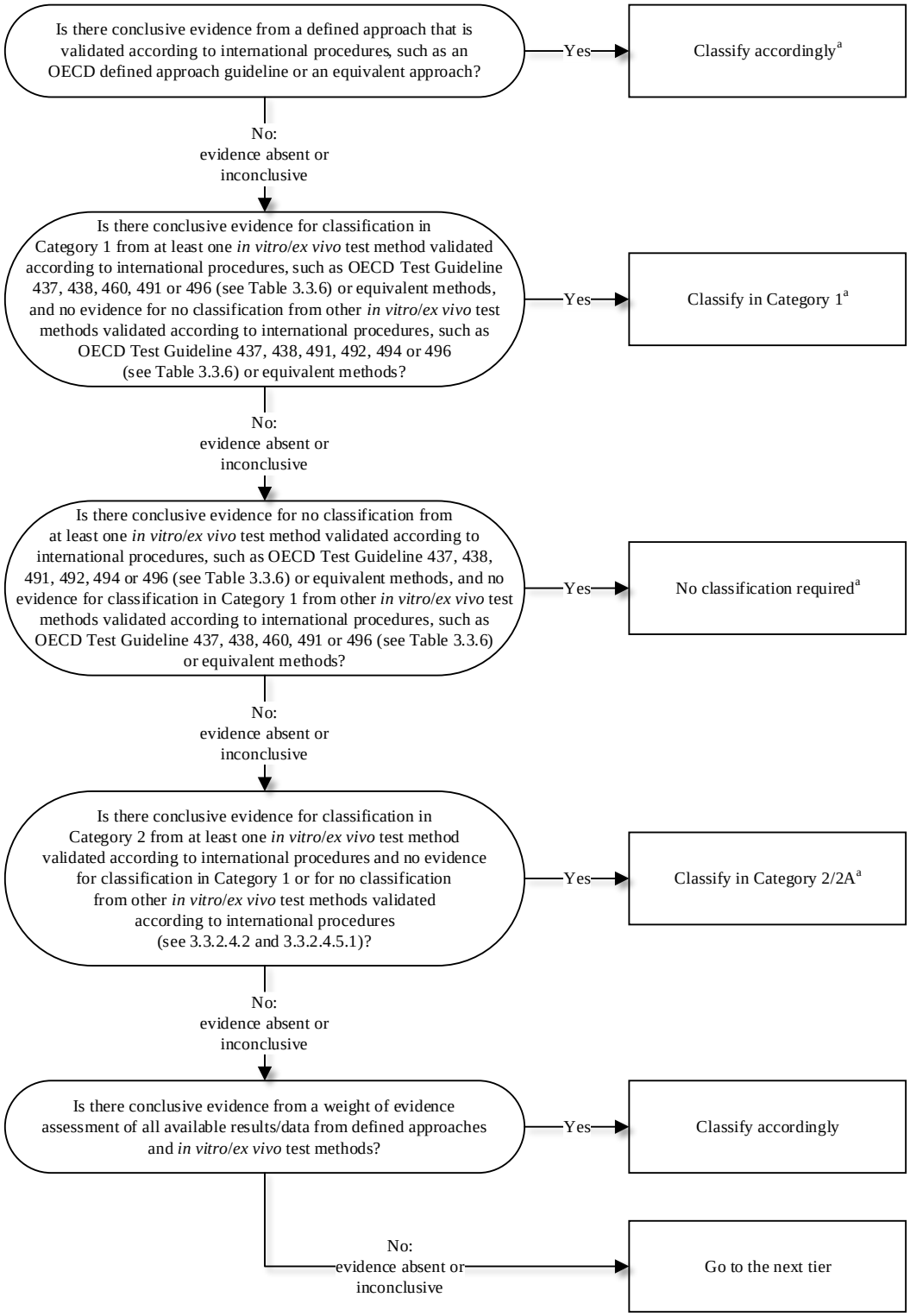
3.3.5.3.4.2 A stepwise approach to the evaluation of information derived from Tier 2 of Figure 3.3.1, i.e. defined approaches and/or *in vitro*/*ex vivo* test methods, should be considered where applicable (Figure 3.3.3), recognizing that not all elements may be relevant. However, all available and relevant information of sufficient quality needs to be examined for consistency with respect to the resulting classification. The outcome of a defined approach containing conclusive animal and/or human data may also eventually be considered during the overall weight of evidence in Tier 7 (see Figure 3.3.1). Where information from several steps is inconsistent and/or conflicting with respect to the resulting classification, information of sufficient quality from a higher step is generally given a higher weight than information from a lower step. However, when information from a lower step would result in a stricter

classification than information from a higher step and there is concern for misclassification, then classification is determined by a within-tier weight of evidence assessment. For example, classifiers concerned with a negative result for serious eye damage in a defined approach when there is a positive result for serious eye damage in an *in vitro*/*ex vivo* method would utilise a within-tier weight of evidence assessment.

