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作为卡塔赫纳生物技术安全议定书缔约方会议的
生物多样性公约缔约方大会
第五次会
2010 年 10 月 11 日至 15 日，日本名古屋
临时议程*项目 13

风险评估和风险管理（第 15 和第 16 条）

执行秘书的说明

一. 导 言

1. 《卡塔赫纳生物技术安全议定书》列出了关于风险评估（第 15 条和附件三）和风险管理（第 16 条）的条款，其中，前者旨在确定和评价改性活生物体对生物多样性的养护和可持续使用的不利影响，同时亦顾及对人类健康构成的风险；后者旨在使各缔约方能够建立并维护适当的机制、措施和战略，用以制约、管理和控制根据该议定书条款开展的风险评估进程所指明的各种风险。

2. 在其第一次会议上，作为议定书缔约方会议的缔约方大会决定在其第五次会议上审议某种能够识别不太可能对养护和可持续利用生物多样性产生不利影响的改性活生物体、同时亦顾及对人类健康构成的风险的方式，以便根据第 7 条第 4 款形成决定 。[1]

3. 在其第四次会议上，缔约方在审议是否需要进一步指导风险评估和风险管理的具体方面时，通过生物技术安全资料交换所建立了一个关于风险评估具体方面的不限成员名额在线论坛与一个风险评估和风险管理问题特设技术专家组（特设技术专家组），专家组的职权范围见决定附件。另外，议定书缔约方请执行秘书：（一）在特设技术专家组每次会议之前召集特设讨论小组，并至少在每个区域召开一次实时在线会议，以确定涉及决定附

* UNEP/CBD/BS/COP-MOP/5/1。

1 第 BS-I/12 号决定附件第 7（a）（一）段。

件所述风险评估和风险管理的具体方面的主要问题；（二）在作为议定书缔约方会议的缔约方大会第五次会议之前召开特设技术专家组的两次会议。[2]

4. 在审议与风险评估有关的能力建设问题时，缔约方第四次会议又请执行秘书：（一）与其他相关的联合国机构和其他国际组织一道，协调并便利开展关于改性活生物体风险评估和风险管理的培训；（二）在缔约方会议第五次会议之前举办区域或次区域培训课程，以使各国能够在根据《议定书》编写和评价风险评估报告时取得实际操作经验；和（三）在太平洋次区域举办一次关于改性活生物体风险评估和风险管理能力建设及经验交流的讲习班。[3]

5. 除如第 3 段所述讨论是否需要进一步指导风险评估的具体方面外，还请特设技术专家组根据缔约方确定的职权范围，审议合作查明可能会对养护和可持续利用生物多样性产生不利影响的改性活生物体或其具体特性的可行方式，同时亦顾及对人类健康构成的风险。为协助特设技术专家组进行审议，作为议定书缔约方会议的缔约方大会请各缔约方、其他国家政府和有关组织提交当时可以得到的有科学依据的资料，以指明可能对养护和可持续利用生物多样性产生不利影响的改性活生物体或其具体特性，同时亦顾及对人类健康构成的风险。缔约方还请执行秘书汇编所收到资料，编写综合报告，供特设技术专家组和缔约方审议。[4]

6. 因此，执行秘书编写了本说明，以协助议定书缔约方审议关于风险评估和风险管理的议程项目。第二节分析了关于风险评估具体方面的进一步指导意见的编制进程取得的主要成果。第三节概述了应缔约方会议要求开展的能力建设活动。第四节概述了一些呈件和建议，内容涉及合作查明*可能会*对养护和可持续利用生物多样性*产生不利影响*的改性活生物体，同时亦顾及对人类健康构成的风险。[5]第五节所列部分要点可能有助于缔约方审议各种方式，以查明*不太可能会*对养护和可持续利用生物多样性产生不利影响的改性活生物体，同时亦顾及对人类健康构成的风险。[6]第六节得出一些结论，并提出了决定草案的部分要点供缔约方审议。

二. 关于风险评估具体方面的进一步指导

7. 为了执行第 BS-IV/11 号决定中关于为风险评估提供进一步指导的各项要点，秘书处经与作为议定书缔约方会议的缔约方大会主席团协商，建立了一个由三类活动组成的持续进程：（一）特设在线讨论小组；（二）实时在线区域会议；和（三）特设技术专家组的面对面会议。

8. 在进程一开始，通过生物技术安全资料交换所开办了风险评估和风险管理问题不限成员名额在线专家论坛（在线论坛）。[7]

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[2] 第 BS-IV/11 号决定第 3、第 4 和第 6 段。

[3] 第 BS-IV/11 号决定第 12 和第 13 段。

[4] 第 BS-IV/11 号决定第 3、第 4 和第 6 段。

[5] 根据第 BS-I/12 号决定附件第 4（b）（三）段。

[6] 根据第 BS-I/12 号决定附件第 7（a）（一）段。

[7] 见http://bch.cbd.int/onlineconferences/forum_RA.shtml。

9. 执行秘书在一份通知中请各缔约方、其他国家政府和有关组织使用生物技术安全专家提名的共同格式，向在线论坛提名风险评估专家。秘书处根据第 BS-IV/4 号决定所列关于生物技术安全专家的标准和最低要求，审查了提名信息的完整性。

10. 共有 229 名专家在不限成员名额在线论坛上登记，其中 153 名专家由共计 48 个缔约方提名，11 名专家由共计五个非缔约方提名，65 名专家以观察员身份登记。[8]

11. 作为特设技术专家组筹备工作的一部分，2008 年 11 月至 2009 年 2 月期间，在在线论坛主持下，召集了八个特设在线讨论小组和四次实时在线区域会议（欧洲、拉丁美洲、非洲和亚洲）。[9]

12. 挑选特设技术专家组参与者的依据是，他们按照第 BS-IV/11 号决定的要求，根据生物多样性公约科学、技术和工艺咨询附属机构（科咨机构）的统一工作方式，[10]经与作为议定书缔约方会议的缔约方大会主席团协商，积极参与在线论坛的各类活动。特设技术专家组参与者名单见本文件附件一。

13. 2009 年 4 月 20 日至 24 日，风险评估和风险管理问题特设技术专家组在蒙特利尔举行了第一次会议。来自十七个缔约方的十八名参与者及来自三个非缔约方和五个组织的八名观察员作为特设技术专家组成员出席了会议。

14. 在特设技术专家组举行的两次会议之间开展了大量活动，以促使针对特设技术专家组第一次会议确定的各项具体问题草拟指导意见，并根据缔约方的授权测试路线图。具体活动如下：

(a) *由不限成员名额在线论坛主持：* 十个特设讨论小组和四次实时在线区域会议（非洲、亚洲和太平洋、西欧和其他国家集团、中东欧以及拉丁美洲和加勒比国家集团）；[11]以及

(b) *由特设技术专家组主持：*在线讨论小组的五轮讨论、特设技术专家组主席团的 2 次电话会议以及路线图问题工作分组与特设技术专家组主席团的面对面会议。[12]

15. 上文第 14 段所列各项活动由不限成员名额在线专家论坛和特设技术专家组交替主持，以形成一个针对特设技术专家组各工作分组编制的指导文件每份新草稿的反馈回路，并使更多专家参与整个进程。

16. 特设技术专家组于 2010 年 4 月 20 日至 24 日在斯洛文尼亚卢布尔雅那举行了第二次会议。在出席会议的特设技术专家组成员中，十四名来自缔约方、两名来自非缔约方、四名来自各组织。

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[8] 参与者名单见：http://bch.cbd.int/onlineconferences/participants_ra.shtml。

[9] 讨论小组记录全文见：http://bch.cbd.int/onlineconferences/archived_discussions_ra.shtml。实时在线会议的文件和记录全文见：http://bch.cbd.int/onlineconferences/realtime_ra.shtml。

[10] 缔约方大会第 VIII/10 号决定附件三第 18 段。

[11] 讨论小组记录全文见：http://bch.cbd.int/onlineconferences/archived_discussions_ra.shtml。实时在线会议文件和记录全文见：http://bch.cbd.int/onlineconferences/realtime_ra.shtml。

[12] 路线图问题工作分组和特设技术专家组主席团于 2009 年 10 月 12 日至 14 日期间在海牙举行了多次会议。

17. 在线论坛和特设技术专家组主持开展的各项活动的完整清单见本文件附件二。

A. 风险评估和风险管理问题不限成员名额在线专家论坛的成果

18. 在线论坛在特设技术专家组第一次会议之前向该专家组提出如下建议：

(a) 就风险评估和风险管理的以下几个具体方面提供指导：（一）鱼类、树木、微生物和药用植物的改性活生物体；（二）有复合基因或特性的改性活生物体；（三）具体的接收环境；及（四）释放后的监测活动和释放到环境中的改性活生物体的长期影响；以及

(b) 就具体的优先方面提供指导材料的行动计划和路线图。

19. 在特设技术专家组第一次会议之后，不限成员名额在线专家论坛主持的讨论帮助推动了路线图的起草和测试，也帮助就特设技术专家组确定为优先事项的风险评估的具体方面（即蚊子的改性活生物体、可承受非生物压力的作物的改性活生物体以及有复合基因的改性活生物体）提供指导意见。

20. 在若干轮讨论期间，在线论坛的专家就路线图的内容和风险评估的具体方面向特设技术专家组提供了实质性援助。在测试路线图时，关于其实用性和相关性的大多数意见都是积极的；关于如何使路线图更方便用户使用，也提出了若干建议。

21. 特设讨论小组的最后一轮讨论还请在线论坛成员就风险评估和风险管理进程的前进之路向缔约方会议提出建议，供其第五次会议审议。论坛的参与者就路线图的实用性和关于风险评估具体方面的指导发表意见，并指出应定期订正和增订这些文件，以确保其相关性并使其与新的事态发展相协调。

22. 在线论坛的参与者还指出有必要为风险评估的其他具体方面提供额外指导。论坛注意到 UNEP/CBD/BS/COP-MOP/5/INF/12 和 UNEP/CBD/BS/COP-MOP/5/INF/13 号资料文件所列的风险评估话题，并将其作为提供进一步指导的起点。[13]另外，参与者还建议审议如下话题：（一）确定风险情形；（二）风险管理战略，包括对释放到环境中的改性活生物体的影响进行释放后监测；（三）不确定性和变异性分析；（四）载有风险评估进程关键内容的“一览表”；以及（五）如何把《议定书》下的风险评估进程与《生物多样性公约》下的条文和决定更好地联系在一起。

23. 在线论坛讨论期间，还有人建议在制订新的指导时，各缔约方应继续进行磋商，并应虑及其他国际机构（如经合组织、植保公约）制订的现有指导意见。

24. 关于引导制订进一步指导意见的机制，许多专家建议采用特设技术专家组、在线讨论和通过生物技术安全资料交换所进行信息交换等方式，抑或兼而有之。引导制订指导意见的其他机制范例包括专家磋商以及在制订指导意见后由顾问专家开展后续培训。

[13] 见http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=3018。

25. 已经对不限成员名额在线专家论坛主持下提出的意见和建议进行汇总并作为资料文件提供，供各缔约方审议（UNEP/CBD/BS/COP-MOP/5/INF/12 和 14）。[14]

B. 风险评估和风险管理问题特设技术专家组的成果

26. 特设技术专家组第一次会议的主要成果包括：（一）路线图草案；（二）为制订指导意见，查明风险评估的另外三个具体方面（蚊子的改性活生物体、可承受非生物压力的作物的改性活生物体以及有复合基因的改性活生物体）并确定了优先次序；（三）建立了四个工作分组，重点处理已确定的问题；以及（四）制订了一项行动计划，由术语摘要和在特设技术专家组第二次会议之前制订指导意见的程序组成。

27. 特设技术专家组各工作分组在闭会期间与不限成员名额在线专家组协商，进一步制订风险评估四个具体问题的指导文件草案，并测试了改性活生物体风险评估路线图草案。

28. 特设技术专家组第二次会议的主要成果包括：

(a) 对题为“改性活生物体风险评估指导意见”的文件定稿，该文件分两部分：“第一部分：改性活生物体风险评估路线图”和“第二部分：改性活生物体及其特性的具体类型”（即可承受非生物压力的作物的改性活生物体、蚊子的改性活生物体以及有复合基因或特性的改性活生物体）。该文件作为附件三附在本文件之后，并将通过生物技术安全资料交换所提供；[15]

(b) 就如何整合和增订特设技术专家组编写的指导文件以及可用于检索生物技术安全资料交换所生物技术安全信息资源中心现有背景材料的工具，向秘书处提出了一些建议；以及

(c) 对第一次会议上制订的行动计划进行了评估。

29. 特设技术专家组还建议缔约方在其第五次会议上就其他风险评估话题，特别是不限成员名额在线论坛和特设技术专家组第一次会议确定并列为优先事项的风险评估具体问题进一步制订指导意见。

