Minutes, Agricultural Biotechnology Research Advisory Committee, Working Group on Aquatic Biotechnology and Environmental Safety : September 28, 1994.

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Agricultural Biotechnology Research Advisory Committee

September 28, 1994

Working Group on Aquatic Biotechnology and Environmental Safety

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U.S. DEPARTMENT OF AGRICULTURE
Agricultural Biotechnology Research Advisory Committee

Working Group on Aquatic Biotechnology and Environmental Safety
Minutes of Meeting
September 28, 1994

The Agricultural Biotechnology Research Advisory Committee (ABRAC) Working Group on Aquatic Biotechnology and Environmental Safety (henceforth referred to as the Working Group) met on September 28, 1994, in Room 108-A of the U.S. Department of Agriculture in Washington, DC. Dr. Anne Kapuscinski chaired the meeting. The meeting was open to the public and had been announced in the *Federal Register*.

Members of the Working Group in attendance were Dr. Anne Kapuscinski, chair; Dr. Susan Ford; Dr. Stanley Pierce; Dr. Harold Kincaid; Dr. Rex Dunham; Dr. George Spangler; Dr. Roger Mann; and Dr. Eric Hallerman. Persons in attendance from the Office of Agricultural Biotechnology (OAB) were Alvin L. Young, Daniel Jones, and Maryln Cordle. Dr. José Amador, Assistant Secretary Designate for Science and Education, also attended the meeting.

Others in attendance were Charles Erikson, U.S. Food and Drug Administration; James Lackey, Animal and Plant Health Inspection Service, USDA; Martin Fitzpatrick, Oregon State University; David MacKenzie, National Biological Impact Assessment Program, USDA; Carmen McCormack, American Veterinary Medical Association; Pat Basu, Food Safety and Inspection Service, USDA; Charles Brown, Animal and Plant Health Inspection Service, USDA; Jane Rissler, Union of Concerned Scientists; Madilyn Fletcher, University of Maryland; Gary Jensen, Extension Service, USDA; Lee Stevens, Sea Grant Association; Meryl Broussard, Cooperative State Research Service, USDA; Althaea Langston, Animal and Plant Health Inspection Service, USDA; and Jim Crosson, U.S. General Accounting Office.

Call to Order and Preliminaries

Dr. Kapuscinski called the meeting to order at 9:00 a.m. She introduced Dr. Alvin Young, Executive Secretary of the ABRAC and Director of the U.S. Department of Agriculture's Office of Agricultural Biotechnology (OAB).

Dr. Young recounted a brief history of the ABRAC for the Working Group. He said that the ABRAC's first task after it was established in 1988 was to develop a set of *Proposed Guidelines for Research Involving Planned Introduction into the Environment of Genetically Modified Organisms* (henceforth referred to as the Guidelines). The ABRAC later realized

that more specific guidelines were needed for fish. For the past 1½ years, the Working Group has been trying to develop appropriate and acceptable performance standards for research on genetically modified fish and shellfish.

Over the past six months, OAB has been involved with rechartering the ABRAC. The full ABRAC is scheduled to meet November 17 and 18 in Monterey, CA, following the "Third International Symposium on Biosafety Results of Field Tests of Genetically Modified Plants and Microorganisms."

Dr. Kapuscinski thanked Dr. Young for his presentation and asked the members of Working Group and the audience to introduce themselves.

Dr. Kapuscinski then asked the Working Group if it approved the agenda. Dr. Hallerman asked if he could take ten minutes later in the day to present a worksheet he had developed to accompany the performance standards. Dr. Hallerman moved that the modified agenda be approved. Dr. Mann seconded the motion, and the agenda was approved unanimously.

Status of Performance Standards

Dr. Kapuscinski said the effort to draft performance standards began 1½ years ago. An initial meeting of the Working Group resulted in an outline of what the standards were to address and plans for a workshop in Minneapolis, MN, in August 1993. About 100 people attended the 3-day workshop, which consisted of both plenary sessions and working groups that dealt with various aspects of the standards.

Dr. Kapuscinski presented the results of the workshop to the full ABRAC at its December 1993 meeting. ABRAC members appeared to agree that a set of performance standards for fish and shellfish was needed, but were concerned that the draft at that point was too restrictive. The key issues upon which the ABRAC focused were:

1. The scope of the performance standards. ABRAC members had differing views on organisms to which the standards should apply. Dr. Kapuscinski has since substituted the word "applicability" for the word "scope" in order to reinforce the idea that these performance standards will be voluntary.

2. Classification of research as high, medium, and low risk with risk management for each risk level. The ABRAC noted that its own efforts to develop risk classifications for the Guidelines had been difficult. Alternatively, the ABRAC suggested that the performance standards be redesigned to identify specific risks and common reasons for concern, and include ways to deal with these specific risks and concerns. Dr. Kapuscinski said she had developed a series of flowcharts (in document #206) designed to do that and to allow the user to figure out what combination of confinement measures would allay risks and concerns.

3. Insufficient flexibility of the performance standards. Participants at the workshop thought some of the recommendations on risk management developed by that Working Group were too prescriptive. ABRAC agreed that there be more flexibility to the user to select combinations of confinement measures to achieve a specific endpoint.

Dr. Kapuscinski said that the purpose of the current meeting was to critique the flowcharts and determine what to do next. She noted that because the full ABRAC is meeting in November, there was little time to complete these tasks.

Ms. Cordle added that the ABRAC would want time to study the flowcharts before the November meeting, and that participants at the Workshop and other interested parties, including members of the international community, had been promised an opportunity to comment on a revised draft. She and Dr. Kapuscinski said that for these reasons, the Working Group needed to finish the performance standards by the end of October.

Overview of Flowcharts

Dr. Kapuscinski explained that the first chart, the *Overview of Performance Standards Flowcharts*, summarizes the logic of the other flowcharts. Each of the other flowcharts represents a subset of questions for researchers to answer as they try to determine the safety of their proposed experiments and develop appropriate confinement measures.