3.3.5.3.4.3 Current *in vitro*/*ex vivo* test methods are not able to distinguish between certain *in vivo* effects, such as corneal opacity, iritis, conjunctiva redness or conjunctiva chemosis, but they have shown to correctly predict substances inducing serious eye damage/eye irritation independently of the types of ocular effects observed *in vivo*. Many of the current *in vitro*/*ex vivo* test methods can thus identify substances or mixtures not requiring classification with high sensitivity but with limited specificity when used to distinguish not classified from classified substances or mixtures. This means that it is reasonably certain that a substance or mixture identified as not requiring classification by OECD Test Guideline 437, 438, 491, 492, 494 or 496 (see Table 3.3.6) is indeed not inducing eye effects warranting classification, whereas some substances or mixtures not requiring classification will be over-predicted by these *in vitro*/*ex vivo* test methods when used in isolation. Furthermore, it should be considered that substances inducing serious eye damage are identified by many of these test methods with a high specificity but a limited sensitivity when used to distinguish Category 1 from Category 2 and not classified. This means that it is reasonably certain that a substance or mixture identified as Category 1 by OECD Test Guideline 437, 438, 460, 491 or 496 (see Table 3.3.6) is indeed inducing irreversible eye effects, whereas some substances or mixtures inducing serious eye damage will be under-predicted by these *in vitro*/*ex vivo* test methods when used in isolation. As a consequence, a single *in vitro*/*ex vivo* OECD test guideline method is currently sufficient to conclude on either Category 1 or no classification according to the criteria defined in Table 3.3.6, but not to conclude Category 2. When the result of an *in vitro*/*ex vivo* method is "no stand-alone prediction can be made" (e.g. see Table 3.3.6), a conclusion cannot be drawn on the basis of that single result and further data are necessary for classification. Some *in vitro/ex vivo* test methods validated according to international procedures but not adopted as OECD test guidelines may be accepted by some competent authorities to classify in Category 2 (see 3.3.5.3.5.2). Moreover, combinations of *in vitro*/*ex vivo* methods in tiered approaches or their integration in defined approaches (see 3.3.2.3) may reduce the number of false predictions and show adequate performance for classification purposes.

3.3.5.3.4.4 In the absence of an adequate defined approach (see 3.3.2.3) or of conclusive *in vitro*/*ex vivo* data (see 3.3.2.4.1 and 3.3.2.4.2), a stand-alone prediction is not possible. In such cases, a within-tier weight of evidence assessment of data from more than one method would be needed to classify within Tier 2. If a within-tier weight of evidence assessment is still not conclusive, then data from lower tiers may be required to reach a conclusion (see Figure 3.3.1).

Figure 3.3.3: Classification based on defined approaches and/or *in vitro*/*ex vivo* data within Tier 2 of Figure 3.3.1



[a] *Evidence is considered conclusive if the data fulfil the criteria of the defined approach or of the method and there is no contradicting in vitro/ex vivo information. When information from a lower step would result in a stricter classification than information from a higher step and there is concern for misclassification, then classification is determined by a within-tier weight of evidence assessment.*

3.3.5.3.5 *Classification criteria based on in vitro/ex vivo data*

3.3.5.3.5.1 Where *in vitro/ex vivo* tests have been undertaken in accordance with OECD test guidelines 437, 438, 460, 491, 492, 494 and/or 496, the criteria for classification in Category 1 for serious eye damage/irreversible effects on the eye and for no classification are set out in Table 3.3.6.

Table 3.3.6: Criteria for serious eye damage/irreversible effects on the eye and for no classification[a] for *in vitro*/*ex vivo* methods