30. 特设技术专家组第一次会议报告和最后报告已作为资料文件提交各缔约方审议。[16]

31. 特设技术专家组向缔约方第五次会议提出的整套建议作为附件四附在本文件之后。

三. 风险评估方面的能力建设

32. 根据各缔约方提出的风险评估方面的能力建设要求，秘书处协调开展了一个多方有关利益方进程，以便与联合国各组织（联合国欧洲经济委员会奥胡斯公约、联合国粮食及农业组织（粮农组织）国际植物保护公约（植保公约）和联合国环境规划署（环境规划

[14] UNEP/CBD/BS/COP-MOP/5/INF/12 和 UNEP/CBD/BS/COP-MOP/5/INF/14 号资料文件见 http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=3018。

[15] 见http://bch.cbd.int/onlineconferences/forum_RA.shtml。

[16] UNEP/CBD/BS/COP-MOP/5/INF/13 和 UNEP/CBD/BS/COP-MOP/5/INF/15 号资料文件见 http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=3018。

署））、其他国际组织（全球工业联盟和第三世界网）及学术部门（坎特伯雷大学和明尼苏达大学）合作，开展培训。

33. 培训工作是逐步展开的。秘书处首先编写培训大纲，请合作者提供资料并发表评论意见。此后，秘书处根据各种反馈意见编写培训手册草案，并请合作者进行同行审议。再之后，秘书处又根据同行审议进程期间提出的反馈和评论意见订正手册草案。

34. 秘书处根据《卡塔赫纳生物技术安全议定书》条文，特别是其附件三起草和审查逐渐成形的培训手册，并试图全面纳入许多国家管制框架和国际组织的经验及现行做法。

35. 该进程取得的成果就是起草了一份题为“改性活生物体风险评估”的培训手册。手册由四个单元组成：（一）生物技术安全和《卡塔赫纳生物技术安全议定书》概述；（二）准备工作——了解开展风险评估的背景；（三）进行风险评估；以及（四）编写风险评估报告。

36. 生物技术安全资料交换所将培训手册作为资料文件提供，供各缔约方审议。[17]

37. 为了进一步响应各缔约方的要求，开展能力建设活动，以使各国能够在根据《议定书》编写和评价风险评估报告时交流经验和取得实际操作知识，在开展下列活动时使用了上述培训手册：

(a) 2010 年 7 月 4 日至 7 日在斐济纳迪举行的关于风险评估能力建设和经验交流的太平洋次区域讲习班；以及

(b) 2010 年 7 月 12 日至 16 日在柬埔寨暹粒举办的关于改性活生物体风险评估的亚洲次区域培训课程。

38. 来自六个议定书缔约方（斐济、基里巴斯、纽埃、萨摩亚、所罗门群岛和汤加）、两个非缔约国（库克群岛和瓦努阿图）和一家组织（新西兰坎特伯雷大学）的十二名参与者出席了太平洋次区域讲习班。来自十五个议定书缔约方（不丹、柬埔寨、印度、印度尼西亚、伊朗伊斯兰共和国、老挝人民民主共和国、马来西亚、蒙古、缅甸、巴基斯坦、阿拉伯叙利亚共和国、泰国、土库曼斯坦、越南和也门）、一家非政府组织（第三世界网）和联合国环境规划署的二十三名参与者参加了亚洲培训课程。此外，参加亚洲培训课程的还包括一名荷兰顾问。

39. 参与者应邀填写调查问卷，以评价太平洋讲习班和亚洲培训课程。问卷结果显示参与者普遍认为这些活动：（一）提供了根据《议定书》条文和附件三编写和评价风险评估报告方面的实际操作培训；（二）帮助培养使用和阐释现有信息以及查明和消除信息差距方面的技能；以及（三）帮助理解如何确定有关风险评估的基线信息。

40. 问卷结果还表明，大多数参与者认为，秘书处与其他联合国机构和有关组织合作编制的培训手册：（一）是一种非常有益的风险评估培训工具；（二）采用了循序渐进的方法，易于理解；（三）适当概述了风险评估进程；以及（四）对广大用户都非常实用。

[17] 培训手册已作为 UNEP/CBD/BS/COP-MOP/5/INF/22 号资料文件在 http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=3018 上提供，并通过生物技术安全资料交换所在 http://bch.cbd.int/protocol/cpb_art15/training 上提供。

41. 在提供进一步反馈意见时，参与者认为培训手册是一种绝佳的教学工具，结构严谨，全面介绍了风险评估进程，对各缔约方、其他国家和有关组织都非常实用。为了提高其实用性，参与者指出，就培训材料而言，应：

(a) 进一步加以完善，除其他外，应增加术语表、缩略语清单、流程图、示意图、其他非作物改性活生物体的范例等；

(b) 纳入特设技术专家组编制的“改性活生物体风险评估指导意见”中的要点，即路线图（如流程图）和关于具体类型的改性活生物体及其特性的指导（即对蚊子的改性活生物体、有复合基因或特性的改性活生物体以及可承受非生物压力的作物的改性活生物体等的风险评估）中的要点；

(c) 通过一种更方便用户使用的学习工具（如互动软件）加以展示；以及

(d) 以所有联合国语文出版。

42. 太平洋讲习班和亚洲培训课程的参与者认为，缔约方可在其第五次会议上对如下内容/活动进行审议：

风险评估方面的能力建设：

(a) 在国家一级，或针对接收环境类似、允许各国国家专家组成的核心小组参与的较小地区（如约 5 至 7 个国家），再举办风险评估培训课程；

(b) 风险评估领域的后续高级培训，重点包括不同类型的有意使用（即引入环境和拟直接用作食品、饲料或用于加工的改性活生物体）和不同类型的改性活生物体；

(c) （一）编写风险评估报告和建议；（二）从通知中提炼相关数据；（三）评估申请所提交数据的质量；以及（四）确定详细基线信息专门培训课程；

(d) 在国家一级对能够深入开展能力建设的培训员进行培训；

关于风险评估的指导意见：

(e) 以所有联合国语文出版和分发特设技术专家组的“改性活生物体风险评估指导意见”，包括通过生物技术安全资料交换所出版分发在线版本；

(f) 根据特设技术专家组的建议，制订关于风险评估的进一步指导意见；

生物技术安全方面的总体能力建设：

(g) 深入开展关于查明改性活生物体的区域培训；以及

(h) 对决策者进行阐释风险评估建议和执行风险管理战略方面的培训。

43. 关于这些能力建设活动的报告已作为资料文件提供，供各缔约方审议（UNEP/CBD/BS/COP-MOP/5/INF/16 和 17）。[18]

四. 合作查明*可能会*对养护和可持续利用生物多样性*产生不利影响*的改性活生物体或其具体特性，同时亦顾及对人类健康构成的风险

44. 执行秘书在一份通知中请各缔约方、其他国家政府和有关组织提交有科学依据的信息，以指明可能会对养护和可持续利用生物多样性产生不利影响的改性活生物体或其具体特性，同时亦顾及对人类健康构成的风险。[19]

45. 秘书处收到的部分呈件提到了一些可能会产生不利影响的改性活生物体或其具体特性，如棉花、鱼、玉米、树木、病毒的改性活生物体以及具有复合基因或特性、抗虫性、非生物压力和杀虫剂耐性、改良性养分吸收能力或载有抗生素抗性标志基因、用于生产药用化合物的改性活生物体。另一方面，一些呈件指出，迄今尚没有科学证据表明已被商品化的改性活生物体可能产生不利影响。

46. 秘书处根据上述呈件，拟订了“呈件汇编：查明可能会对养护和可持续利用生物多样性产生不利影响的改性活生物体或其具体特性，同时亦顾及对人类健康构成的风险”，供特设技术专家组和缔约方审议。[20]

47. 审议过该问题之后，特设技术专家组确定了如下合作方式：（一）通过生物技术安全资料交换所交换信息；（二）讲习班；（三）特设技术专家组；以及（四）合作检测改性活生物体。

48. 特设技术专家组的许多成员还认为，应为此目的确定一种循序渐进的办法，第一阶段是收集信息，第二阶段是分析信息。

49. 如下文附件四（f）段和（g）（四）段所示，特设技术专家组还就该问题提出了进一步的具体建议。

五. 查明*不太可能*对养护和可持续利用生物多样性*产生不利影响*的改性活生物体，同时亦顾及对人类健康构成的风险

50. 《议定书》第 7 条第 4 段规定，“事先知情同意程序不应适用于经作为本议定书缔约方会议的缔约方大会的一项决定认定在亦顾及对人类健康构成的风险的情况下不太可能对生物多样性的养护和可持续使用产生不利影响的改性活生物体的有意越境转移”。

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[18] UNEP/CBD/BS/COP-MOP/5/INF/16 和 UNEP/CBD/BS/COP-MOP/5/INF/17 号资料文件见：http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=3018。

[19] SCBD/BS/MPDM/jh/67587（2009-056）号通知见：http://bch.cbd.int/protocol/notifications/。

[20] 作为 UNEP/CBD/BS/COP-MOP/5/INF/11 号资料文件提供，见：http://bch.cbd.int/protocol/meetings/documents.shtml?eventid=3018。

51. 在审议有助于在亦顾及对人类健康构成的风险的情况下查明不太可能对生物多样性的养护和可持续使用产生不利影响的改性活生物体的方式时，除其他外，缔约方可在其第五次会议上审议各缔约方根据免除对进口改性活生物体采用事先知情同意程序的简化程序（第 13 条），通过生物技术安全资料交换所提交的下列资料。[21]

52. 截至 2010 年 6 月 10 日，生物技术安全资料交换所收到了根据简化程序提交的如下改性活生物体资料：

适用简化程序的改性活生物体	国家	生物技术安全资料交换所记录号
Bollgard™棉花	哥伦比亚	8151
Roundup Ready™棉花	哥伦比亚	8155
Bollgard II™棉花（MON-15985-7）	南非	5666
Bollgard™棉花（MON-00531-6）	南非	5679
YieldGard™玉米（MON-00810-6）	南非	5712
YieldGard™ 玉米（SYN-BT011-1）	南非	5715
Roundup Ready™ 玉米（MON-00603-6）	南非	8164
Roundup Ready™大豆（MON-04032-6）	南非	8167
Roundup Ready™ 棉花（MON-01445-2）	南非	8170
Roundup Ready™ YieldGard™ 玉米（MON-00603-6 x MON-00810-6）	南非	40513
Roundup Ready™ Flex™ 棉花（MON-88913-8）	南非	40514
Roundup Ready™ Bollgard™ 棉花（MON-00531-6 x MON-01445-2）	南非	40516

六. 结论和决定草案基本要点

A. 关于风险评估具体方面的进一步指导

53. 缔约方在在线论坛和特设技术专家组的职权范围中指派了制订关于风险评估的进一步指导的任务，通过一个包括在线审议和面对面审议在内的进程，任务得以圆满完成。

54. 许多专家通过特设讨论小组和实时会议进行在线审议，并向一个人数较少的小组，即特设技术专家组提出建议。该小组举行面对面会议。这一进程有利于与风险评估相关的各种科学和技术领域里的许多专家提供协助，从而利用现有有限的财政资源，以具有成本效益的方式编制指导材料。

55. 该进程取得的成果之一就是题为“改性活生物体风险评估指导意见”的文件。特设技术专家组和在线论坛建议，就该指导文件而言，应：（一）以所有联合国语文出版和分发该文件，包括通过生物技术安全资料交换所出版分发在线版本；（二）进行进一步测试，例如在举办区域讲习班时进行测试，包括酌情与现有的能力建设和培训倡议合作；（三）在两年之内对其进行重新审议，并在一年内评估是否需要更新背景资料清单。

[21] 第 13 条第 1（b）段。

56. 虽然通过编制上述文件，在讨论是否需要为风险评估提供指导方面取得了重大进展，但特设技术专家组和在线论坛的许多成员都认为仍需进一步提供指导，因此，建议继续推进结合了在线论坛和特设技术专家组的进程。

57. 基于上述信息并特别考虑到在线论坛和特设技术专家组的建议，谨建议作为议定书缔约方会议的缔约方大会：

(a) 支持并批准不限成员名额在线专家论坛与风险评估和风险管理问题特设技术专家组继续开展工作，以便：（一）制订关于具体类型的改性活生物体及其特性的额外指导，同时特别顾及下文附件五所列专题；（二）订正“改性活生物体风险评估指导意见”的案文，例如根据能力建设活动期间对指导意见进行测试，并增订背景资料清单；