I. Applicability of Performance Standards

The researcher first answers questions with respect to the applicability of the performance standards (Flowchart I). There are three conditions under which a researcher can exit the performance standards at this point:

(1) the research organisms are not finfish, crustaceans or molluscs;

(2) the organisms are modified solely by intraspecific selective breeding or captive breeding; or

(3) the organisms are modified solely by interspecific hybridization and the hybrid is widespread in the accessible ecosystems and has not shown adverse effects.

Dr. Kapuscinski noted that ABRAC had decided not to deal with aquatic plants. Most current aquatic biotechnology deals with finfish, crustaceans, and molluscs. Ms. Cordle added that there was not enough money available to convene experts to address aquatic plants.

Dr. Spangler asked what would happen if a way were found to introduce into a fish stock a bacterium that nullified the effects of a pathogen. Dr. Mann responded that USDA's Animal and Plant Health Inspection Service (APHIS) already deals with that type of question.

II. Survival and Reproduction Assessment

This set of charts poses questions on survival and reproduction that the researcher must answer to determine whether the organism poses any risk. These questions focus on the attributes of the genetically modified organism (GMO). Specifically, the researcher is asked whether the organism was modified through deliberate gene changes (Flowchart II.A.), deliberate chromosomal manipulation (Flowchart II.B.), or interspecific hybridization (Flowchart II.C.). After proceeding through one or more of three paths that correspond to the method of genetic modification, the researcher will reach one of three conclusions:

1. There are specific reasons to feel confident that the modified organism is safe, in which case the researcher can exit the standards.

2. One or more specific risks have been identified, in which case the researcher proceeds to the appropriate flowcharts that address risk management.

3. There is insufficient information to determine safety or risk at this point, in which case the researcher proceeds to one or more of the flowcharts that address how the organism affects the ecosystem.

III. Ecosystem Effects Assessment

Questions in this section address: 1) impacts of introgression of the modified gene in natural populations, 2) interference with reproduction of natural populations, and 3) impacts on ecosystem structure and processes. As in the previous section, three outcomes are possible. You identify a reason for safety and exit the standards, you identify specific risks and go to risk management, or you find the information is insufficient to answer critical questions and go to risk management.

Dr. Kapuscinski pointed out that a researcher would not have to use every flowchart. She and other members suggested that the flowcharts be put into a computerized expert system. She then asked the Working Group to comment on the overall approach to the performance standards.

Dr. Hallerman said he was pleased with the overall approach. Dr. Mann said the flowcharts made the process of determining risk or safety much easier. Drs. Ford, Pierce, and Kincaid said that Dr. Kapuscinski's explanation convinced them that the flowcharts were much less complicated than they initially appeared to be. Drs. Dunham and Spangler also liked the approach and thought it was a major improvement. Several members responded enthusiastically to the idea of putting the flowcharts onto an expert system. Drs. Ford and Kincaid noted that duplication in risk management charts could be eliminated.

Dr. Kincaid asked how an expert system would put the logic behind the answers to questions in written form that could be added to a research proposal. Dr. Hallerman said his worksheet would help; Dr. Kapuscinski said that expert systems usually contain a printable file or trace of decision points that shows how the user arrives at his or her answers.

Dr. Rissler said that she was glad to see agreement on the form the performance standards should take, but she expressed concern about the criteria for exiting the standards or continuing with them.

Dr. Basu asked how the standards would be enforced. Dr. Kapuscinski reiterated that the standards were voluntary - a feature with which Ms. Rissler expressed dissatisfaction - but noted that Institutional Biosafety Committees (IBC's) could play a role in implementing the standards. Dr. Mann noted that State regulatory agencies play the main enforcement role in aquatic biotechnology, and that having the performance standards in expert system form would be very useful to these agencies. Ms. Cordle noted that USDA's National Biotechnology Impact Assessment Program (NBIAP) already has expert systems to provide guidance for field testing transgenic plants and generating permit applications for APHIS.

Dr. Langston said that the inclusion of interspecific hybridization in the performance standards expanded the Working Group's purview beyond biotechnology. Dr. Kapuscinski explained that the August 1993 workshop participants expressed interest in including these organisms in the performance standards.

Dr. Young introduced Dr. José Amador, Acting Assistant Secretary Designate for Science and Education. Dr. Amador welcomed the Working Group and commended the work of the OAB staff. Dr. Kapuscinski thanked Dr. Amador for joining the meeting.

After a short break, the Working Group moved to a substantive discussion of the Applicability Flowchart, Chart I.

Applicability

Dr. Kapuscinski asked the Working Group for opinions on the genetically modified organisms that stay within applicability versus the ones that exit, any comments on those concepts, and wording of the questions in Flowchart I.

Ms. Cordle asked whether the narrative for the flowcharts should include a section on the rationale behind the questions in the flowcharts and, if so, whether any technical changes should be made in the draft narrative in Attachment A. She also suggested that the examples in the applicability definition in Attachment A be deleted, noting that they caused some difficulty in the ABRAC meeting.

Dr. Kapuscinski thought the ABRAC would find examples important; they found the earlier draft vague. Dr. Mann noted that another reason examples had been added was to address concerns over limiting the standards to three categories of risk. The proposed restructuring makes the standards easier to understand, so including examples is less important. Dr. Spangler said that documentation of rationale should be included in the expert system, and should be simplified at the interface between the user and the expert system. Dr. Kincaid noted that if the performance standards were incorporated into an expert system, instructions would be needed. A rationale could be added at that point. Dr. Hallerman agreed. Dr. Pierce said that the flowcharts should be as simple as possible.