Category	OECD Test Guideline 437 Bovine Corneal Opacity and Permeability test method	OECD Test Guideline 438 Isolated Chicken Eye test method	OECD Test Guideline 460 Fluorescein Leakage test method	OECD Test Guideline 491 Short Time Exposure test method	OECD Test Guideline 492 Reconstructed human Cornea-like Epithelium (RhCE)-based test methods: Methods 1, 2, 3 and 4 as numbered in Annex II of OECD Test Guideline 492	OECD Test Guideline 494 Vitrigel-Eye Irritancy Test Method	OECD Test Guideline 496 *In vitro* Macromolecular Test Method (test method 1)
	Organotypic *ex vivo* assay using isolated corneas from the eyes of freshly slaughtered cattle. Test chemicals are applied to the epithelial surface of the cornea. Damage by the test chemical is assessed by quantitative measurements of: - Corneal opacity changes measured using a light transmission opacitometer (opacitometer 1) or a laserlight-based opacitometer (LLBO, opacitometer 2) - Permeability (sodium fluorescein dye). Both measurements are used to calculate an *In Vitro* Irritancy Score (IVIS) when using opocitometer 1 or a LLBO Irritancy Score (LIS) when using opacitometer 2. **Criteria based on IVIS or LIS.**	Organotypic *ex vivo* assay based on the short-term maintenance of chicken eyes *in vitro*. Test chemicals are applied to the epithelial surface of the cornea. Damage by the test chemical is assessed by (i) a quantitative measurement of increased corneal thickness (swelling), (ii) a qualitative assessment of corneal opacity, (iii) a qualitative assessment of damage to epithelium based on application of fluorescein to the eye, and (iv) a qualitative evaluation of macroscopic morphological damage to the surface. Histopathology can be used to increase the sensitivity of the method for identifying Category 1 non-extreme pH ($2 < pH < 11.5$) detergents and surfactants. [b] **Criteria based on the scores of corneal swelling, opacity and fluorescein retention, which are used to assign ICE classes (I, II, III or IV) to each endpoint, and on macroscopic and histopathology assessment** [b]	Cytotoxicity and cell-function based *in vitro* assay that is performed on a confluent monolayer of Madin-Darby Canine Kidney (MDCK) CB997 tubular epithelial cells cultured on permeable inserts. The toxic effects of a test chemical are measured after a short exposure time (1 minute) by an increase in permeability of sodium fluorescein through the epithelial monolayer of MDCK cells. The amount of fluorescein leakage that occurs is proportional to the chemical-induced damage to the tight junctions, desmosomal junctions and cell membranes, and is used to estimate the ocular toxicity potential of a test chemical. **Criteria based on mean percent fluorescein leakage following a defined exposure period**	Cytotoxicity-based *in vitro* assay that is performed on a confluent monolayer of Statens Seruminstitut Rabbit Cornea (SIRC) cells. Each test chemical is tested at both 5 % and 0.05 % concentrations. Following five-minute exposure, cell viability is assessed by the enzymatic conversion in viable cells of the vital dye MTT into a blue formazan salt that is quantitatively measured after extraction from cells. **Criteria based on mean percent cell viability following a defined exposure period**	Three-dimensional RhCE tissues are reconstructed from either primary human cells or human immortalised corneal epithelial cells, which have been cultured for several days to form a stratified, highly differentiated squamous epithelium, consisting of at least 3 viable layers of cells and a non-keratinised surface, showing a cornea-like structure morphologically similar to that found in the human cornea. Following exposure and post-treatment incubation (where applicable), tissue viability is assessed by the enzymatic conversion in viable cells of the vital dye MTT into a blue formazan salt that is quantitatively measured after extraction from the tissues. **Criteria based on mean percent tissue viability following defined exposure and post-exposure (where applicable) periods**	*In vitro* assay using human corneal epithelium models fabricated in a collagen vitrigel membrane (CVM) chamber. The eye irritation potential of the test chemical is predicted by analysing time-dependent changes in transepithelial electrical resistance values using the value of three indexes. Resistance values are measured at intervals of 10 seconds for a period of three minutes after exposure to the test chemical preparation. **Criteria based on the 3 measured indexes: time lag, intensity and plateau level of electrical resistance**.	*In vitro* assay consisting of a macromolecular plant-based matrix obtained from jack bean *Canavalis enisformis*. This matrix serves as the target for the test chemical and is composed of a mixture of proteins, glycoproteins, carbohydrates, lipids and low molecular weight components, which form a highly ordered and transparent gel structure upon rehydration. Test chemicals causing ocular damage lead to the disruption and disaggregation of the highly organized macromolecular reagent matrix, and produce turbidity of the macromolecular reagent. Such phenomena is quantified, by measuring changes in light scattering. **Criteria based on a Maximum Qualified Score (MQS) derived from the Optical Density readings at different concentrations, calculated via a software.**