(b) 请执行秘书：（一）以所有联合国语文出版和分发“改性活生物体风险评估指导意见”文件，包括通过生物技术安全资料交换所出版分发在线版本；（二）在举办区域讲习班期间测试指导文件，包括酌情与现有的能力建设和培训倡议合作；（三）订正向生物技术安全资料交换所生物技术安全信息资源中心提交记录的共同格式，以便把生物技术安全信息资源中心关于风险评估的各项记录与指导文件的具体部分联系在一起；

(c) 继续在风险评估和风险管理问题不限成员名额在线专家论坛的主持下展开讨论，并要求执行秘书邀请更多专家参加；

(d) 建立风险评估和风险管理问题特设技术专家组，并请执行秘书在挑选专家时采用与先前的进程相同的工作方式。

B. 风险评估方面的能力建设

58. 关于能力建设，与一些相关的联合国组织和国际组织合作编制了培训手册。手册是太平洋和亚洲次区域开展能力建设活动的依据。讲习班和培训课程的参与者就如何提高培训手册的实用性及如何使其更加方便用户使用提出了若干建议。此外，参与者建议把手册制成互动培训材料（如 CD-ROM），翻译成所有联合国语文并加以分发。

59. 基于上述信息并特别考虑到能力建设活动参与者的建议，谨建议作为议定书缔约方会议的缔约方大会：

(a) 请执行秘书在有资金可用的情况下，尽早在方便的时候再举办区域或次区域培训课程，以使各国能够在根据《议定书》条文和附件三编写和评价风险评估报告方面取得实际操作经验；

(b) 又请执行秘书与有关的联合国组织及其他组织合作，通过以下方式提高“改性活生物体风险评估”培训手册的实用性：（一）定期根据区域和次区域能力建设活动期间提出的建议修订手册；（二）将手册制作成互动学习工具，如 CD-ROM，并通过生物技术安全资料交换所发布；和（三）出版并向各缔约方、其他国家政府和有关组织分发手册。

C. 查明（一）可能会或（二）不太可能会对养护和可持续利用生物多样性产生不利影响的改性活生物体或其具体特性，同时亦顾及对人类健康构成的风险

60. 对于查明可能会对养护和可持续利用生物多样性产生不利影响的改性活生物体或其具体特性，同时亦顾及对人类健康构成的风险，各缔约方、其他国家政府和有关组织发表了不同意见。特设技术专家组确定了以下几种可用于解决该问题的方式：（一）通过生物技术安全资料交换所进一步交换信息；（二）讲习班；（三）特设技术专家组；以及（四）合作评估改性活生物体的潜在不利影响。可逐步启动该进程：第一阶段，收集信息，随后，对信息进行分析。

61. 关于查明不太可能会对养护和可持续利用生物多样性产生不利影响的改性活生物体，同时亦顾及对人类健康构成的风险，各缔约方应特别注意到根据关于免除对进口改性活生物体采用事先知情同意程序的简化程序做出并已提交生物技术安全资料交换所的决定。

62. 基于上述信息并特别考虑到各缔约方、其他国家政府和有关组织的意见以及不限成员名额在线论坛和特设技术专家组的建议，谨建议作为议定书缔约方会议的缔约方大会：建立一种或多种机制，如信息交换、讲习班和/或专家组，以使各缔约方能就查明（一）*可能会*或（二）*不太可能会*对养护和可持续利用生物多样性产生不利影响的改性活生物体或其具体特性，同时亦顾及对人类健康构成的风险做出决定。

Annex I

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Annex II

ACTIVITIES CARRIED OUT UNDER THE OPEN-ENDED ONLINE EXPERT GROUP ON RISK ASSESSMENT AND RISK MANAGEMENT AND BY THE AD HOC TECHNICAL EXPERT GROUP ON RISK ASSESSMENT AND RISK MANAGEMENT

Activity	Date / Location
Opening of the Online Forum and announcement of the topics and calendar of the discussion groups	6 November 2008, online
Ad hoc discussion groups under the Open-ended Online Forum on risk assessment and risk management of: (i) living modified (LM) fish; (ii) LM trees; (iii) LM microorganisms and viruses; (iv) LM pharmaplants; (v) living modified organisms (LMOs) with stacked genes or traits; (vi) post-release monitoring and long-term effects of LMOs released into the environment; and (vi) specific receiving environments; as well as on a Flowchart ("Roadmap") for risk assessment: the necessary steps to conduct risk assessment according to Annex III of the Protocol	10 November – 19 December 2008, online
First Series of Regional Real-time Online Conferences (for Europe, Latin America, Africa and Asia)	28 January – 17 February 2009, online
First Meeting of the Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management	20 – 24 April 2009, Montreal, Canada
Meeting of the AHTEG Bureau.	24 April 2009, Montreal, Canada
Ad hoc discussion groups within the AHTEG Sub-working Groups for further drafting of the guidance documents	May – June 2009, online
Ad hoc discussion groups under the Open-ended Online Forum for input to the work of the AHTEG Sub-working Groups	22 June – 12 July 2009, online
Teleconference of the AHTEG Bureau	24 July 2009
Ad hoc discussion groups within the AHTEG Sub-working Groups for further drafting of the guidance documents and testing of the Roadmap	August – October 2009, online
Progress reports on the work of the AHTEG Sub-working Groups	October 2009
Meetings of the AHTEG Sub-working Group on the Roadmap and AHTEG Bureau	12 – 14 October 2009, The Hague, Netherlands
Ad hoc discussion groups within the AHTEG Sub-working Groups for further drafting of the guidance documents and testing of the Roadmap	November 2009, online
Ad hoc discussion groups under the Open-ended Online Forum for further input to the work of the AHTEG Sub-working Groups	23 November – 14 December 2009, online

Activity	Date / Location
Ad hoc discussion group under the Open-ended Online Forum on "The way forward for the development of further guidance on risk assessment and risk management of LMOs"	7 – 14 December 2009
Ad hoc discussion groups within the AHTEG sub-working groups for further drafting of the guidance documents	January 2010, online
Second series of Regional Real-time Online Conferences (for Africa, Asia and the Pacific, WEOG and CEE, and Latin America and the Caribbean)	2 – 11 February 2010, online
Ad hoc discussion group under the AHTEG for final drafting of the guidance documents in preparation for the second AHTEG meeting	March 2010, online
Teleconference of the AHTEG Bureau	7 April 2010
Preparatory meetings of the AHTEG Sub-working Groups	19 April 2010, Ljubljana
Second meeting of the Ad Hoc Technical Expert Group	20-23 April 2010, Ljubljana

Annex III

GUIDANCE ON RISK ASSESSMENT OF LIVING MODIFIED ORGANISMS

This document was developed by the Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management under the Cartagena Protocol on Biosafety.[22]

This is intended to be a **"**living document**"** that will be improved with time as new experience becomes available and new developments in the field of applications of living modified organisms (LMOs) occur, as and when mandated by the Parties to the Cartagena Protocol on Biosafety.

PART I:

ROADMAP FOR RISK ASSESSMENT OF LIVING MODIFIED ORGANISMS

This "Roadmap" provides an overview of the process of environmental risk assessment for a living modified organism (LMO) in accordance with Annex III[23] to the Cartagena Protocol on Biosafety (hereinafter "the Protocol") and all other articles related to risk assessment. This Roadmap was developed in response to decision BS-IV/11[24] of the Conference of the Parties serving as the meeting of the Parties to the Protocol (COP-MOP). Annex III is the basis of the Roadmap. Accordingly, this Roadmap is a guidance document and does not replace Annex III. The overall aim of the Roadmap is facilitating and enhancing the effective use of Annex III by elaborating the technical and scientific process of how to apply the steps and points to consider in the process of risk assessment.

The purpose of this Roadmap is to provide further guidance on using Annex III with additional background material and links to useful references relevant to risk assessment. The Roadmap may be useful as a reference for risk assessors when conducting or reviewing risk assessments and in capacity-building activities.

The Roadmap applies to all types of LMOs[25] and their intended uses within the scope and objective of the Protocol, and in accordance with Annex III. However, it has been developed based largely on living modified crop plants because of the extensive experience to date with environmental risk assessments for these organisms. It is intended to be a "living document" that will be modified and improved on over time as and when mandated by COP-MOP, and in the light of new experience, information and developments in the field of applications of LMOs, e.g. when other types of LMOs have been evaluated more extensively in environmental risk assessments.

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[22] The AHTEG on Risk Assessment and Risk Management was established by the Conference of the Parties serving as the meeting of the Parties to the Cartagena Protocol on Biosafety (COP-MOP) in its decision BS-IV/11. The terms of reference for the AHTEG as set out by the Parties may be found in the annex to decision BS-IV/11 (http://bch.cbd.int/protocol/decisions/decision.shtml?decisionID=11690).

[23] http://www.cbd.int/biosafety/articles.shtml?a=cpb-43 .

[24] http://www.cbd.int/biosafety/cop-mop/results/?id=11690 .

[25] Including products thereof, as described in paragraph 5 of Annex III to the Protocol.

INTRODUCTION

General introduction

Background

In accordance with the precautionary approach[26] the objective of the Protocol is "to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of LMOs resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, specifically focusing on transboundary movements".[27]

For this purpose, Parties shall ensure that risk assessments are carried out when making informed decisions regarding LMOs.

An LMO and its use may have several effects, which may be intended or unintended, taking into account that some unintended effects may be predictable. The objective of risk assessment is to *identify* and *evaluate* the potential adverse effects of LMOs on the conservation and sustainable use of biological diversity in the likely potential receiving environment, taking also into account risks to human health.[28] The risk assessment is performed on a case-by-case basis. What is considered an adverse effect depends on protection goals and assessment end-points taken into consideration when scoping the risk assessment. The choice of protection goals by the Party could be informed by Articles 7(a), 7(b) and 8(g) and Annex 1 of the Convention on Biological Diversity.

According to the general principles of Annex III of the Protocol, risk assessments shall be based, at a minimum, on information provided in accordance with Article 8 and other available scientific evidence in order to identify and evaluate the possible adverse effects of LMOs on the conservation and sustainable use of biological diversity, taking also into account risks to human health.[29]

Annex III states that "risk assessment should be carried out in a scientifically sound and transparent manner, and can take into account expert advice of, and guidelines developed by, relevant international organizations. Lack of scientific knowledge or scientific consensus should not necessarily be interpreted as indicating a particular level of risk, an absence of risk, or an acceptable risk. (…) Risk assessment should be carried out on a case-by-case basis. The required information may vary in nature and level of detail from case to case, depending on the LMO concerned, its intended use and the likely potential receiving environment".[30]

The risk assessment process

Risk assessment is a structured process. Paragraph 8 of Annex III provides a description of the key steps of the risk assessment process to identify and evaluate the potential adverse effects and manage risks.

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[26] "In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation" (Principle 15 of the Rio Declaration on Environment and Development) at: (http://www.unep.org/Documents.Multilingual/Default.asp?DocumentID=78&ArticleID=1163), and in line with Articles 10.6 and 11.8 of the Protocol.

[27] http://www.cbd.int/biosafety/articles.shtml?a=cpb-01 .

[28] Annex III, paragraph 1.

[29] Article 15, paragraph 1.

[30] Annex III, paragraphs 3, 4 and 6.

Paragraph 9 describes, depending on the case, points to consider in this process. The steps describe an integrated process whereby the results of one step may be relevant to other steps. Also, risk assessment may need to be conducted in an iterative manner, where certain steps may be repeated or re-examined to increase or re-evaluate the confidence in the conclusions of the risk assessment. When new information arises that could change its conclusions, the risk assessment may need to be re-examined accordingly. Similarly, the issues mentioned in the 'overarching issues' section below can be taken into consideration again at the end of the risk assessment process to determine whether the objectives and criteria that were set out at the beginning of the risk assessment have been met.

Risk assessment is done in a comparative manner, meaning that risks associated with living modified organisms should be considered in the context of the risks posed by the non-modified recipient organism in the likely potential receiving environment.[31] Additionally, experience with the same, or, as appropriate, similar, genotypic or phenotypic characteristics may be taken into consideration along with the non-modified recipient organism in the risk assessment of an LMO. For instance, the comparison with the (near-)isogenic or closely related non-modified recipient is used in step 1 of the risk assessment (see below) where the novel genotypic or phenotypic characteristics associated with the LMO are identified. But when the potential consequences of adverse effects are evaluated, broader experience, such as mentioned in step 3 (a), may be taken into account, when establishing a baseline. Results from experimental field trials or other environmental information and experience with the same LMO may be taken into account as information elements in a new risk assessment for that LMO. In all cases where information, including baseline data, is derived from other sources, it is important to establish the validity and relevance of the information for the risk assessment. For instance, it should be taken into account that the behavior of a transgene,[32] as that of any other gene, may vary because it depends on the genetic and physiological background of the recipient as well as on the ecological characteristics of the environment that the LMO is introduced into.