Dr. Pierce said that he shared Dr. Langston's concern about including interspecific hybrids in the standards, pointing out that interspecific hybrids refer to breeding, not biotechnology. Dr. Hallerman noted that the Scope document published by the Bush Administration (Fed. Register Vol. 57 No. 39, Feb. 27, 1992 p. 6753-6762) said that biotechnology was not different from other methods, and that results, not methodology, were the key to scope or applicability. If the organisms are not found in nature, they are eligible for treatment under the performance standards.

Dr. Kapuscinski and Ms. Cordle noted that fisheries professionals have concerns about interspecific hybrids in part because of their longer experience with these types of manipulations. Dr. Hallerman noted that an entire species of cutthroat trout had been lost as a result of interspecific hybridization.

Dr. Spangler said that the Working Group should make a recommendation, but it would be up to the ABRAC to accept or reject the definitions of what organisms would be applicable. He reiterated that participants in the August 1993 workshop had very vocal concerns about the inclusion of interspecific hybrids under the standards.

Dr. Dunham said that if interspecific hybrids continue to be a form of modification to which the Standards apply, the third diamond on Flowchart I should read "or has not shown adverse effects" rather than "and ..." Otherwise, he thought research on a very common hybrid could be restricted because of lack of information of its effects on the environment.

Dr. Dunham also suggested that the word "solely" in the third diamond be deleted. Both Drs. Dunham and Kincaid noted that an organism produced by both interspecific hybridization and selective breeding could be prevented from exiting the standards early, even if there were no safety concerns.

Dr. Kapuscinski said that she would try to find a way to ensure that interspecific hybrids could exit earlier in the process, even if the word "solely" were not removed. She also agreed to change the last "and" in the third diamond to "or."

Survival and Reproduction Assessment

Dr. Kapuscinski began the discussion of the survival and reproduction assessment flowcharts by explaining the design of Flowchart II.A, Deliberate Gene Changes. She reminded the group that there are three pathways based on the type of genetic modification, (i.e., deliberate gene changes, chromosome manipulation, and interspecific hybridization) which are roughly parallel with each other. For illustration, she described the deliberate gene change path in some detail.

The flowchart starts with the question, "Does the GMO result from deliberate changes of genes?" A negative answer takes the researcher to Flowchart II.B, Deliberate Chromosomal Manipulations, to assess other possible modifications. All of the questions are designed to enable the researcher to exit the standards at this point in the process if at all possible; the questions become more complicated as the standards progress.

Dr. Kapuscinski asked the Working Group its opinions on the questions posed in this set of flowcharts (II.A, II.B, and II.C), particularly with respect to how the questions are worded as well as the notes and definitions.

Dr. Ford asked what would happen if a researcher didn't know whether an organism could survive in a natural ecosystem. Dr. Kapuscinski said that the researcher would proceed to the risk management flowcharts. She agreed to go through the flowchart questions and add paths to risk management for cases where a definitive yes or no answer may not be given. Alternatively, a general instruction to this effect may be appropriate in the introduction.

Dr. Hallerman suggested editing the third diamond on the left of chart II.A to read as follows: "Is/are the accessible ecosystem(s) isolated from other aquatic systems and of low enough concern that killing of all fish/shellfish in the event of a GMO escape would be **possible and practical**? *(Rapporteur's note: Modified wording is in boldface.)* Dr. Mann pointed out that killing research fish and shellfish would be impractical in marine systems.

Dr. Kapuscinski then asked for opinions on the information box dealing with scale in Flowchart II.A. She noted that the question of scale is vague and left to the user's interpretation. Dr. Mann cited an example of how the scale of an experiment was used to determine how many triploid oysters could be put into the Chesapeake Bay. Researchers estimated the probability of error that the oysters were all triploid, the possibility of their reversion to diploidy, the number of oysters that would revert in a given time frame, the number of reversions that would produce viable gametes at the same time, their distribution, and possibility of those gametes coming together, and so on. This process estimated such vanishingly small numbers that it was not difficult to justify safety of the experiment. He recommended a case-by-case decisions regarding scale of experiments.

Most of the Working Group felt that information boxes should not be preceded by an arrow (as is the case with the box about scale). Dr. Spangler suggested that the box be converted to

a decision diamond asking the researcher to decide whether the project is large-scale or small-scale. If the project were small-scale, the researcher could exit the standards; if not, the researcher would proceed to Flowchart II.A.1.

In discussing Flowchart II.A.1, Impact of Deliberate Gene Changes, the Working Group decided that the initial decision diamond, which allows exit for marker genes only if they had no physiological effect, should be changed to read as follows: Is the only gene change a gene deletion, or the addition of a marker sequence with **no phenotypic effect of the types listed in Table 1**? Table 1 was developed at the Workshop to identify traits of potential concern. Dr. Hallerman mentioned beta-galactosidase as an example of a marker gene posing no concern.

Flowchart II.A.1 provided an exit if the gene change were not present in the germ line. After discussing the potential significance of risks from genetic changes which are not in the germ line, the Working Group agreed to eliminate the early exit for organisms with such changes.

Dr. Hallerman questioned the presentation of the note on Flowchart II.A.1. about compliance with the Aquatic Nuisance Species Protocol. He suggested that in an expert system the user could be routed directly to the protocol. This point precipitated an extensive discussion about the relationship between the Aquatic Nuisance Species (ANS) Protocol and the standards.

Dr. Kapuscinski said some researchers have suggested that the performance standards should not require users to follow the ANS Protocol if their research organisms are sterile and have no conspecifics or closely related species present in the accessible environment, because there would be no potential for reproductive interference or gene introgression. Dr. Hallerman said that the standards should not preempt the ANS protocol by instructing researchers not to consult the Protocol. He said that researchers using non-indigenous species should consult the ANS Protocol, and should be instructed to do so in the standards.

Dr. Kapuscinski said she would add a decision diamond between the "sterility question" and the exit circle asking whether the GMO fits the definition of non-indigenous species in the ANS Protocol. If the answer is yes, a circle will instruct the user to consult the ANS Protocol. If no, the user will exit the standards.