Category	OECD Test Guideline 437 Bovine Corneal Opacity and Permeability test method		OECD Test Guideline 438 Isolated Chicken Eye test method	OECD Test Guideline 460 Fluorescein Leakage test method	OECD Test Guideline 491 Short Time Exposure test method	OECD Test Guideline 492 Reconstructed human Cornea-like Epithelium (RhCE)-based test methods: Methods 1, 2, 3 and 4 as numbered in Annex II of OECD Test Guideline 492				OECD Test Guideline 494 Vitrigel-Eye Irritancy Test Method	OECD Test Guideline 496 *In vitro* Macromolecular Test Method (test method 1)
1	Opacitometer 1 IVIS > 55	Opacitometer 2 LIS > 30 and lux/7 ≤ 145 and OD490 > 2.5, OR LIS > 30 and lux/7 > 145	At least 2 ICE class IV, OR Corneal opacity = 3 at 30 min (in at least 2 eyes), OR Corneal opacity = 4 at any time point (in at least 2 eyes), OR Severe loosening of the epithelium (in at least 1 eye), OR Certain histopathological effects[b]	Chemical concentration causing 20 % of Fluorescein Leakage (FL_{20}) ≤ 100 mg/mL	Viability ≤ 70 % at 5 % and 0.05 %	No stand-alone prediction can be made				No stand-alone prediction can be made	MQS > 30.0
2/2A/2B	No stand-alone prediction can be made.	No stand-alone prediction can be made	No stand-alone prediction can be made	No stand-alone prediction can be made	No stand-alone prediction can be made	No stand-alone prediction can be made				No stand-alone prediction can be made	No stand-alone prediction can be made
Not classified	Opacitometer 1 IVIS ≤ 3	Opacitometer 2 LIS ⩽ 30	ICE class I for all 3 endpoints, OR ICE class I for 2 endpoints and ICE class II for the other endpoint, OR ICE class II for 2 endpoints and ICE class I for the other endpoint	No stand-alone prediction can be made	Viability > 70 % at 5 % and 0.05 %	Test method 1 Liquids and Solids: Viability > 60 %	Test method 2 Liquids: Viability > 60 %; Solids: Viability > 50 %	Test method 3 Liquids and Solids: Viability > 40 %	Test method 4 Liquids: Viability > 35 %; Solids: Viability > 60 %	Time lag > 180 seconds and Intensity < 0.05 %/seconds and Plateau level ≤ 5.0 %	MQS ≤ 12.5

[a] *Grading criteria are understood as described in OECD test guidelines 437, 438, 460, 491, 492, 494 and 496.*

[b] *For criteria, please consult OECD Test Guideline 438*

3.3.5.3.5.2 A non-exhaustive list of other validated *in vitro*/*ex vivo* test methods accepted by some competent authorities but not adopted as OECD test guidelines are listed below. A competent authority may decide which classification criteria, if any, should be applied for these test methods:

- Time to Toxicity (ET_{50}) tests using the Reconstructed human Cornea-like Epithelia (RhCE) described in OECD Test Guideline 492 (Kandarova et al., 2018; Alépée et al., 2020);
- *Ex Vivo* Eye Irritation Test (EVEIT): an *ex vivo* assay that uses excised rabbit corneal tissues kept in culture for several days and monitors tissue recovery to model both reversible and non-reversible eye effects. Full-thickness tissue recovery is monitored non-invasively using optical coherence tomography (OCT) (Frentz et al., 2008; Spöler et al., 2007; Spöler et al., 2015);
- Porcine Ocular Cornea Opacity/Reversibility Assay (PorCORA): an *ex vivo* assay that uses excised porcine corneal tissues kept in culture for up to 21 days and monitors tissue recovery to model both reversible and non-reversible eye effects. The tissues are stained with fluorescent dye and effects on the corneal epithelia are visualised by the retention of fluorescent dye (Piehl et al., 2010; Piehl et al., 2011);
- EyeIRR-IS assay: a genomic approach applied to a RhCE model (Cottrez et al., 2021);
- *In vitro* Macromolecular Test Method (test method 2), similar to test method 1 described in OECD Test Guideline 496 (Choksi et al., 2020);
- Metabolic activity assay: *In vitro* assay consisting of measuring changes to metabolic rate in test-material treated L929 cell monolayer (Harbell et al., 1999; EURL ECVAM, 2004a; Hartung et al., 2010; Nash et al., 2014);
- Hen's Egg Test on the Chorio-Allantoic Membrane (HET-CAM): an organotypic assay that uses the vascularised membrane of fertile chicken eggs to assess a test material's potential to cause vascular changes (Spielmann et al., 1993; Balls et al., 1995; Spielmann et al., 1996; Brantom et al., 1997; ICCVAM, 2007; ICCVAM, 2010);
- Chorio-Allantoic Membrane Vascular Assay (CAMVA): an organotypic assay that uses the vascularised membrane of fertile chicken eggs to assess a test material's potential to cause vascular changes (Bagley et al., 1994; Brantom et al., 1997; Bagley et al., 1999; Donahue et al., 2011);
- Neutral Red Release (NRR) assay: *In vitro* assay that quantitatively measures a substance's ability to induce damage to cell membranes in a monolayer of normal human epidermal keratinocytes (NHEK) (Reader et al. 1989; Reader et al., 1990; Zuang, 2001; EURL ECVAM, 2004b; Settivari et al., 2016); and
- Isolated Rabbit Eye (IRE) test, similar to OECD Test Guideline 438 but using isolated rabbit eyes instead of isolated chicken eyes (Burton et al., 1981; Whittle et al. 1992; Balls et al., 1995; Brantom et al., 1997; ICCVAM, 2007; ICCVAM, 2010).