The concluding recommendations derived from the risk assessment in step 5 are required to be taken into account in the decision-making process on an LMO. In the decision-making process, other Articles of the Protocol or other relevant issues may also be taken into account and are addressed in the last paragraph of this Roadmap: 'Related Issues'.

A flowchart illustrating the risk assessment process according to this Roadmap is annexed hereto.

(*See references relevant to "General Introduction"*).

Overarching issues in the risk assessment process

There are some overarching issues to consider in the design/planning phase of the risk assessment process to ensure the quality and relevance of the information used. These entail, among others:

- Setting criteria for relevancy in the context of a risk assessment – e.g. data may be considered relevant if they can affect the outcome of the risk assessment.

- Establishment of scientifically robust criteria for the inclusion of scientific information.

    - Data should be of an acceptable scientific quality. Data quality should be consistent with the accepted practices of scientific evidence-gathering and reporting and may include

[31] Annex III, paragraph 5.

[32] For the purpose of this document, a transgene is a nucleic acid sequence in an LMO that results from the application of modern biotechnology as described in Article 3 (i) (a) of the Protocol.

independent review of the methods and designs of studies. Data may be derived from a variety of sources, e.g. new experimental data as well as data from relevant peer reviewed scientific literature.

- Sound science is based on transparency, verifiability, and reproducibility (e.g. reporting of methods and data in sufficient detail, so that the resulting data and information could be confirmed independently), and on the accessibility of data (e.g. the availability of relevant, required data or information or, if requested and as appropriate, of sample material), taking into account the provisions of Article 21 of the Protocol on the confidentiality of information. The provisions of sound science serve to ensure and verify that the risk assessment is carried out in a scientifically sound and transparent manner.

- Identification and consideration of uncertainty.

According to the Protocol, "where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the living modified organism in the receiving environment".[33]

Uncertainty is inherent in the concept of risk. To date, "there is no internationally agreed definition of 'scientific uncertainty', nor are there internationally agreed general rules or guidelines to determine its occurrence. Those matters are thus dealt with – sometimes differently – in each international instrument incorporating precautionary measures".[34, 35]

It should be kept in mind that uncertainty cannot always be reduced by providing additional information. For example, new uncertainties may arise as a result of the provision of additional information.

Considerations of uncertainty strengthen the confidence and scientific soundness of a risk assessment. In communicating the results of a risk assessment, it is important to consider and analyze in a systematic way the various forms of uncertainty that can arise at each step and in combination at step 4 of the Roadmap. An analysis of uncertainty includes considerations of its source and nature.

The *source(s)* of uncertainty may stem from the data/information itself and/or the choice of study design including the methods used, and the analysis of the information.

The *nature* of uncertainty may be described for each identified source of uncertainty arising from: (i) imperfect knowledge or lack of available information, which may be reduced with more research/information, and (ii) inherent variability.

(*See references relevant to "Identification and consideration of uncertainty"*).

[33] Annex III, paragraph 8 (f).

[34] *An Explanatory Guide to the Cartagena Protocol on Biosafety*, paragraph 57 (http://data.iucn.org/dbtw-wpd/edocs/EPLP-046.pdf).

[35] Article 10, paragraph 6, of the Protocol: "Lack of scientific certainty due to insufficient relevant scientific information and knowledge regarding the extent of the potential adverse effects of a living modified organism on the conservation and sustainable use of biological diversity in the Party of import, taking also into account risks to human health, shall not prevent that Party from taking a decision, as appropriate, with regard to the import of that living modified organism intended for direct use as food or feed, or for processing, in order to avoid or minimize such potential adverse effects."

Context and scoping of the risk assessment

In setting the context and scope for a risk assessment, a number of aspects should be taken into consideration, as appropriate, that are specific to the Party involved and to the specific case of risk assessment. These aspects include:

- Existing policies and strategies based on, for instance, regulations and the international obligations of the Party involved; (ii) Guidelines or regulatory frameworks that the Party has adopted; and (iii) Protection goals, assessment end-points, risk thresholds and management strategies. Setting the context and scope for a risk assessment that are consistent with these policies, strategies and protection goals may involve a process that includes risk assessors, decision-makers and various stakeholders prior to conducting the actual risk assessment;

- (i) Framing the risk assessment process; (ii) Taking into account the expected (potential) conditions of handling and use of the LMO; (iii) Taking into account customary practices and habits that could affect the protection goals or end-points; identification of relevant questions to be asked for that purpose;

- Identification of methodological and analytical requirements, including any reviewing mechanisms, that is required to achieve the objective of the risk assessment as laid down, for instance, in guidelines published or adopted by the Party that is responsible for conducting the risk assessment (i.e. typically the Party of import according to the Protocol);

- The nature and level of detail of the information required may depend on the intended use of the LMO and the likely potential receiving environment. For small scale field releases, especially at early experimental stages, less information may be available compared to the information available for large scale environmental release, and for commercial scale planting;

- Experience and history of use of the non-modified recipient, taking into account its ecological function;[36] and

- Establishing criteria for describing the level of the (potential) environmental adverse effects of LMOs, as well as criteria for the terms that are used to describe the levels of likelihood (step 2), the magnitude of consequences (step 3) and risks (step 4) and the manageability of risks (step 5; see risk assessment steps below).

(*See references relevant to "Context and scoping of the risk assessment"*).

THE RISK ASSESSMENT

To fulfill its objective under Annex III, as well as other relevant Articles of the Protocol, risk assessment is performed in five steps, as appropriate. These five steps are indicated in Paragraph 8 (a)-(e) of Annex III and also detailed below. Their titles have been taken directly from the paragraphs 8 (a)-(e) of Annex III.

For each step a rationale and points to consider are provided. Some points to consider are taken from paragraph 9 of Annex III, whereas others have been added based on generally accepted methodology of

[36] The term "ecological function" (or: "ecological services") provided by an organism refers to the role of the organism in ecological processes. Which ecological functions or services are taken into account here will be dependent on the protection goals set for the risk assessment. For example, organisms may be part of the decomposer network playing an important role in nutrient cycling in soils or be important as a pollen source for pollinators and pollen feeders.

LMO risk assessment and risk management. The relevance of each point to consider will depend on the case being analyzed.

(*See references relevant to "Risk Assessment in general"*).

Step 1: "An identification of any novel genotypic and phenotypic characteristics associated with the living modified organism that may have adverse effects on biological diversity in the likely potential receiving environment, taking also into account risks to human health." [37]

Rationale:

The purpose of this step is to identify biological changes resulting from the genetic modification(s), including any deletions, compared to the non-modified organism, and identify what, if any, changes could cause adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health. This step is similar to the 'hazard identification step' in other risk assessment guidance. The comparison of the LMO is performed with the non-modified recipient, or a (near-)isogenic line or, as appropriate, with a non-modified organism of the same species, taking into consideration the new trait(s) of the LMO.

In this step, scientifically plausible scenarios are identified in which novel characteristics of the LMO could give rise to adverse effects in an interaction with the likely potential receiving environment. The novel characteristics of the LMO to be considered can be genotypic or phenotypic, biological. They may be intended or unintended, predicted or unpredicted. The points to consider below provide information elements on which hazard identification can be built.

The type and level of detail of the information required in this step may vary from case to case depending on the nature of the modification of the LMO and on the scale of the intended use of the LMO. For small scale field releases, especially at early experimental stages, less information may be available and some of the resulting uncertainty may typically be addressed by risk management measures (see step 5).

Points to consider regarding the characterization of the LMO:

(a) Relevant characteristics of the non-modified recipient (e.g. (i) its biological characteristics, in particular those that, if changed, or interacting with the new gene products or traits of the LMO, could cause changes in the behavior of the non-modified recipient in the environment in a way that may cause adverse effects; (ii) its taxonomic relationships, (iii) its origin, centers of origin and centers of genetic diversity); (iv) ecological function, and (v) as a component of biological diversity that is important for the conservation and sustainable use of the biological diversity in the context of Article 7(a) and Annex I of the Convention;

(b) Relevant characteristics of the genes and of other functional sequences, such as promoters, that have been inserted into the LMO (e.g. functions of the gene and its gene product in the donor organism with particular attention to characteristics that could cause adverse effects in the recipient);

(c) Molecular characteristics of the LMO related to the modification (e.g. (a) characteristics of the insert(s) which may include (i) gene products (intended and unintended), (ii) levels of expression, (iii) functions, (iv) insertion site in the genome of the recipient and any effects of insertion, (v) stability or integrity within the genome of the recipient; (b) (i) the transformation method, (ii) the characteristics of the vector if and, as far as it is present in the LMO, including its identity, source or origin and host range) with particular attention paid to any characteristics

[37] The bold printed headings of each step are direct quotes from Annex III of the Protocol.

that are related to potential adverse effects. The availability and relevance of this information may vary according to the type of application. Characteristics related to adverse effects may also result from changed expression levels of endogenous genes due to effects of a transgene or from combinatorial effects;[38]

(d) Consideration of genotypic (see point to consider (c) above) and phenotypic, biological changes in the LMO, either intended or unintended, in comparison with the non-modified recipient, considering those changes that could cause adverse effects. These may include changes at the transcriptional and translational level and may be due to the insert itself or to genomic changes due to the transformation or recombination processes.

Point to consider regarding the receiving environment:

(e) Characteristics of the likely potential receiving environment, in particular its attributes that are relevant to potential interactions of the LMO that could lead to adverse effects (see also paragraph (g) below),[39] taking into account the characteristics that are components of biological diversity;

(f) The intended scale and duration of the environmental release.

Points to consider regarding the potential adverse effects resulting from the interaction between the LMO and the receiving environment:

(g) Characteristics of the LMO in relation to the receiving environment (e.g. information on phenotypic traits that are relevant for its survival in, or its potential adverse effects on the likely receiving environment – see also paragraph (e) above);

(h) Considerations for unmanaged and managed ecosystems (such as agricultural, forest and aquaculture systems) that are relevant for the likely potential receiving environment. These include the potential for dispersal of the LMO through, for instance, seed dispersal or outcrossing within or between species, or through transfer into habitats where the LMO may persist or proliferate;

(i) Potential consequences of outcrossing and flow of transgenes from an LMO to other sexually compatible species, which could lead to introgression of the transgene(s) into the population of sexually compatible species;

(j) Effects on non-target organisms;

(k) Cumulative effects;[40]

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[38] For the purpose of this document, the term "combinatorial effects" refers to effects that may arise from the interactions between two (or more) genes. The effects may occur at the level of gene expression, or through interactions between RNA, or among gene products. The effects may be qualitative or quantitative; quantitative effects are often referred to as resulting in antagonistic, additive or synergistic effects.

[39] Examples of relevant attributes of the receiving environment include, among others: (i) ecosystem type (e.g., agroecosystem, horticultural or forest ecosystems, soil or aquatic ecosystems, urban or rural environments); (ii) extension of dimension (small, medium, large or mixed scale); (iii) previous use/history (intensive or extensive use for agronomic purposes, natural ecosystem, or no prior managed use in the ecosystem); (iv) the geographical zone(s) in which the release is intended, including climatic and geographic conditions and the properties of soil, water and/or sediment; (v) specific characteristics of the prevailing faunal, floral and microbial communities including information on sexually compatible wild or cultivated species; and (vi) biodiversity status, including the status as centre of origin and diversity of the recipient organism and the occurrence of rare, endangered, protected species and/or species of cultural value.

[40] For the purpose of this document, the term "cumulative effects" refers to effects that occur due to the presence of multiple LMOs in the receiving environment.

(l) Effects of the incidental exposure of humans to (parts of) the LMO (e.g. exposure to pollen), and the toxic or allergenic effects that may ensue;

(m) Potential adverse effects as a consequence of horizontal gene transfer (HGT) of transgenic sequences from the LMO to any other organism in the likely receiving environment. With regard to HGT to micro-organisms (including viruses), particular attention may be given to cases where the LMO is also a micro-organism; and

(n) A consideration of uncertainty arising in step 1 that may significantly impact the identification of hazards in this step (see "Identification and consideration of uncertainty" under Context and scoping of the risk assessment above).

(*See references relevant to "Step 1"*).

Step 2: "An evaluation of the likelihood of adverse effects being realized, taking into account the level and kind of exposure of the likely potential receiving environment to the living modified organism."

Rationale:

The potential adverse effects identified in step 1 may result in risks, but this depends on the likelihood and the consequence of the effects. In order to determine and characterize the overall risk (in step 4), the likelihood of each adverse effect being realized has to be assessed and evaluated beforehand.