Mr. Brown suggested that the ANS Protocol be mentioned much earlier in the introduction to the Standards.

Dr. Kapuscinski said that Flowchart II.A.1 enables the researcher to reach one of three conclusions:

1. If there are conspecifics, the GMO is not sterile, and at least one natural population in the ecosystem is threatened, the researcher should proceed to Flowchart IV, Risk Management for Protected Populations.

In this Risk Management flowchart, the objective is to reduce the risk to protected populations to a negligible level. The researcher chooses barriers from among those described in the flowchart which would achieve that objective.

2. If the GMO is fertile and there are conspecifics, but none of those conspecifics is threatened or endangered, more information would be needed, and the researcher would proceed to Flowchart V.A. of the Ecosystems Effects Assessment.

3. If there are no conspecifics present, but the GMO is fertile and could found a new population if it escaped into the accessible environment, the researcher would proceed to Flowchart V.B. of the Ecosystem Effects Assessment. The Working Group decided to delete the portion of this square which gives the researcher the option to exit to the ANS Protocol. Instead, the researcher would be directed to continue with the standards.

Dr. Ford asked how the researcher would proceed through the flowcharts if he or she did not know the answers to the questions being posed. She asked whether the researcher should choose the most conservative answer to the given question and proceed further through the standards. Dr. Kapuscinski said she would find a way to provide the choice of "answer unknown" which would then lead to the conservative path, throughout the flowcharts.

The Working Group decided that the Barriers box should include five categories; physical or chemical barriers, mechanical barriers, biological barriers, scale of the experiment and operations. Water temperature and pH would be examples of physical and chemical barriers respectively.

Dr. Ford suggested that information be included on how to design barriers. Dr. Dunham said that the literature contains considerable information on how to build fresh water barriers, but that most sea water barriers are mostly chemical. Dr. Kapuscinski asked Dr. Ford and Dr. Mann to prepare a list of references on barrier construction for inclusion in the standards, perhaps as an appendix in the written version.

Dr. Kapuscinski said she was concerned about using GMO sterility as a form of risk management, because of recent reports of reversal of induced sterility in research organisms. Dr. Mann explained that, in experiments he and Drs. Allen and Ford recently conducted, triploid oysters did revert to diploidy over the course of the research period. This suggests that sterility resulting from induced triploidy may have reverted as well. However, reproductive activity of the now-diploid oysters was not directly assessed.

Dr. Dunham commented that, in his opinion, all chemical and physical techniques of inducing sterility, other than removal of gonads, should not be considered permanent. He suggested rephrasing flowchart questions about sterility to ask about **permanent** sterility, in order to emphasize that reversal of sterility must be addressed. Dr. Kapuscinski agreed. She and other members agreed that the performance standards text must address this point. She asked the Working Group members to provide references on this topic.

Dr. Spangler suggested that researchers might control reproduction in their research organisms by using a monosex population, rather than inducing sterility. He agreed with Dr. Kapuscinski that this strategy would be effective only if no conspecifics were present. Dr. Kincaid pointed out that monosex populations could present a higher risk than induced sterility. If even a single individual of the other sex is present, either because sex-determination is not 100% effective or because conspecifics are present, there would be a very high likelihood of successful mating.

The Working Group then proceeded to discuss the flowcharts dealing with the Ecosystems Effects Assessment.

Ecosystem Effects Assessment

Dr. Kapuscinski started this discussion with Flowchart V.A., Ecosystem Effects - Deliberate Gene Changes. She noted that the questions in the initial diamond are designed to enable the researcher to exit the standards early. This option applied only to GMOs with genetic changes which do not result in phenotypic changes in Table 1. Dr. Kapuscinski emphasized that Table 1 is a very comprehensive list, therefore very few projects could exit the standards here. She suggested that a gene change resulting in change in flesh color might be one example of a phenotypic change not included in Table 1. Ms. Cordle noted that this section of the flowcharts addresses how the presence of organisms with these genetic changes might affect the ecosystem.

The Working Group agreed that the second decision diamond in Flowchart V.A. could cause confusion because it would be difficult for a researcher to answer whether there is a "high degree of familiarity with the ... accessible ecosystem." The group decided to replace the diamond with an information box that instructing researchers to proceed to the risk management flowcharts if they do not have enough information to answer the next set of questions (Flowchart V.A.1, Ecosystem Effects - Impacts of Introgression of Modified Gene).

Dr. Kapuscinski said that she had thought quite a bit about the order of the questions on Flowchart V.A.1. She explained that she asked questions about frequency of gene flow before questions about estimating fitness, because she thought it would be a little bit easier to estimate gene flow. Gene flow frequency can then be analyzed for potential effects on the fitness of GMOs themselves, or on the fitness of introgressed individuals compared to non-modified conspecifics. In response to a questions from Ms. Cordle, Dr. Kapuscinski said that fitness of an organism is defined as the number of successful progeny the organism produces, where successful progeny are defined as those which survive and reproduce. She added that it is quite difficult to estimate fitness in a natural setting. Dr Dunham stated that he felt that researchers wanting to conduct transgenic fish research must be serious enough to commit themselves to addressing these questions of ecological risk.

Effects on Ecosystem Structure and Processes

Dr. Kapuscinski explained that the user reaching this part of the flowcharts is assessing how the GMO and other organisms will interact - not whether the interaction will take place. She explained that potential adverse effects will depend on the scale of the experiment. Dr. Ford asked why the question of scale is posed in Flowchart II.A. if it is posed again in Flowchart VI, Effects on Ecosystem Structure and Processes. Dr. Kapuscinski explained that Flowchart II.A. poses the question of scale in order to provide an early exit for small-scale experiments accessible to an ecosystem through indirect pathways only. Flowchart VI. asks the question of scale for a different set of cases: those GMO experiments which have directly-accessible ecosystems, and which are likely to cause ecological effects related to the scale of the experiment.