3.3.5.3.6 *Guidance on the use of other existing skin or eye data in animals for classification as serious eye damage or eye irritation*

3.3.5.3.6.1 The availability of other animal data for serious eye damage/eye irritation may be limited as tests with the eye as the route of exposure are not normally performed. An exception could be historical data from the Low Volume Eye Test (LVET) that might be used in a weight of evidence assessment. The LVET is a modification of the standard OECD Test Guideline 405 test method.

3.3.5.3.6.2 Existing data from the LVET test could be considered for the purpose of classification and labelling but must be carefully evaluated. The differences between the LVET and OECD Test Guideline 405 may result in a classification in a lower category (or no classification) based on LVET data, than if the classification was based on data derived from the standard in vivo test (OECD Test Guideline 405). Thus, positive data from the LVET test could be a trigger for considering classification in Category 1 on its own, but data from this test are not conclusive for a Category 2 classification or no classification (ECHA, 2017). Such data may, however, be used in an overall weight of evidence assessment. It is noted that the applicability domain of the LVET is limited to household detergent and cleaning products and their main ingredients (surfactants) (ESAC, 2009).

3.3.5.3.6.3 Effects on the eyes may be observed in acute or repeated dose inhalation studies with full body exposure. However, normally no scoring according to the Draize criteria is performed and the follow-up period may be shorter than 21 days. Also, the effects on the eyes will likely depend upon the concentration of the substance/mixture and the exposure duration. As there are no criteria for minimal concentration and duration, the absence of effects on the eyes or eye irritation may not be conclusive for the absence of serious eye damage. The presence of irreversible effects on the eye should be considered within a weight of evidence assessment.

3.3.5.3.7 *Guidance on the use of pH and acid/alkaline reserve for classification as serious eye damage*

3.3.5.3.7.1 Methods to determine the pH value such as OECD Test Guideline 122 and the method described by Young et al. (1988) differ in the concentration of the substance or mixture for which the pH is determined and include values of 1%, 10% and 100%. These methods also differ in the way the acid/alkaline reserve is determined, namely up to a pH of 7 for both acids and bases (OECD Test Guideline 122) or up to a pH of 4 for acids and a pH of 10 for bases (Young et al., 1988). Furthermore, there are differences between OECD Test Guideline 122 and Young et al. (1988) in the units used to express the acid/alkaline reserve.

3.3.5.3.7.2 Criteria to identify substances and mixtures requiring classification in Category 1 based on pH and acid/alkaline reserve have been developed for effects on the skin (Young et al., 1988) and the same criteria are applied for effects on the eye. These criteria were developed using a combination of pH and acid/alkaline reserve values that were determined in a specific way (Young et al., 1988). Therefore, these criteria may not be directly applicable when other test concentrations or methods are used to measure pH and acid/alkaline reserve. Furthermore, the calibration and validation of these criteria was based on a limited dataset for effects on the skin. Thus, the predictive value of the combination of pH and acid/alkaline reserve for classification in Category 1 for effects on the eye is limited, especially for substances and mixtures with an extreme pH but a non-significant acid/alkaline reserve. The criteria developed by Young et al. (1988) for classification in Category 1 may be used as a starting point for determining whether a substance or a mixture has a significant acid/alkaline reserve or a non-significant acid/alkaline reserve. A competent authority may decide which criteria for significant acid/alkaline reserve can be applied.

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* *References:*

Alépée, N., E. Adriaens, T. Abo, D. Bagley, B. Desprez, J. Hibatallah, K. Mewes, U. Pfannenbecker, À. Sala, A.R. Van Rompay, S. Verstraelen, and P. McNamee. 2019a. Development of a defined approach for eye irritation or serious eye damage for liquids, neat and in dilution, based on Cosmetics

Europe analysis of in vitro STE and BCOP test methods. Toxicol. In Vitro, 57: 154-163. doi: 10.1016/j.tiv.2019.02.019.

Alépée, N., E. Adriaens, T. Abo, D. Bagley, B. Desprez, J. Hibatallah, K. Mewes, U. Pfannenbecker, À. Sala, A.R. Van Rompay, S. Verstraelen, and P. McNamee. 2019b. Development of a defined approach for eye irritation or serious eye damage for neat liquids based on Cosmetics Europe analysis of in vitro RhCE and BCOP test methods. Toxicol. In Vitro, 59: 100-114. doi: 10.1016/j.tiv.2019.04.011.

Alépée, N., V. Leblanc, M.H. Grandidier, S. Teluob, V. Tagliati, E. Adriaens, and V. Michaut. 2020. Development of the SkinEthic HCE Time-to-Toxicity test method for identifying liquid chemicals not requiring classification and labelling and liquids inducing serious eye damage and eye irritation. Toxicol. In Vitro, 69: 104960. doi: 10.1016/j.tiv.2020.104960.