One aspect to be considered is whether the receiving environment will be exposed to the LMO in such a way that the identified adverse effects may actually occur, e.g. taking into consideration the intended use of the LMO, and the expression level, dose and environmental fate of transgene products as well as plausible pathways leading to adverse effects.

Other aspects to be considered here are (i) the potential of the LMO (or its derivatives resulting from outcrossing) to spread and establish beyond the receiving environment (in particular into protected areas), and whether that could result in adverse effects; and (ii) the possibility of occurrence of adverse (e.g. toxic) effects on organisms (or on organisms other than the 'target organism' for some types of LMOs).

The levels of likelihood may be expressed, for example, by the terms 'highly likely', 'likely', 'unlikely', 'highly unlikely'. Parties may consider describing these terms and their uses in risk assessment guidelines published and/or adopted by them.

Points to consider:

(a) Information relating to the type and intended use of the LMO, including the scale and duration of the release, bearing in mind, as appropriate, user habits, patterns and agronomic practices;

(b) The relevant characteristics of the likely potential receiving environment that may experience or may be a factor in the occurrence of the potential adverse effects (see also step 1 (e), (f) and (g)), taking into account the variability of the environmental conditions and any long-term adverse effects. Levels of expression in the LMO and persistence and accumulation in the environment (e.g. in the food chain) of substances with potentially adverse effects newly produced by the LMO, such as insecticidal proteins, toxins and allergens;

(c) Available information on the location of the release and the receiving environment (such as geographic and biogeographic information, including, as appropriate, coordinates, information on the sexually compatible species and whether they are co-localized with the LMO and whether flowering occurs at the same time, or in general, interbreeding can occur);

(d) For the case of outcrossing and outbreeding from an LMO to sexually compatible species, the considerations would include: (i) the biology of the sexually compatible species; (ii) the potential environment where the sexually compatible species may be located; (iii) the chance of introgression of the transgene into the sexually compatible species;

(e) Expected exposure to the environment where the LMO is released and means by which incidental exposure could occur at that location or elsewhere (e.g. gene flow or incidental exposure due to losses during transport and handling);

(f) A consideration of uncertainty arising in step 2 (see "Identification and consideration of uncertainty" under "Context and scoping of the risk assessment" above).

(*See references relevant to "Step 2"*).

Step 3: "An evaluation of the consequences should these adverse effects be realized."

Rationale:

This step describes an evaluation of the magnitude of the consequences in the likely potential receiving environment, taking into account, among others, results of tests done under different conditions such as laboratory experiments or experimental field releases. The evaluation is comparative and should be considered in the context of the adverse effects caused by the non-modified recipient or, if more appropriate, by a near-isogenic or other non-modified organism of the same species. The evaluation may also be considered in the context of the adverse effects that occur in the environment and which are associated with existing practices such as various agronomic practices, for example, for pest or weed management if such information is available and relevant. The evaluation of the consequence of adverse effects may be expressed as, for instance, 'major', 'intermediate', 'minor' or 'marginal'. Parties may consider describing these terms and their uses in risk assessment guidelines published and/or adopted by them.

Points to consider:

(a) Relevant experience with the consequences of existing practices with the non-modified recipient or, if more appropriate, with a non-modified organism of the same species in the likely potential receiving environment, may be useful in order to establish baselines to evaluate, for example, the consequences of (i) agricultural practices, such as the level of inter- and intra-species gene flow, dissemination of the recipient, abundance of volunteer plants in crop rotation; occurrence of pests and/or beneficial organisms such as pollinators and pest predators; or (ii) pest management, including effects on non-target organisms in pesticide applications while following accepted agronomic practices;

(b) Adverse effects which may be direct and indirect, immediate and delayed. Some of these adverse effects may result from combinatorial and cumulative effects;

(c) Results from laboratory experiments examining, *inter alia*, dose-response relationships (e.g., EC 50s, LD 50s) and from field trials evaluating, for instance, potential invasiveness;

(d) For the case of outcrossing to sexually compatible species, the possible adverse effects that may occur, after introgression, due to the expression of the transgenes in the sexually compatible species; and

(e) A consideration of uncertainty arising in step 3 that may significantly impact the evaluation of consequences should the adverse effects be realized (see "Identification and consideration of uncertainty" under Context and scoping of the risk assessment above).

(*See references relevant to "Step 3"*).

Step 4: "An estimation of the overall risk posed by the living modified organism based on the evaluation of the likelihood and consequences of the identified adverse effects being realized."

Rationale:

The purpose of this step is to determine and characterize the level of the overall risk based on the identified individual risks posed by the LMO on the conservation and sustainable use of biological diversity, taking also into account human health. The individual risks are determined on the basis of an analysis of the potential adverse effects identified in step 1, their likelihood (step 2) and consequences (step 3), and also taking into consideration any relevant uncertainty that emerged in the preceding steps.

It should then be determined whether the assessed risks meet the criteria set out in the protection goals, assessment endpoints and thresholds, as established in relevant legislation of the Party or in its practice. Where there is uncertainty regarding the level of risk, it may be addressed by requesting further information on the specific issues of concern or by implementing appropriate risk management strategies and/or monitoring the LMO in the receiving environment (see also step 5). Description of the risk characterization may be expressed as, for instance, 'high', 'medium', 'low', 'negligible' or 'indeterminate due to uncertainty or lack of knowledge'. Parties may consider describing these terms and their uses in risk assessment guidelines published and/or adopted by them.

To date, there is no universally accepted method to estimate the overall risk but rather a number of methods are available for this purpose. The outcome of this step may be, for example, a description explaining how the estimation of the overall risk was performed.

Points to consider:

(a) The identified potential adverse effects (step 1);

(b) The assessments of likelihood (step 2);

(c) The evaluation of the consequences (step 3);

(d) Any interaction between the identified individual risks;

(e) Any cumulative effect due to the presence of multiple LMOs in the receiving environment; and

(f) A consideration of uncertainty arising in this and the previous steps (see "Identification and consideration of uncertainty" under Context and scoping of the risk assessment above).

(*See references relevant to "Step 4"*).

Step 5: "A recommendation as to whether or not the risks are acceptable or manageable, including, where necessary, identification of strategies to manage these risks"

Rationale:

In this way, step 5 provides an interface between the process of risk assessment and the process of determining whether risk management measures are necessary and, if so, which measures could be implemented to manage the risks associated with the LMO.

The evaluation of the overall risk on the basis of the identified individual risks conducted in the previous step may lead to the conclusion that the identified risks are not acceptable in relation to the established protection goals, assessment end-points and risk thresholds, also when taking into account risks posed by

the non-modified recipient and its use. Then the question arises whether risk management options can be identified that have the potential to remove the identified risks or reduce their magnitude. In the process of the formulation of risk management options, the effect of the proposed options on the identified risks should be explained. The appropriate steps of the risk assessment should then be reiterated by taking into account the implementation of the risk management options to estimate the new levels of likelihood, consequence and risk and to assess if the risk management measures are appropriate and sufficient.

The issues mentioned in the 'overarching issues' section can be taken into consideration again at the end of the risk assessment process to evaluate whether the objectives and criteria that were set out at the beginning of the risk assessment have been met.

The recommendation of acceptability of risk(s) should acknowledge the previously identified uncertainties. Some uncertainties may be reduced by monitoring (e.g. checking the validity of assumptions about the ecological effects of the LMO), requests for more information, or implementing the appropriate risk management options.

The recommendation(s) as to whether or not the risks are acceptable or manageable and recommendations for risk management options are submitted for consideration in the decision-making process.

Points to consider related to the acceptability of risks:

(a) The criteria for the establishment of acceptable/unacceptable levels of risk, including those set out in national legislation or guidelines, as well as the protection goals of the Party, as identified when setting the context and scope for a risk assessment;

(b) In establishing a baseline for the comparison of the LMO, any relevant experience with the use of the non-modified recipient, and practices associated with its use in the potential receiving environment; and

(c) The feasibility of the adoption of risk management or monitoring strategies.

Points to consider related to the risk management strategies:

(d) Existing management practices, if applicable, that are in use for the non-modified recipient organism or for other organisms that require comparable risk management and that might be appropriate for the LMO being assessed, e.g. isolation distances to reduce outcrossing potential of the LMO, modifications in herbicide or pesticide management, crop rotation, soil tillage, etc.;

(e) Methods to detect and identify the LMO and their specificity, sensitivity and reliability in the context of environmental monitoring (e.g. monitoring for short- and long-term, immediate and delayed effects; specific monitoring on the basis of scientific hypotheses and supposed cause/effect relationship as well as general monitoring) including plans for appropriate contingency measures to be applied in case the results from monitoring call for them;

(f) Management options in the context of the intended use (e.g. mitigating the effect of an LMO producing insecticidal proteins by the use of refuge areas to minimize the development of resistance against these proteins).

(*See references relevant to "Step 5"*).

RELATED ISSUES

Some members of the AHTEG considered some issues to be related to risk assessment and decision-making process but outside the scope of this Roadmap. These issues were, *inter alia*:

- Risk management (Article 16);
- Capacity-building (Article 22);
- Public awareness and participation (Article 23);
- Socio-economic considerations (Article 26);
- Liability and redress (Article 27);
- Co-existence;
- Ethical issues.

Annex

FLOWCHART FOR RISK ASSESSMENT

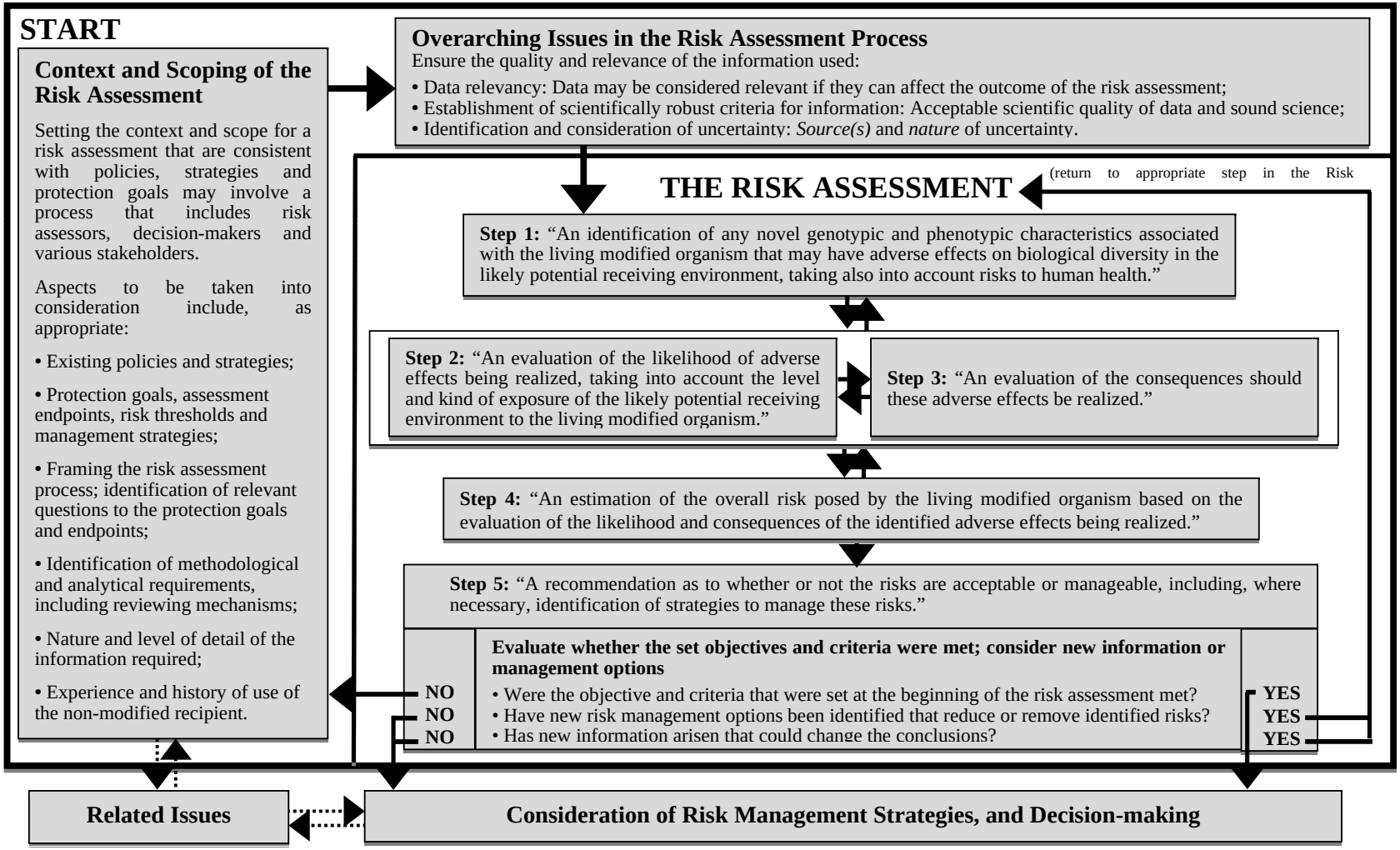

Figure 1. The Roadmap for Risk Assessment. The flowchart represents the steps to *identify* and *evaluate* the potential adverse effects of LMOs on the conservation and sustainable use of biological diversity in the likely potential receiving environment, taking also into account risks to human health. The box around steps 2 and 3 shows that these steps may sometimes be considered simultaneously or in reverse order.