Dr. Spangler was uncomfortable with the use of the word "keystone" in the first decision diamond of Flowchart VI. "Keystone" species are very difficult to identify, and ecological risks are important regardless of whether or not a known "keystone" species is involved. The Working Group decided to delete this diamond and the information below it (on the left side of the chart), since this specific case would be addressed in the question on the rest of the flowchart. The group also decided to change the phrasing on the boxes at the bottom to say, "adverse alterations are 'clearly **improbable**' rather than 'clearly impossible'." Ms. Cordle recommended including explanatory text about comparing the ecological impacts of a GMO to those of its non-modified parental organism.

Dr. Spangler raised the question of the voluntary nature of the performance standards, and suggested that if state natural resources management agencies conducting stocking projects do not follow the standards, researchers who comply with the standards may be at a disadvantage in terms of seeking funding. Dr. Kapuscinski emphasized that the performance standards are voluntary, and that she hopes that U.S. fisheries professionals in all institutions will follow them, but that this is out of the scope of the Working Group's discussion. In response to another question by Dr. Spangler, Dr. Kapuscinski explained that concerns of whether other countries are moving ahead of U.S. transgenic fish researchers are also beyond the scope of the Working Group. She noted that the international community is very interested in the outcome of the effort to develop the performance standards.

Dr. Kapuscinski was concerned that Flowchart VI.A., Assess Ecosystem Resiliency, contained many uncompleted questions, and asked whether it should be included in the standards at all. She explained that this flowchart applied only to those cases where the user anticipates adverse ecological effects that will occur on a scale large enough that they must be managed, and is attempting to determine whether the ecosystem will recover from the adverse impact. She argued that, because ecosystem resiliency would be extremely difficult to determine, and because ecosystem recovery might not be complete, responses to these questions should not allow the user to exit the standards.

Drs. Dunham and Spangler suggested Flowchart VI.A. is unnecessary because answering its questions would not further illuminate risk management decisions. Drs. Spangler and Mann commented that resiliency of an ecosystem is extremely difficult to understand, and nearly impossible to measure, because of the variability of ecosystems. Dr. Kincaid added that if the introduction of the GMO will be known to cause an adverse effect, at that point the decision to proceed should not rest with the researcher, but with resource management agencies. Dr. Kapuscinski agreed, and the group decided to eliminate Flowchart VI.A.

Ms. Cordle asked whether an ecosystem interaction affecting a threatened or endangered species was addressed specifically. Dr. Kapuscinski agreed that it should be addressed specifically, and said she would clarify the flowcharts so that in that case, the user would be instructed to go to Risk Management for Protected Populations.

Dr. Hallerman asked whether the user is responsible to consult with natural resource management agencies about the adverse effects of a project. Dr. Kapuscinski replied that she had recommended that the user do so, at several points throughout the flowcharts. She said she will further revise the flowcharts to emphasize that point.

Dr. Kapuscinski then asked Dr. Hallerman to discuss the worksheet he drafted to accompany the performance standards.

Worksheet to Accompany Flowcharts

Dr. Hallerman said that researchers using the performance standards may find an accompanying worksheet helpful. The worksheet would provide written documentation that could be included in a presentation of a research proposal to an IBC or other oversight body. He explained that the person filling out the worksheet should show how he or she proceeded through the performance standards and selected confinement measures. Ms. Cordle said that the worksheet should also include documentation of the user's explanations for exiting the standards. Dr. Kapuscinski asked Dr. Hallerman to add the word "trace" to the worksheet title, to signify that the worksheet will also be a direct output of a researcher's completion of the expert system form of the performance standards

Dr. Kapuscinski said that members of the full ABRAC would probably find the worksheet useful at the November meeting, and the Working Group agreed.

Dr. Mann said that the effectiveness of the worksheet might be enhanced if an example were included. Dr. Hallerman said he could add two examples and complete the revised worksheet by the end of October.

Dr. Kapuscinski said that Dr. Jensen had suggested that the final version of the standards should have a place to list persons who could be consulted for help. She suggested that

people from State natural resource agencies and the American Fisheries Society might be the best sources of assistance to users of the standards.

Ms. Cordle suggested that the standards recommend review of a proposed project and the performance standards by a peer group such as an IBC. She said she would find language in the Guidelines for duplication in the standards. Dr. Kapuscinski asked Dr. Hallerman to include the question "Have you submitted this to peer review?" on his worksheet.

Risk Management

Dr. Kapuscinski asked that Working Group members send her any editorial comments with respect to the risk management flowcharts by October 10. In response to a recommendation from Dr. Ford, Dr. Kapuscinski said she would condense all of the risk management flowcharts into one flowchart, and would list the different goals or endpoints at the top of the chart.

Dr. Dunham said that Flowchart V.A.3, Manage Risk of Decline in Population Abundance, was very similar to Flowchart IV, Manage Risk to Protected Populations. Dr. Kapuscinski said that the goals of the two charts differed. In Flowchart V.A.3, some escaped GMOs are permitted, and the user must calculate the number of acceptable escapees.

Dr. Kapuscinski said that Dr. John Colt's draft text on risk management guidance should be used to define the criteria for barriers. Ms. Cordle said that the Working Group should go beyond Dr. Colt's text to call attention to events that might take place at the research site, such as flooding. She also suggested that if the necessary risk management goes beyond standard practices, the standards should provide qualitative guidance, rather than quantitative requirement, on how to reach that level of protection.

Dr. Dunham suggested that for low-risk situations, at least one barrier be required; for high risk, multiple barriers should be required. He and Dr. Kincaid suggested that the medium-risk category be eliminated or combined with the low-risk category in Dr. Colt's text.

Dr. Kapuscinski agreed that the risk management material must be revised to address the concept of different conditions (flooding, wind loading, snow loading) and of different water systems (freshwater, marine, estuarine), but must be less prescriptive than Dr. Colt's text.