Bagley, D.M., D. Waters, and B.M. Kong. 1994. Development of a 10-day chorioallantoic membrane vascular assay as an alternative to the Draize rabbit eye irritation test. Food Chem. Toxicol., 32(12): 1155-1160. doi: 10.1016/0278-6915(94)90131-7.

Bagley, D.M., D. Cerven, and J. Harbell. 1999. Assessment of the chorioallantoic membrane vascular assay (CAMVA) in the COLIPA in vitro eye irritation validation study. Toxicol. In Vitro, 13(2): 285-293. doi: 10.1016/s0887-2333(98)00089-7.

Balls, M., P.A. Botham, L.H. Bruner, and H. Spielmann. 1995. The EC/HO international validation study on alternatives to the draize eye irritation test. Toxicol. In Vitro, 9(6): 871-929. doi: 10.1016/0887-2333(95)00092-5.

Brantom, P.G., L.H. Bruner, M. Chamberlain, O. De Silva, J. Dupuis, L.K. Earl, D.P. Lovell, W.J. Pape, M. Uttley, D.M. Bagley, F.W. Baker, M. Bracher, P. Courtellemont, L. Declercq, S. Freeman, W. Steiling, A.P. Walker, G.J. Carr, N. Dami, G. Thomas, J. Harbell, P.A. Jones, U. Pfannenbecker, J.A. Southee, M. Tcheng, H. Argembeaux, D. Castelli, R. Clothier, D.J. Esdaile, H. Itigaki, K. Jung, Y. Kasai, H. Kojima, U. Kristen, M. Larnicol, R.W. Lewis, K. Marenus, O. Moreno, A. Peterson, E.S. Rasmussen, C. Robles, and M. Stern. 1997. A summary report of the COLIPA international validation.study on alternatives to the draize rabbit eye irritation test. Toxicol. In Vitro, 11: 141-179. doi:10.1016/S0887-2333(96)00069-0.

Burton, A.B., M. York, and R.S. Lawrence. 1981. The in vitro assessment of severe eye irritants. Food Cosmet. Toxicol., 19(4): 471-480. doi: 10.1016/0015-6264(81)90452-1.

Choksi, N., S. Lebrun, M. Nguyen, A. Daniel, G. DeGeorge, J. Willoughby, A. Layton, D. Lowther, J. Merrill, J. Matheson, J. Barroso, K. Yozzo, W. Casey, and D. Allen. 2020. Validation of the OptiSafe™ eye irritation test. Cutan. Ocul. Toxicol., 39(3): 180-192. doi: 10.1080/15569527.2020.1787431.

Cottrez, F., V. Leblanc, E. Boitel, H. Groux, and N. Alépée. 2021. The EyeIRR-IS assay: Development and evaluation of an in vitro assay to measure the eye irritation sub-categorization of liquid chemicals. Toxicol. In Vitro, 71: 105072. doi: 10.1016/j.tiv.2020.105072.

Donahue, D.A., L.E. Kaufman, J. Avalos, F.A. Simion, and D.R Cerven. 2011. Survey of ocular irritation predictive capacity using Chorioallantoic Membrane Vascular Assay (CAMVA) and Bovine Corneal Opacity and Permeability (BCOP) test historical data for 319 personal care products over fourteen years. Toxicol. In Vitro, 25(2): 563-572. doi: 10.1016/j.tiv.2010.12.003.

ECHA. 2017. Guidance on the Application of the CLP Criteria. Version 5.0. Reference ECHA-17-G-21-EN. doi: 10.2823/124801. Available at: https://echa.europa.eu/guidance-documents/guidance-on-clp.

ESAC. 2019. Statement on the use of existing low volume eye test (LVET) data for weight of evidence decisions on classification and labelling of cleaning products and their main ingredients. Statement of the ECVAM Scientific Advisory Committee (ESAC) of 9th July 2009. Available at: https://ec.europa.eu/jrc/sites/jrcsh/files/esac31_lvet_20090922.pdf.

EURL ECAM. 2004a. Tracking System for Alternative Methods Towards Regulatory Acceptance (TSAR). Method TM2004-01. The cytosensor microphysiometer toxicity test. Available at: https://tsar.jrc.ec.europa.eu/test-method/tm2004-01.

EURL ECAM. 2004b. Tracking System for Alternative Methods Towards Regulatory Acceptance (TSAR). Method TM2004-03. Neutral Red Release Assay. Available at: https://tsar.jrc.ec.europa.eu/test-method/tm2004-03.

Frentz, M., M. Goss, M. Reim, and N.F. Schrage. 2008. Repeated exposure to benzalkonium chloride in the Ex Vivo Eye Irritation Test (EVEIT): observation of isolated corneal damage and healing. Altern. Lab. Anim., 36(1): 25-32. doi: 10.1177/026119290803600105.