PART II

SPECIFIC TYPES OF LMOs AND TRAITS

A. RISK ASSESSMENT OF LIVING MODIFIED ORGANISMS WITH STACKED GENES OR TRAITS

INTRODUCTION

Worldwide, a growing number of LMOs with stacked transgenic traits, particularly LM crops, are being developed for commercial uses. As a result, the number of stacked genes in a single LMO and the number of LMOs with two or more transgenic traits is growing.

Stacked transgenic traits can be produced through different approaches. In addition to the cross-hybridising of two LMOs, multiple trait characters can be achieved by transformation with a multigene cassette, retransformation of an LMO or simultaneous transformation with different transgene cassettes (i.e., cotransformation).

This guidance document focuses on stacked transgenic traits that have been produced through cross-breeding of two or more LMOs.

LMOs with multiple transgenic traits resulting from re-transformation, co-transformation or transformation with a multigene cassette should be assessed according to the Roadmap.

This guidance document complements the Roadmap for Risk Assessment developed by the AHTEG on Risk Assessment and Risk Management, and focuses on issues that are of particular relevance to the risk assessment of LMOs with stacked events generated through cross breeding of single or multiple event LMO.

This is intended to be a "living document" that will be shaped and improved with time as new information and/or experience becomes available and new developments in the field of applications of LMOs occur, as and when mandated by the Parties to the Protocol.

OBJECTIVE

The objective of this document is to give additional guidance on the risk assessment (RA) of LMOs with stacked events generated through conventional crossing of single or multiple event LMOs. Accordingly, it is meant to complement the Roadmap for Risk Assessment[41] and address special aspects of LMOs with stacked transgenes/traits resulting from the conventional crossing. For the time being it will be restricted to plant LMOs.[42]

[41] In accordance with a mandate from the Parties to the Cartagena Protocol on Biosafety (the Protocol), the AHTEG has developed 'a "roadmap", such as a flowchart, on the necessary steps to conduct a risk assessment in accordance with Annex III to the Protocol and, for each of these steps,' has provided 'examples of relevant guidance documents'. The Roadmap is presented, together with the present document, to the Parties of the Protocol on the occasion of the fifth meeeting of the Conference of the Parties serving as the meeting of the Parties.

[42] It is also restricted to those LMO generated through the methods of Modern Biotechnology as defined in Art. 3 (i) (a) of the Protocol. LMOs derived from fusion of cells are not covered in this document.

USE OF TERMS

Transformation event (TraEv)

For the purpose of this document, a transformation event (TraEv) is an LM plant which results from the use of modern biotechnology applying *in vitro* nucleic acid techniques[43] that may involve, but is not limited to, single or multiple gene transformation cassettes. In either case, the result will be one transformation event.

Stacked event (StaEv)

For the purpose of this document, a stacked event (StaEv) is an LM plant generated through conventional cross breeding of two or more single parental transformation events (TraEvs) or two already stacked events. Accordingly the transgene[44] cassettes may be physically unlinked (i.e. located separately in the genome) and may segregate independently.

Unintentional stacked event

Unintentional stacked events are the result of outcrossing of stacked events into other LMOs or compatible relatives in the receiving environment. Depending on the segregation pattern of the stacked genes this may result in new and/or different combinations of TraEvs.

SCOPE

This guidance document focuses on stacked events (StaEv) resulting from conventional crossings between two or more single transformation events (TraEv) as parental lines so that the resulting LMO contains two or more transgenic traits. It is understood that the individual TraEvs making up the StaEv have been assessed previously in accordance with Annex III of the Cartagena Protocol on Biosafety and as described in the Roadmap.

ISSUES TO BE CONSIDERED IN THE RISK ASSESSMENT

Assessment of sequence characteristics at the insertion sites and genotypic stability *(see step 1, Point to consider (c) of the Roadmap for Risk Assessment)*

Rationale:

Although recombination, mutation and rearrangements are not limited to LMOs, the combination of transgenic traits via cross breeding may further change the molecular characteristics of the inserted genes/gene fragments at the insertion site and/or influence the regulation of the expression of the transgenes. In addition, changes to the molecular characteristics may influence the ability to detect the LMO, which may be needed in the context of risk management measures (see step 5 of the Roadmap. The reappraisal of the molecular sequence at the insertion sites, and the intactness of the transgenes may be confirmative to the molecular characteristics of the parental LMOs, but may also be a basis for assessing any intended or unintended possibly adverse effects on the conservation and sustainable use of biological diversity in the likely potential receiving environment and of potential adverse effects on human health. The extent of the reexamination may vary case by case and take into account the results of the parental LMO risk assessment.

[43] See Article 3 (i) (a) of the Protocol.

[44] For the purpose of this document, a transgene is a nucleic acid sequence that results from the application of modern biotechnology as described in Article 3 (i) (a) of the Protocol.

Assessment of potential interactions between combined events and the resulting phenotypic effects *(see step 1, point to consider (d) of the Roadmap for Risk Assessment)*

Rationale:

The combination of two or more TraEvs resulting in a StaEv may influence the expression level of each of the transgenes and there may be interaction between the genes and the expressed products of the different transgenes. In addition, the stacked transgenes may alter the expression of endogenous genes.

Therefore, in addition to information about the characteristics of the parental single-TraEv LMOs, specific information on potential for interactions between the altered or inserted genes, stacked proteins or modified traits and endogenous genes and their products in the StaEv LMO should be considered and assessed. For example, it should be assessed whether the different transgenes affect the same biochemical pathways or physiological processes, or are expected to or may have any combinatorial effects that may result in potential for new or increased adverse effects relative to the parent LMOs.

Assessment of combinatorial and cumulative effects of stacked event LMOs on the conservation and sustainable use of biological diversity in the likely potential receiving environment, taking also into account potential adverse effects to human health *(see step 1, point to consider (c), step 2, point to consider (c) and step 3, point to consider (b) of the Roadmap for Risk Assessment)*

Rationale:

Assessment of combinatorial and cumulative effects[45] is based on the environmental risk assessment data for the StaEv LMO in comparison to the closely related non-modified recipient species and the parent LMOs in the likely receiving environment, taking into consideration the results of the genotypic and phenotypic assessments outlined above.

If potential new or increased adverse effects on the conservation and sustainable use of biological diversity or on human health are identified in relation to the StaEv through the above analysis of possible interactions, additional supporting data on StaEv may be required, such as:

(a) Phenotypic characteristics, including the levels of expression of any introduced gene products or modified traits, compared to the parent LMOs and to relevant non-modified recipient organisms (plants);

(b) Compositional analysis (e.g. levels of expression in the LMO and persistence and accumulation in the environment, such as in the food chain) of substances with potentially harmful effects newly produced by the StaEv, (e.g. insecticidal proteins, allergens, anti-nutritional factors, etc.) in amounts that differ from those produced by the parental LMOs or non-modified recipient organisms;

(c) Additional information depending on the nature of the combined traits. For example, further toxicological analysis of the StaEv may be required to address any combinatorial effects arising from the stacking of two or more insecticidal traits that result in a broadened target range or increased toxicity.

Also, indirect effects due to changed agricultural management procedures, combined with the use of the transgenic stacked event LMO, should be taken into consideration.

[45] See definition of combinatorial and cumulative effects in the Roadmap (footnotes 38 and 40, respectively).

Intentional and unintentional StaEvs may have altered environmental impacts as a result of cumulative and combinatorial effects of the stacked traits prevalent in different LMOs of the same species in the receiving environment. Unintentional StaEvs may arise from outcrossing with other LMOs of the same species or cross-compatible relatives (see "Use of terms"). If a number of different StaEvs are cultivated in the same environment a number of varying unintentional StaEvs may occur. Changed impacts on non-target organisms or a change in the range of non-target organisms in the likely receiving environment should be taken into account.

Development of specific methods for distinguishing the combined transgenes in a stacked event from the parental LMOs *(see step 5, point to consider (d) of the Roadmap for Risk Assessment)*

Rationale:

Some of the risk management strategies for StaEvs may involve methods for the detection and identification of these LMOs in the context of environmental monitoring. Currently, many detection methods for LMOs rely on DNA-based techniques, such as polymerase chain reaction (PCR) or protein based ELISA tests targeted to single transformation events. The methods used to detect the transgene in the parental lines may not be sensitive or specific enough to differentiate between single parental transformation events and the same event being part of a stacked event. A special problem may arise particularly in the cases where the StaEv contains multiple transgenes with similar DNA sequences. Therefore, the detection of each and all individual transgenes in a StaEv may become a challenge and need special consideration.

BIBLIOGRAPHIC REFERENCES

See references relevant to the "*Guidance Document on Risk Assessment of LMOs with Stacked Genes or Traits*".

B. RISK ASSESSMENT OF LIVING MODIFIED CROPS WITH TOLERANCE TO ABIOTIC STRESS

INTRODUCTION

The aim of this document is to provide further guidance for the risk assessment of living modified (LM) crops with improved tolerance to abiotic stress.

This guidance document should be considered in the context of the Cartagena Protocol on Biosafety. The elements of Articles 15 Annex III of the Protocol also apply to LM crops with tolerance to abiotic stress. Accordingly, the methodology and points to consider[46] contained in Annex III are also applicable to this type of LMO.

The potential environmental adverse effects of an LM crop with abiotic stress tolerance depends on (i) the receiving environment; (ii) the modified crop, (iii) phenotypic changes resulting from the genotypic changes made to the plant and (iv) its intended use. A risk assessment would be performed on a case-by-case basis in accordance with Annex III of the Protocol.

This guidance document complements the Roadmap for Risk Assessment developed by the AHTEG on Risk Assessment and Risk Management, and focuses on issues that are of particular relevance to the risk assessment of LM crops tolerant to abiotic stress.

USE OF TERMS

"Abiotic stresses" are environmental conditions caused by non-living factors that are detrimental or suboptimal to the growth, development and/or reproduction of a living organism. Types of abiotic stresses include, for example, drought, salinity, cold, heat, soil pollution and air pollution (e.g., nitrous oxides, ozone).

RISK ASSESSMENT

While the same general principles used in the risk assessments of other types of LMOs also apply to LM crops with increased tolerance to abiotic stress, there are a number of specific issues that may be of particular importance when assessing the risks of LM crops tolerant to abiotic stresses.

Questions that may be relevant to the risk assessment of LM crops with tolerance to abiotic stress in connection with the intended use and receiving environment include:

- Would the tolerance trait have the potential to increase the invasiveness, persistence or weediness of the LM crop that causes adverse effects to other organisms?
- Would a LM plant expressing tolerance to a particular abiotic stress have other advantages in the targeted receiving environment that cause adverse effects?
- Would any LMO arising from outcrossing with the abiotic stress tolerant LM crop, have the potential to colonize an ecosystem beyond the targeted receiving environment?
- Would the abiotic stress tolerance trait, for example, via pleitropic effects, have the potential to affect, *inter alia*, pest and disease resistance mechanisms of the LM crop?

[46] Paragraphs 8 and 9 of Annex III, respectively.

Some of the potential adverse effects to be evaluated in the risk assessment, from the introduction of crops tolerant to abiotic stress into the environment include, for example: a) increased selective advantage(s) other than the intended tolerance trait; b) increased persistence in agricultural areas and increased invasiveness in natural habitats; c) adverse effects on organisms exposed to the crop; and d) consequences of potential gene flow to wild or conventional relatives. While these adverse effects may exist regardless of whether the tolerant crop is a product of modern biotechnology or conventional breeding, some specific issues may be more relevant in the case of abiotic stress tolerant LM crops.

Characterization of the LM crop with tolerance to abiotic stress in comparison with its non-modified crop *(see step 1 of the Roadmap for Risk Assessment)*

Rationale:

The first step in the risk assessment process involves the characterization of genotypic or phenotypic, biological, intended and unintended changes associated with the abiotic stress tolerant LM crop that may have adverse effects on biodiversity in the likely receiving environment, taking into account risks to human health. This step is the 'hazard identification step' in other risk assessment guidance.