Ms. Cordle said that some of Dr. Colt's criteria were not very realistic with respect to marine biotechnology. Dr. Dunham agreed, and questioned the quantitative recommendations for flooding events, arguing that few facilities could meet those criteria. Dr. Kapuscinski suggested that such figures might not be needed at all. Ms. Cordle suggested that instead of providing figures, the text should describe ways to cope with flooding events, such as relocating a facility away from a flood area. Dr. Ford suggested that experiments should be kept small so that such moves could be accomplished quickly and easily, or that experiments

be kept very short in duration. She added that researchers of oysters must use flow-through rearing systems, which raises the difficult problem of controlling escape of gametes. Dr. Dunham said he felt the equipment logs suggested in Dr. Colt's text were excessive.

Dr. Kapuscinski asked Drs. Ford and Dunham to submit detailed comments to her for incorporation into the performance standards.

Ms. Cordle thanked Dr. Kapuscinski and the Working Group for their work on the performance standards. Dr. Kapuscinski adjourned the meeting at 4:52 p.m.

Approved:

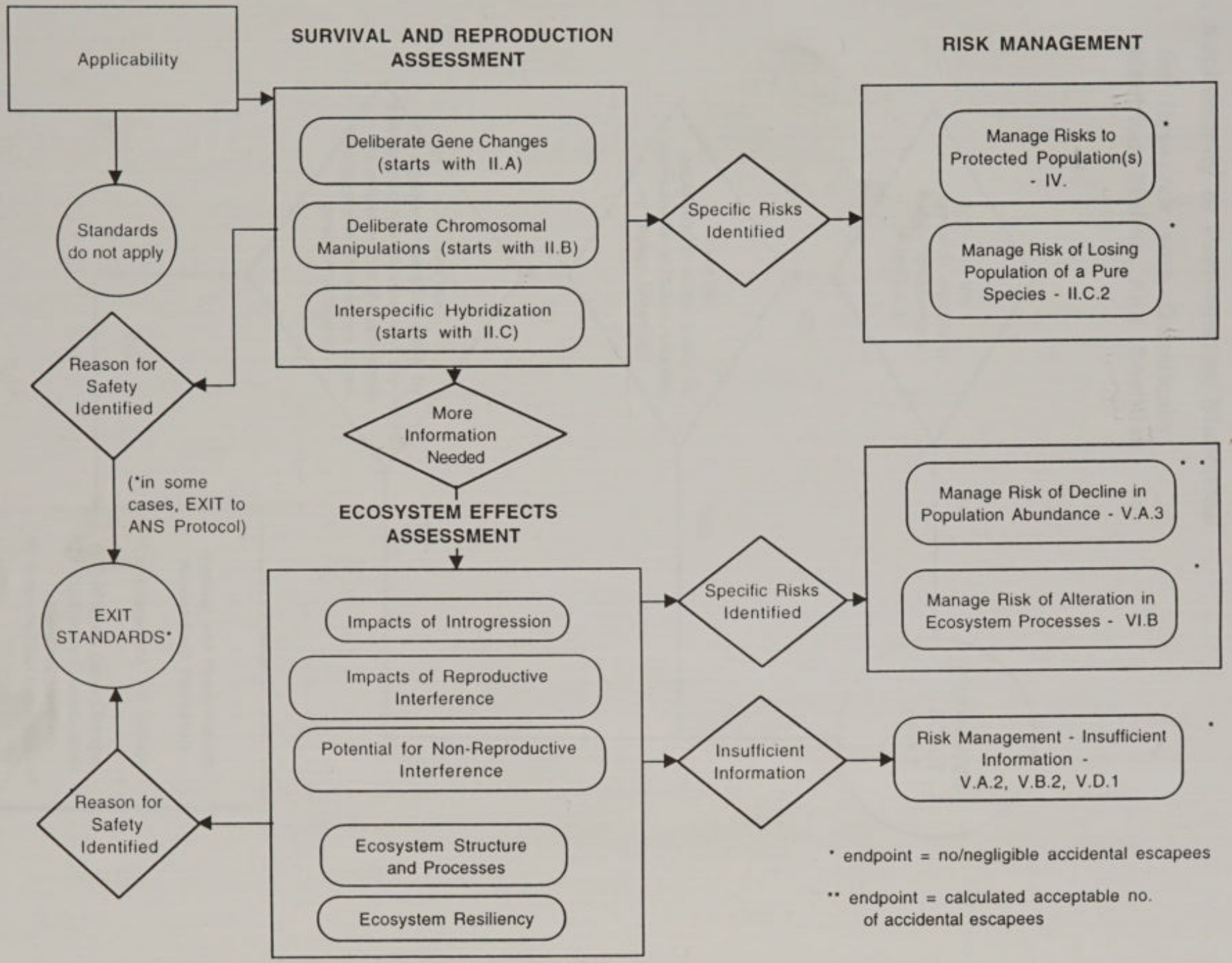
SUSAN McCULLOUGH
Rapporteur

DANIEL JONES
Editor

ALVIN YOUNG
Executive Secretary

ANNE KAPUSCINSKI
Chair

OVERVIEW of Performance Standards Flowcharts 9/20/94 DRAFT

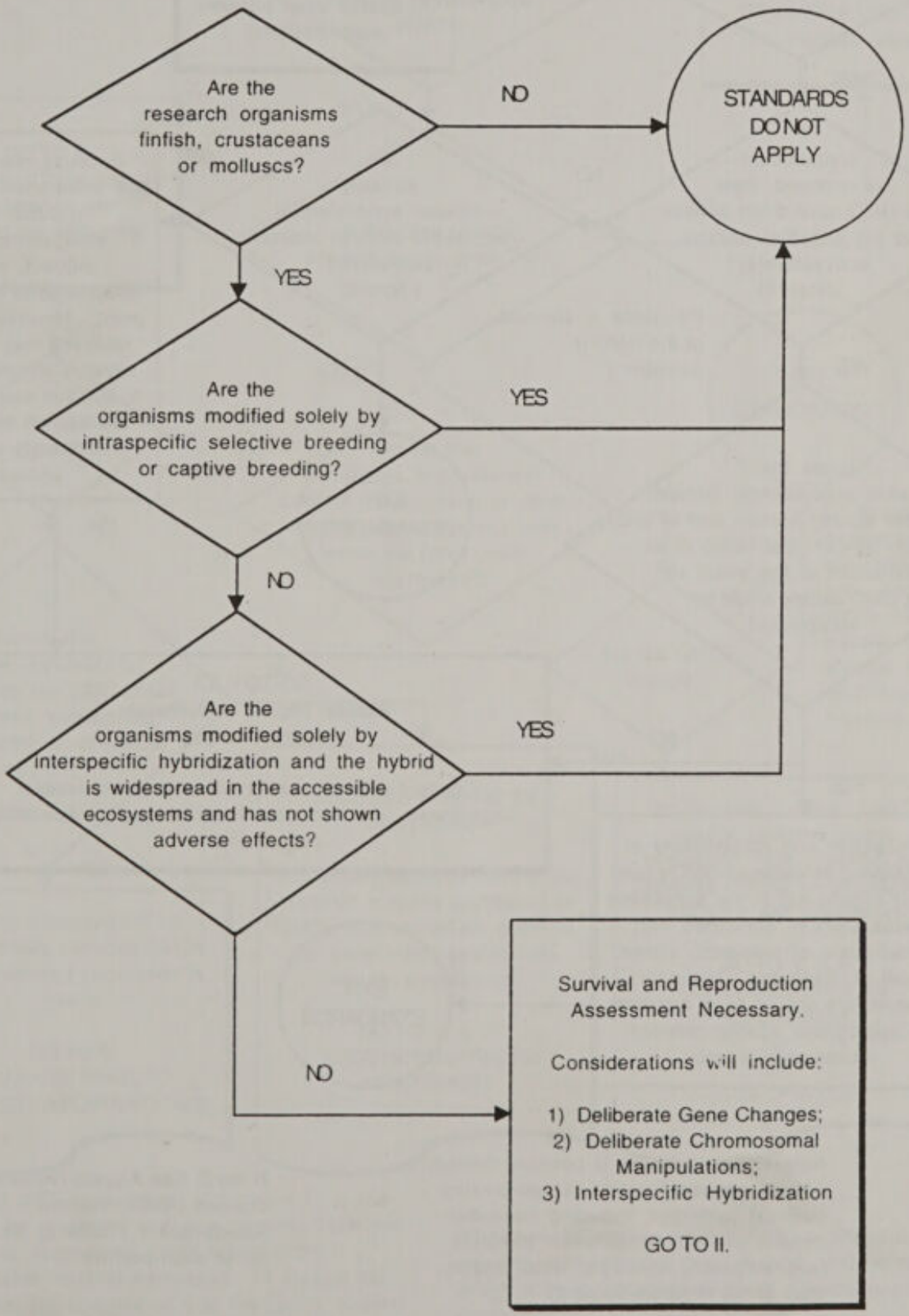


* endpoint = no/negligible accidental escapees

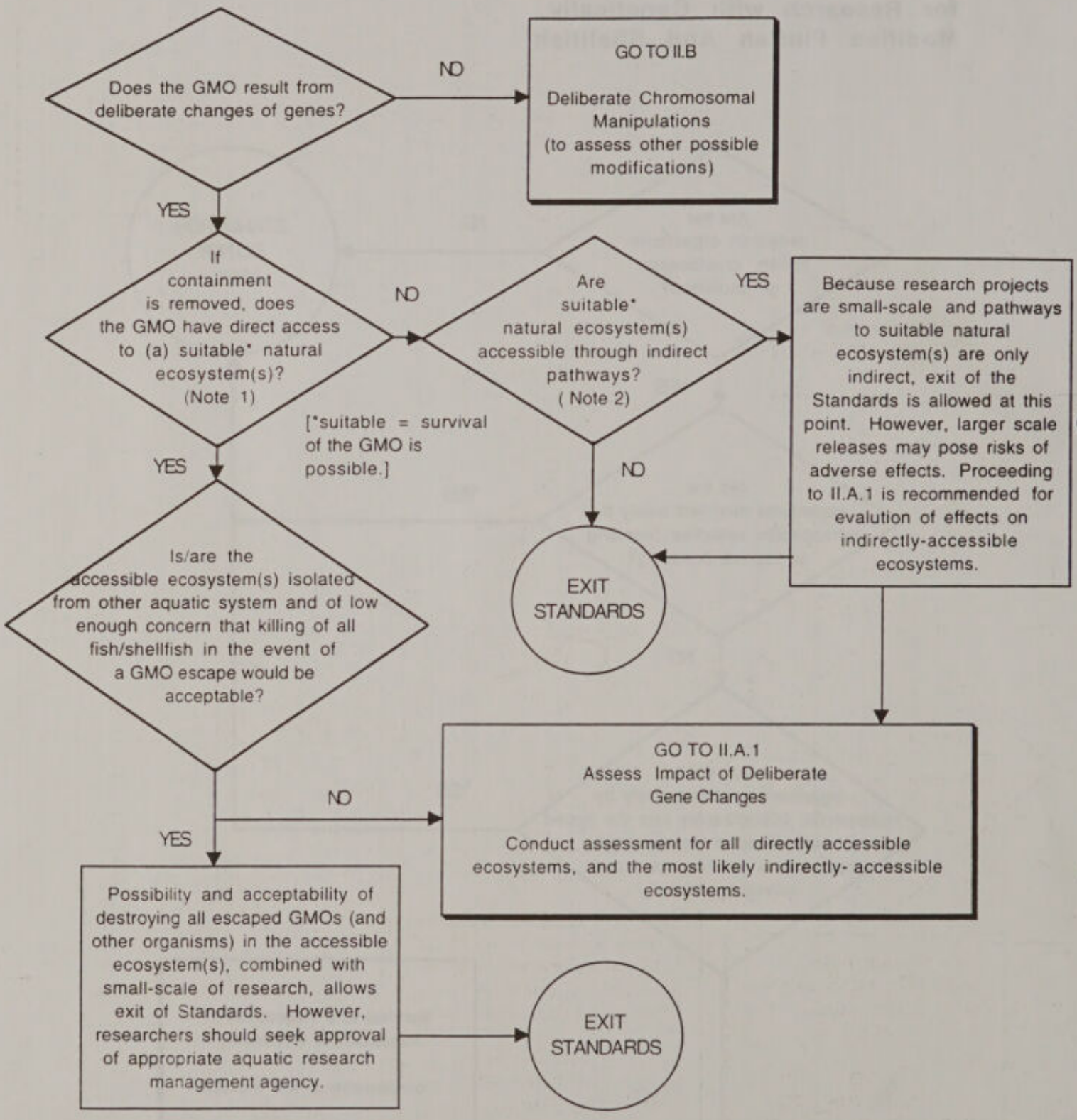
** endpoint = calculated acceptable no. of accidental escapees