Harbell, J.W., R. Osborne, G.J. Carr, and A. Peterson. 1999. Assessment of the Cytosensor Microphysiometer Assay in the COLIPA In Vitro Eye Irritation Validation Study. Toxicol. In Vitro, 13(2): 313-323. doi: 10.1016/s0887-2333(98)00090-3.

Hartung, T., L. Bruner, R. Curren, C. Eskes, A. Goldberg, P. McNamee, L. Scott, and V. Zuang. 2010. First alternative method validated by a retrospective weight-of-evidence approach to replace the Draize eye test for the identification of non-irritant substances for a defined applicability domain. ALTEX, 27(1): 43-51. doi: 10.14573/altex.2010.1.43.

ICCVAM. 2007. ICCVAM test method evaluation report: in vitro ocular toxicity test methods for identifying ocular severe irritants and corrosives. NIH Publication No. 07–4517. National institute of environmental health sciences, research Triangle Park, North Carolina, USA.

ICCVAM. 2010. ICCVAM test method evaluation report: current validation status of in vitro test methods proposed for identifying eye injury hazard potential of chemicals and products. NIH Publication No. 10-7553. National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA.

Kandarova, H., S. Letasiova, E. Adriaens, R. Guest, J.A. Willoughby Sr., A. Drzewiecka, K. Gruszka, N. Alépée, S. Verstraelen, and A.R. Van Rompay. 2018. CON4EI: CONsortium for in vitro Eye Irritation testing strategy - EpiOcular™ time-to-toxicity (EpiOcular ET-50) protocols for hazard identification and labelling of eye irritating chemicals. Toxicol. In Vitro, 49: 34-52. doi: 10.1016/j.tiv.2017.08.019.

Nash, J.R., G. Mun, H.A. Raabe, and R. Curren. 2014. Using the cytosensor microphysiometer to assess ocular toxicity. Curr. Protoc. Toxicol. 61: 1.13.1-11. doi: 10.1002/0471140856.tx0113s61.

Piehl, M., A. Gilotti, A. Donovan, G. DeGeorge, and D. Cerven. 2010. Novel cultured porcine corneal irritancy assay with reversibility endpoint. Toxicol. In Vitro 24: 231-239. doi:10.1016/j.tiv.2009.08.033.

Piehl, M., M. Carathers, R. Soda, D. Cerven, and G. DeGeorge. 2011. Porcine corneal ocular reversibility assay (PorCORA) predicts ocular damage and

recovery for global regulatory agency hazard categories. Toxicol. In Vitro, 25: 1912-1918. doi:10.1016/j.tiv.2011.06.008.

Reader, S.J., V. Blackwell, R. O'Hara, R.H. Clothier, G. Griffin, and M. Balls. 1989. A vital dye release method for assessing the short-term cytotoxic effects of chemicals and formulations. Altern. Lab. Anim., 17: 28-33. doi: 10.1177/026119298901700106.

Reader, S.J., V. Blackwell, R. O'Hara, R.H. Clothier, G. Griffin, and M. Balls. 1990. Neutral red release from pre-loaded cells as an in vitro approach to testing for eye irritancy potential. Toxicol. In Vitro, 4(4-5): 264-266. doi: 10.1016/0887-2333(90)90060-7.

Settivari, R.S., R.A. Amado, M. Corvaro, N.R. Visconti, L. Kan, E.W. Carney, D.R. Boverhof, and S.C. Gehen. 2016. Tiered application of the neutral red release and EpiOcular™ assays for evaluating the eye irritation potential of agrochemical formulations. Regul. Toxicol. Pharmacol., 81: 407-420. doi: 10.1016/j.yrtph.2016.09.028.

Spielmann, H., S. Kalweit, M. Liebsch, T. Wirnsberger, I. Gerner, E. Bertram-Neis, K. Krauser, R. Kreiling, H.G. Miltenburger, W. Pape, and W. Steiling. 1993. Validation study of alternatives to the Draize eye irritation test in Germany: Cytotoxicity testing and HET-CAM test with 136 industrial chemicals. Toxicol. In Vitro, 7(4): 505-510. doi: 10.1016/0887-2333(93)90055-a.

Spielmann, H., M. Liebsch, S. Kalweit, F. Moldenhauer, T. Wirnsberger, H.-G. Holzhütter, B. Schneider, S. Glaser, I. Gerner, W.J.W. Pape, R. Kreiling, K. Krauser, H.G. Miltenburger, W. Steiling, N.P. Luepke, N. Müller, H. Kreuzer, P. Mürmann, J. Spengler, E. Bertram-Neis, B. Siegemund, and F.J. Wiebel. 1996. Results of a validation study in Germany on two in vitro alternatives to the Draize eye irritation test, HET-CAM test and the 3T3 NRU cytotoxicity test. Altern. Lab. Anim., 24: 741-858.