The identification of genotypic and phenotypic changes in the abiotic stress tolerant LM crop, either intended or unintended, is typically done in comparison with the non-modified recipient organism (see step 1 of the Roadmap). The non-modified comparator provides the baseline information for comparison of trials when it is grown at the same time and location as the LM crop. Comparisons with the observed range of changes in the non-modified crop in different environments, also provides baseline information.

Challenges with respect to experimental design: Abiotic stress crops may present unique challenges in experimental design for risk assessment. In some cases, for instance, an approach uses different reference plant lines, which typically include a range of genotypes representative of the natural variation in the crop species. In such conditions, choosing appropriate comparators could be a challenge and there are several proposals on whether and how the comparative approach can be used to characterize LM crops tolerant to abiotic stress in these likely receiving environments. Another important consideration is whether the experimental design properly controlled for the effect of the abiotic stress trait. In the extreme case, when the non-modified crop has never been grown in the range of conditions of the receiving environment because the abiotic stress conditions prevent or severely affect the growth of the non-modified crop, a comparative approach between the LM crop and the non-modified crop will need to be adjusted.

The use of non-isogenic reference lines can make it more difficult to identify statistically meaningful differences. In some situations when a comparator may not be available to carry out a meaningful comparison, a characterization of the abiotic stress tolerant LM crop as a novel genotype in the receiving environment may be conducted. In the future, information available from "omics" technologies, for example, "transcriptomics" and "metabolomics", if available, may help to detect phenotypes (e.g., the production of a novel allergen or anti-nutrient) that cannot be detected using a comparison between field grown plants at a suboptimal condition.

Points to consider:

(a) Characteristics of the LM crop under the abiotic stress and non-stress conditions and under different stresses, if applicable;

(b) Likelihood of gene flow to wild or domestic relatives; and

(c) Whether one or more suitable comparators are available and the possibility of their use in the appropriate experimental design.

Unintended characteristics *(see step 1 of the Roadmap for Risk Assessment)*

Rationale:

Both intended and unintended changes to the LM crop which are directly or indirectly associated with the abiotic stress tolerance that may have adverse effects should be identified. These include changes to the biology of the crop plant (e.g. if the genes alter multiple characteristics of the plant) or to its distribution range in relation to the potential receiving environment (e.g. if the plant can grow where it has not grown before), that may cause adverse effects.

The abiotic-stress-tolerant LM crop may have unintended characteristics such as tolerances to other types of biotic and abiotic stresses, which could lead to a selective advantage of these crop plants under conditions other than that related to the modified trait. For instance, crops modified to become tolerant to drought or salinity may be able to compete better than their counterparts at lower and higher growing temperatures.

It is also possible the LM crops with enhanced tolerance to an abiotic stress could have changes in seed dormancy, viability, and/or germination rates under other types of stresses. Particularly if genes involved in abiotic stress are also involved in crucial steps in physiology, modifications involving these genes may, therefore, have pleiotropic effects. Such LM crops may also transfer genes for stress tolerance at higher frequencies than observed in non-modified crops.

A potential mechanism for interactions between abiotic and biotic stresses may exist in plants. For example, drought or salinity-tolerant LM crops may acquire a changed tolerance to biotic stresses, which could result in changed interactions with their predators, parasitoids and pathogens, and, therefore, have both direct and indirect effects on organisms that interact with them.

Points to consider:

(a) Any intended or unintended change that may lead to selective advantage or disadvantage acquired by the LM crop under other abiotic or biotic stress conditions that could cause adverse effects;

(b) Any change in the resistance to biotic stresses and how these could affect the population of organisms interacting with the LM crop; and

(c) A change in the substances (e.g., toxin, allergen, or nutrient profile) of the LM crop that could cause adverse effects.

Increased persistency in agricultural areas and invasiveness of natural habitats *(see steps 1, 3 and 5 of the Roadmap for Risk Assessment)*

Rationale:

Climate change, water depletion or elevated salt content are examples of factors that limit the growth, productivity, spread or persistence of a crop. Expression of the genes for abiotic stress tolerance could result in increased persistence of the modified crop in agricultural areas. Expression of these genes may also alter the capacity of LM crops to spread to and establish in climatic and geographic zones beyond those initially considered as the likely or potential receiving environments.

The gene(s) inserted for tolerance to, for instance, drought and salinity might also affect molecular response mechanisms to other forms of abiotic stress, such as cold temperatures. For example, when the genetic modification affects genes that also regulate key processes in seeds, such as abscisic acid (ABA) metabolism, physiological characteristics such as dormancy and accumulation of storage lipids may also be changed. In such cases, the seeds of a tolerant crop, modified for drought or salinity tolerance, may acquire in addition tolerance to cold resulting in an increased winter survivability of the seeds. Therefore, an abiotic stress-tolerant crop may acquire the potential to persist better than its conventional counterpart under different abiotic-stress conditions.

Points to consider:

(a) Consequences of the increased potential for persistency of the modified crop in agricultural habitats and consequences of increased potential for invasiveness in natural habitats;

(b) Need for control measures if the abiotic stress-tolerant crop shows a higher potential for persistency in agricultural or natural habitats, that could cause adverse effects;

(c) Characteristics that are generally associated with weediness such as prolonged seed dormancy, long persistence of seeds in the soil, germination under a broad range of environmental conditions, rapid vegetative growth, short lifecycle, very high seed output, high seed dispersal and long-distance seed dispersal; and

(d) Effects of climate change on agriculture and biodiversity and how this could change the habitat range of the LM crop in comparison to the non modified crop.

(e) If the LM crop expressing tolerance, would have a change in its agriculture practices.

BIBLIOGRAPHIC REFERENCES

See references relevant to the "Guidance Document on Risk Assessment of LM Crops with Tolerance to Abiotic Stress".

C. RISK ASSESSMENT OF LIVING MODIFIED MOSQUITOESINTRODUCTION

Living modified (LM) mosquitoes are being developed through modern biotechnology to reduce transmission of vector borne human pathogens, particularly those that cause malaria, dengue and chikungunya. Control, including eradication of such diseases, is a recognized public health goal. Some of the strategies being developed are to control mosquito vectors by suppressing their population or reducing their competence. These strategies can be subcategorized according to the technology involved and the method used. Some are intended to develop LM mosquitoes that are genetically modified to be sterile or self-limiting (i.e., unable to pass the modified trait on indefinitely through subsequent generations). Modern biotechnology techniques for developing sterile LM mosquitoes are different from those based on the use of irradiation to induce male sterility.

Other modern biotechnology strategies are also being used for developing LM mosquito populations that are self-sustaining or self-propagating (i.e., heritable modifications intended to spread through the target population). The strategy used is an important factor to be considered in the risk assessment and risk management process since there might be different points to be considered, depending on the specific strategy used.

The biology and ecology of mosquitoes on the one hand, and their impact on public health as vectors of human and animal diseases on the other hand, pose new considerations and challenges during the risk assessment process, which have mainly dealt with LM crop plants thus far.

This guidance document provides information for the risk assessment of environmental releases of LM mosquitoes and aims at helping to conduct risk assessments for environmental releases of LM mosquitoes. Although the focus of this guidance is on LM mosquitoes, in principle, it may also be useful for the risk assessment of similar non-LM mosquito strategies.

The main emphasis of this guidance document is the assessment of potential risks to biodiversity. Nevertheless, the potential adverse effects to human health arising from environmental releases of LM mosquitoes should also be considered.

This guidance document complements the Roadmap for Risk Assessment developed by the AHTEG on Risk Assessment and Risk Management and focuses on specific issues that may need special consideration on the risk assessment for environmental releases of LM mosquitoes.

OBJECTIVE

The objective of this document is to give additional guidance on the risk assessment (RA) of LM mosquitoes in accordance with Annex III to the Cartagena Protocol on Biosafety.[47] Accordingly, it aims at complementing the Roadmap for Risk Assessment on specific issues that may need special consideration for the environmental release of LM mosquitoes.

SCOPE

This document focuses on the specifics aspects of risk assessment of LM mosquitoes developed to be used in the control of human and zoonotic diseases such as malaria, dengue, chikungunya, yellow fever and West Nile.

[47] The Parties to the Cartagena Protocol on Biosafety have mandated the AHTEG to 'develop a "roadmap", such as a flowchart, on the necessary steps to conduct a risk assessment in accordance with Annex III to the Protocol and, for each of these steps, provide examples of relevant guidance documents'. The Roadmap is meant to provide reasoned guidance on how, in practice, to apply the necessary steps for environmental risk assessment as set out in Annex III of the Protocol. The Roadmap also demonstrates how these steps are interlinked.

ISSUES TO BE CONSIDERED IN THE RISK ASSESSMENT

(See step 1 of the Roadmap for Risk Assessment of LMOs)

Specific and comprehensive considerations should be undertaken with respect to the potential adverse effects of a particular LM mosquito, taking into account the species of the mosquito, the LM trait, the intended receiving environment, and the objective and scale of the intended release. These considerations should focus on, for instance: (a) description of the genetic modification; (b) the kinds of possible adverse effects for which there are scientifically plausible scenarios; (c) the species and ecological processes that could be affected by the introduction of the LM mosquitoes; (d) the protection goals of the country where the LM mosquitoes will be introduced; and (e) a conceptual link between the identified protection goals and the introduction of the LM mosquito into the environment.

The biology and, to some extent, the ecology of the mosquito species that transmit malaria and dengue are well known in many regions of the world. However, in certain regions and in the environment where the LM mosquito is likely be released, more information may be needed depending on the nature and scale of the LM strategy to be deployed. In many of these environments few studies have been conducted to examine gene flow among vectors, their mating behaviour, the interactions between vectors sharing one habitat, how pathogens respond to the introduction of new vectors, etc. Such information may be needed to establish a baseline in order to successfully assess the risks of LM mosquitoes. Additionally, methods for the identification of specific ecological or environmental hazards are also needed.

Effects on biological diversity (species, habitats, ecosystems, and ecosystem services)

(*See step 2 of the Roadmap for Risk Assessment of LMOs*)

Rationale:

The release of LM mosquitoes may have a negative impact on the target vector and pathogen[48] and other species, such as:

New or more vigorous pests, especially those that have adverse effects on human health: (i) the released LM mosquitoes may not function as expected, for example gene silencing or production failures could result in the release of non-sterile or competent mosquitoes and thus increase the vector population or disease transmission; (ii) the released LM mosquitoes could transmit another disease more efficiently than indigenous non-LM mosquitoes, such diseases might include yellow fever, chikungunya, etc.; (iii) suppression of the target mosquito might result in the population of another vector species to increase and result in higher levels of the target disease or the development of a new disease in humans and/or animals. These other vector species may include other mosquito vectors of other diseases; (iv) the released LM mosquitoes might become pests; (v) the released LM mosquitoes might cause other pests to become more serious, including agricultural pests and other pests that affect human activities.

Harm to or loss of other species: The released LM mosquitoes might cause other species (for instance fish that rely seasonally on mosquitoes for food) to become less abundant. These include species of ecological, economic, cultural and/or social importance such as wild food, endangered, keystone, iconic and other relevant wildlife species. Ecological effects might result from competitive release if the target mosquito population is reduced or from trophic consequences of species that rely on mosquitoes for food at specific times of the year. Effects may also occur if (i) the target mosquitoes transmit a disease to animal species, (ii) the released LM mosquitoes transmit a disease to animal species more efficiently, (iii) another vector of an animal disease was released from control when the target mosquito population was reduced, or (iv)

[48] For the purpose of this guidance, the term “target vector” refers to the mosquito that transmits the disease and “target pathogen” is the disease causing agent transmitted by the target mosquito.

the population of a target pathogen is reduced or lost and this may affect other organisms that interact with it.

Although mosquitoes, like other insects, typically have strong reproductive isolating mechanisms that will not allow interspecific gene flow, if sterile interspecific mating between released LM mosquitoes and other mosquito species should occur, it could disrupt the population dynamics of these other species, leading to harm or loss of valued ecological species. Moreover, cessation of transmission of pathogens to other animals (e.g., West Nile virus to birds, Rift Valley fever virus to African mammals) might alter the population dynamics of those species, favouring increases in their numbers.

Disruption of ecological communities and ecosystem processes: The ecological communities in the ephemeral, small aquatic habitats occupied by the non-LM mosquitoes are unlikely to be disrupted beyond the possibilities already addressed above under "harm to or loss of other species." However, if the released LM mosquitoes were to inhabit natural habitats (e.g. tree-holes), disruption of the associated community is a possibility. The released LM mosquitoes might degrade some valued ecosystem process. This might include processes such as pollination or support of normal ecosystem functioning. These processes are often referred to as "ecosystem services". However, the valued ecosystem processes may also be culturally or socially specific. Under some circumstances, mosquito species are significant pollinators. In those cases, mosquito control of any kind might reduce the rate of pollination of some plant species or cause a shift to different kinds of pollinators. Habitats in which mosquitoes are the dominant insect fauna (e.g., high Arctic tundra, tree holes) would be changed if mosquitoes were eliminated; however, the common target vector species are usually associated with human activity and therefore not as closely tied to ecosystem services.

Points to consider:

(a) Impacts on the target mosquitoes and pathogens resulting from the use of the strategy under consideration;

(b) Whether the LM mosquitoes have the potential of causing adverse effects on other species which will result in the other species becoming agricultural, aquacultural, public health or environmental pests, or nuisance or health hazards;

(c) Whether the target mosquito species is native or invasive to a given area;

(d) The habitat range of the target mosquito species and whether the habitat range is likely to be affected by climate change;

(e) Any other species (e.g. animal hosts, larval pathogens or predators of mosquitoes) in addition to the pathogen, that typically interact with the LM mosquito in the likely receiving environment;

(f) Whether the release of LM mosquitoes is likely to affect other mosquito species that are pollinators or otherwise known to be beneficial to ecosystem processes;

(g) Whether the LM mosquitoes are likely to have an adverse effect on other interacting organisms, e.g. predators of mosquitoes;

(h) Whether species replacement by other disease vector species may occur, and if so, whether it can result in an increased incidence of the target disease or new diseases in humans or animals.

Gene Flow

(*See steps 2 and 3 of the Roadmap for Risk Assessment of LMOs*)

Rationale:

With regard to the biosafety of LM mosquitoes, gene flow refers to the transfer of transgenes[49] or genetic elements from the LM mosquitoes to non-LM mosquitoes. It can occur via cross-fertilisation or other movement of the transgenes or genetic elements. Various factors may influence gene flow and any associated adverse effects, such as, the strategy, the transgenes, the gene drive system [50] and the stability of the trait(s) carried by the mosquito over generations, as well as the receiving environment, etc.

Gene flow through cross-fertilization: Some LM mosquitoes are being developed to spread the introduced trait rapidly through the target mosquito population. For instance, when introduced into *Anopheles gambiae*, the trait may be expected to spread throughout the *A. gambiae* species complex. Other LM mosquito technologies are designed to be self-limiting and, in such cases, spread of the transgenes or genetic elements in the target mosquito population is not intended or expected. For the self-limiting technologies, the potential for an unexpected spread of the introduced trait should be considered by focusing on the assumption that any management strategy to limit the spread could fail. Gene flow between different species should be considered for all of the LM mosquito technologies in spite of the fact that mosquitoes, like other insects, typically have strong reproductive isolating mechanisms that will not allow interspecific gene flow. Identifying the key reproductive isolating mechanisms and possible conditions that could lead to the breakdown of such mechanisms is of particular importance in the risk assessment of LM mosquitoes with this trait. In addition, the fitness conferred by the introduced trait and the population size and frequency of the introduction of the LM mosquito into the environment will also determine the likelihood and rate of spread of the transgenes or genetic elements.

Horizontal gene flow: For the purpose of this document, "horizontal gene flow", is the movement of genetic information from one organism to another through means other than sexual transmission. Gene drive systems for moving genes into wild populations may be the initial focus of the risk assessment. The risk of horizontal gene flow in LM mosquitoes that do not contain a gene drive system is likely to be smaller but should nevertheless be assessed on a case-by-case basis.

Persistence of the transgene in the environment. Some of the transgenes in LM mosquitoes are designed not to persist whereas others are expected to spread rapidly and/or persist through wild populations. In cases where the LM mosquitoes have been found through the risk assessment process to have the potential to cause adverse effects to the biological diversity, taking also into account human health, methods to reduce the persistence of the transgene in the environment needs to be considered

Points to consider:

(a) Whether LM mosquitoes have the potential to transfer the modified traits to wild mosquito populations (when it is not an intended strategy) and/or to non-related organisms, and if so, the occurrence of any potential undesirable consequences;

(b) Whether the LM mosquitoes have the potential to induce undesirable characteristics, functions, or behaviour within the target mosquito species, other wild related species or non-related organisms;

(c) Any undesirable consequence should the transgene persist in the environment.

Evolutionary responses (especially in target mosquito vectors or pathogens of humans and animals)

(*See step 1 of the Roadmap for Risk Assessment of LMOs*)

[49] For the purpose of this document, a transgene is a nucleic acid sequence in an LMO that results from the application of modern biotechnology as described in Article 3 (i) a of the Protocol.

[50] Gene drive systems are methods of effectively introducing the desired gene into a mosquito population (Selfish DNA versus Vector-Borne Disease, Environmental Health Perspectives (2008) 116 - http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2235231/pdf/ehp0116-a00066.pdf).

Rationale:

Any strong ecological effect also exerts an evolutionary selection pressure on the human and animal pathogens and the mosquito vectors. The main evolutionary effects are those that could result in a breakdown in the effectiveness of the technology and the resumption of previous disease levels. Some LM mosquito strategies aim at modifying the mosquito vector's ability to transmit diseases through changes in its physiological mechanisms. An evolutionary effect resulting in the development of resistance to physiological mechanisms in the targeted pathogen might occur when modifying mosquito vector competence. This might harm the effectiveness of the strategy used and result in a population of pathogens that may be transmitted more easily by all types of vectors.

Other evolutionary effects could be hypothesized, including effects resulting from climate change, but they would first require the occurrence of some adverse effect on a species, community or ecosystem effect. Therefore, consideration of secondary evolutionary effects can be postponed until such effects are identified and found to be significant.

Points to consider:

(a) Whether the target mosquito vector has the potential to evolve and avoid population suppression, regain vector competence or acquire new or enhanced competence to another disease agent, and if so, the occurrence of any possible undesirable consequences;

(b) Whether the trait has the potential to evolve and thus lose its effectiveness, or the pathogen to evolve and overcome the limitation posed by the genetic modification, and if so, the occurrence of any possible undesirable consequences.

RISK-MANAGEMENT STRATEGIES

(*See step 5 of the Roadmap for Risk Assessment of LMOs*)

Risk assessors may want to consider risk-management strategies such as the quality control of the released LM mosquitoes and monitoring them and the environment for potential unintended adverse effects. There should also be strategies in place for halting the release and application of mitigation methods if an unanticipated effect occurs. Careful implementation of the technology including the availability of mitigations measures (such as an alternative set of control measures should a problem occur) and the integration of other population control methods should be considered. In some circumstances methods to reduce the persistence of the transgene in the environment or to mitigate adverse effects resulting from the expression of the transgene might be needed. Monitoring during and after the environmental release of the LM mosquitoes so as to address prompt detection of unexpected adverse effects may also be considered.

Points to consider:

(a) Availability of monitoring methods to:

  (i) Measure the efficacy and effectiveness of LM mosquito technology;

  (ii) Assess the potential evolutionary breakdown of the LM mosquito technology (monitoring for transgene stability and proper function over time);

  (iii) Determine the level to which the identified adverse effects may be realized, including detection of unexpected and undesirable spread of the transgenic trait (monitor for undesirable functions or behaviours within target species and other wild related species).

(b) Availability of mechanisms to recall the LM mosquitoes and transgenes in case they spread unexpectedly (e.g. mass release of wild-type mosquitoes above a certain threshold, alternative control methods including genetic control).

(c) Availability of methods for managing the dispersal of the LM mosquitoes and ensuring that they do not establish themselves beyond the intended receiving environment (eg. vegetation-free zones, traps, high threshold gene drive systems).

(d) Availability of methods to manage potential development of resistance, e.g. in the target vector or pathogen.

OTHER ISSUES

There are other factors that may be taken into consideration in the decision for environmental releases of LM mosquitoes which are not covered by Annex III of the Protocol. They encompass, *inter alia*, social, economic, cultural and health issues associated with the application and acceptance of the technology.

BIBLIOGRAPHIC REFERENCES

See references relevant to the "*Guidance Document on Risk Assessment of LM Mosquitoes*".

Annex IV

RECOMMENDATIONS TO THE CONFERENCE OF THE PARTIES SERVING AS THE MEETING OF THE PARTIES TO THE CARTAGENA PROTOCOL ON BIOSAFETY AT ITS FIFTH MEETING

1. The Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management took note of the deliberations under the Open-ended Online Expert Forum on Risk Assessment and Risk Management in particular about the need for further guidance on specific aspects of risk assessment and considered the existing guidance materials on risk assessment of living modified organisms.

2. The AHTEG recognized the importance of involving experts in the various scientific and technical fields relevant to risk assessment in any future activity taking into account the limited financial and human resources.

3. The following recommendations were made by the AHTEG:

(a) The document "Guidance on Risk Assessment of Living Modified Organisms" should be published and distributed, including an online version under the Biosafety Clearing-House (BCH), in all UN languages;

(b) The "Guidance on Risk Assessment of Living Modified Organisms" should be further tested for example during regional workshops including cooperation with existing initiatives for capacity-building and training, as appropriate;

(c) The "Guidance on Risk Assessment of Living Modified Organisms" should be revisited within two years and the need for an update of the list of background materials should be assessed within a year;

(d) Further development of guidance on risk assessment of living modified organisms should be considered. The topics identified and prioritized during the first meeting of the AHTEG as well as those mentioned at the second meeting could be the starting point for the further development of guidance on risk assessment (see list annexed hereto as annex V);

(e) A process should be established for the incorporation of background materials, available in the Biosafety Information Resources Centre of the Biosafety Clearing-House, that are relevant in the different sections of the "Guidance on Risk Assessment of Living Modified Organisms". In order to assist this process, the Secretariat should be requested to revise the common format for submission of records to the Biosafety Information Resources Centre (BIRC) of the BCH with the view to identifying and including a mechanism to link BIRC records on risk assessment to specific sections of the guidance document;

(f) Recognizing that the exchange of information is a central element for identifying living modified organisms or specific traits that have been assessed as having the potential to cause adverse effects on the conservation and sustainable use of biological diversity taking also into account risks to human health, a process should be established by:

(i) Urging Parties and inviting non-Parties to submit relevant information to the BCH on experiences in conducting risk assessment with regard to this topic;

(ii) Requesting the Secretariat to undertake a regular analysis of the information contained in the BCH within the context of this process and reporting to the COP-MOP for that purpose;

(iii) Organizing workshops where the information submitted would be analyzed through a guided-process.

(g) The goals of the above recommendations (a) to (f) could be achieved by a combination of an extended Open-ended Online Expert Forum on Risk Assessment and Risk Management and an AHTEG on Risk Assessment and Risk Management, as well as a combination of online conferences, ad hoc discussion groups and face-to-face meetings with a view to:

(i) Developing additional guidance documents on the basis of the "Guidance on Risk Assessment of Living Modified Organisms" on specific types of living modified organisms and traits;

(ii) Reviewing the text of the "Guidance on Risk Assessment of Living Modified Organisms" and updating the lists of background materials;

(iii) Incorporating background materials, available in the Biosafety Information Resources Centre of the Biosafety Clearing-House, that are relevant to the different sections of the "Guidance on Risk Assessment of Living Modified Organisms";

(iv) Analysing the results of the workshops on living modified organisms or specific traits that have been assessed as having the potential to cause adverse effects.

(h) Human and financial resource implications should be considered for the process set up to achieve the above goals.

Annex V

TOPICS FOR THE DEVELOPMENT OF GUIDANCE MATERIALS ON RISK ASSESSMENT

Further topics indentified in the first meeting of the AHTEG as priorities for the development of guidance:[51]

- Post-release monitoring and long-term effects of LMOs released into the environment;
- Risk assessment and risk management in specific receiving environments;
- Risk assessment of living modified microorganisms and viruses;
- Risk assessment of living modified pharmaplants;
- Risk assessment of living modified crops;
- Risk assessment of living modified trees;
- Risk assessment of living modified fish;
- Risk assessment living modified organisms for production of pharmaceutical and industrial products;
- "Co-existence" between LMOs and non-LMOs in the context of small scale farming;
- Risk assessment of living modified plants for biofuels;
- Risk assessment of living modified organisms produced through synthetic biology.

Further topics identified in the second meeting of the AHTEG as possible priorities for the development of guidance:

- Uncertainty analysis;
- Establishment of criteria for transparency and reproducibility of information;
- Interface between risk assessment and risk management;
- Environmental risk assessment and monitoring taking into account human health;
- Unintentional transboundary movements;
- ***Risk assessment and management of LMOs intended for introduction into unmanaged environments.***

[51] From annex II of the report of the first meeting of the Ad Hoc Technical Expert Group on Risk Assessment and Risk Management (UNEP/CBD/BS/COP-MOP/5/INF/13).