Spöler, F., M. Först, H. Kurz, M. Frentz, and N.F. Schrage. 2007. Dynamic analysis of chemical eye burns using high-resolution optical coherence tomography. J. Biomed. Opt., 12: 041203. doi:10.1117/1.2768018.

Spöler, F., O. Kray, S. Kray, C. Panfil, and N.F. Schrage. 2015. The Ex Vivo Eye Irritation Test as an alternative test method for serious eye damage/eye irritation. Altern. Lab. Anim., 43(3): 163-179. doi: 10.1177/026119291504300306.

Whittle, E., D. Basketter, M. York, L. Kelly, T. Hall, J. McCall, P. Botham, D. Esdaile, and J. Gardner. 1992. Findings of an interlaboratory trial of the enucleated eye method as an alternative eye irritation test. Toxicol. Mech. Methods., 2: 30-41.

Young, J.R., M.J. How, A.P. Walker, and W.M. Worth. 1988. Classification as corrosive or irritant to skin of preparations containing acidic or alkaline substances, without testing on animals. Toxicol. In Vitro, 2(1): 19-26. doi: 10.1016/0887-2333(88)90032-x.

Zuang, V. 2001. The neutral red release assay: a review. Altern. Lab. Anim., 29(5): 575-599. doi: 10.1177/026119290102900513.".

(Ref. Document: ST/SG/AC.10/C.4/2021/4)

附属 3

第 1 節, 表 A3.1.2

H317, column (3)

Replace “Sensitization, skin (chapter 3.4)” with “Skin sensitization (chapter 3.4)”.

(Ref. Doc: ST/SG/AC.10/C.4/2021/2, paragraphs 31 to 34)

H334, column (3)

Replace “Sensitization, respiratory (chapter 3.4)” with “Respiratory sensitization (chapter 3.4)”.

(Ref. Doc: ST/SG/AC.10/C.4/2021/2, paragraphs 31 to 34)

第 2 節, 表 A3.2.2

P262, column (4)

Insert: “3” after: “1, 2”.

(Ref. Document: ST/SG/AC.10/C.4/2021/2, paragraphs 6 to 9)

P264 and P270, column (4)

For the hazard class acute toxicity (dermal), insert: “3” after: “1, 2”.

(Ref. Document: ST/SG/AC.10/C.4/2021/2, paragraphs 6 to 9)

第 3 節

Tables for flammable gases (Chapter 2.2)

Delete the note under the tables for pyrophoric gases and chemically unstable gases

(Ref. Doc: ST/SG/AC.10/C.4/2021/2 as amended by informal document INF.19)

Table for “Acute toxicity - dermal (Chapter 3.1)”, hazard category 3, column “Prevention”

Insert the following entries:

> “P262
> **Do not get in eyes, on skin, or on clothing.**
>
> P264
> **Wash hands [and ...] thoroughly after handling.**
> text in square brackets to be used when the manufacturer/supplier or competent authority specify other parts of the body to be washed after handling.
>
> P270
> **Do not eat, drink or smoke when using this product.**”.

(Ref. Doc: ST/SG/AC.10/C.4/2021/2, paragraphs 6 to 9)

Tables for “Sensitization – respiratory (Chapter 3.4)

Amend the heading to read as follows: “RESPIRATORY SENSITIZATION (CHAPTER 3.4)”.

(Ref. Doc: ST/SG/AC.10/C.4/2021/2, paragraphs 31 to 34)

Table for “Sensitization – skin (Chapter 3.4)”,

Amend the heading to read as follows: “SKIN SENSITIZATION (CHAPTER 3.4)”.

(Ref. Doc: ST/SG/AC.10/C.4/2021/2, paragraphs 31 to 34)

付属書II

[オリジナル:英語と仏語]

化学品の分類および表示に関する世界調和システム改訂9版（ST/SG/AC.10/30/Rev.9）の修正（実際の翻訳物と齟齬が出るとよろしくないため、和訳はしない）

第2.17章

1. Paragraph 2.17.1.1, last sentence, text between brackets

For see also Note 2 of paragraph 2.1.2.2 *read* see paragraph 2.1.1.2.2

(Reference document: ST/SG/AC.10/C.4/2021/6)

2. Footnote 1 to paragraph 2.17.1.1

The first sentence should read*:*

Explosives that are too sensitive to be assigned Category 2 of Chapter 2.1 can also be desensitized and consequently may be classified as desensitized explosives, provided all criteria of Chapter 2.17 are met.

(Reference document: ST/SG/AC.10/C.4/2021/6)

3. Paragraph 2.17.4.1, decision logic 2.17.1, in the two text boxes on the right-hand side with the “exploding bomb” symbol

For Division 1.1 *read* Sub-category A

(Reference document: ST/SG/AC.10/C.4/2021/6)