I. Applicability of Performance Standards

for Research with Genetically Modified Finfish And Shellfish



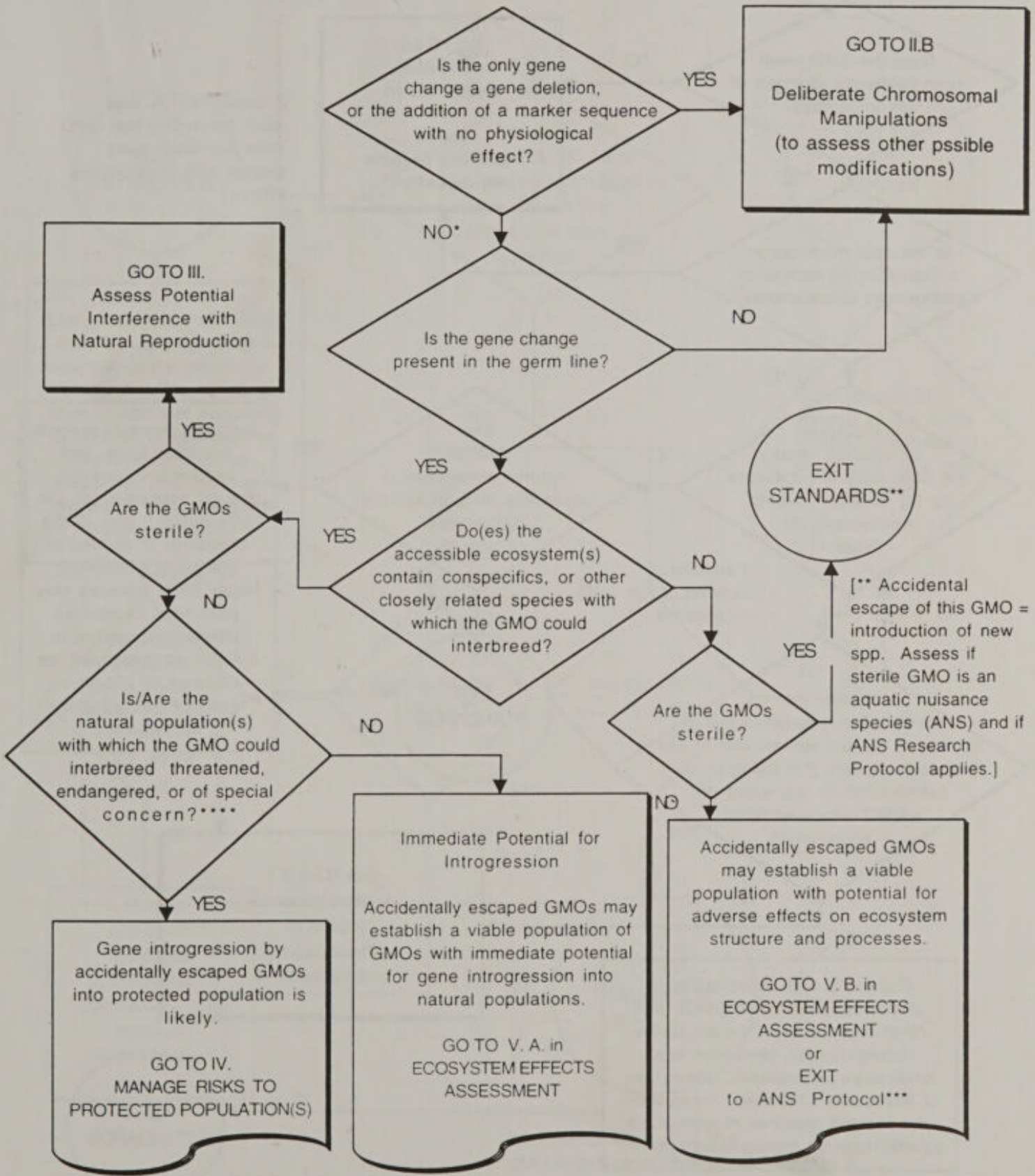
II.A Survival and Reproduction Assessment - Deliberate Gene Changes



Note 1: Direct access is possible through natural waterbodies and human-created physical pathways, including navigation canals, and interbasin water transfers (e.g. irrigation, municipal water supply, etc.) (ANS Protocol Table 2).

N ote 2: See Aquatic Nuisance Species (ANS) Program - Attachment 1 (Table 2) for full list of such pathways.

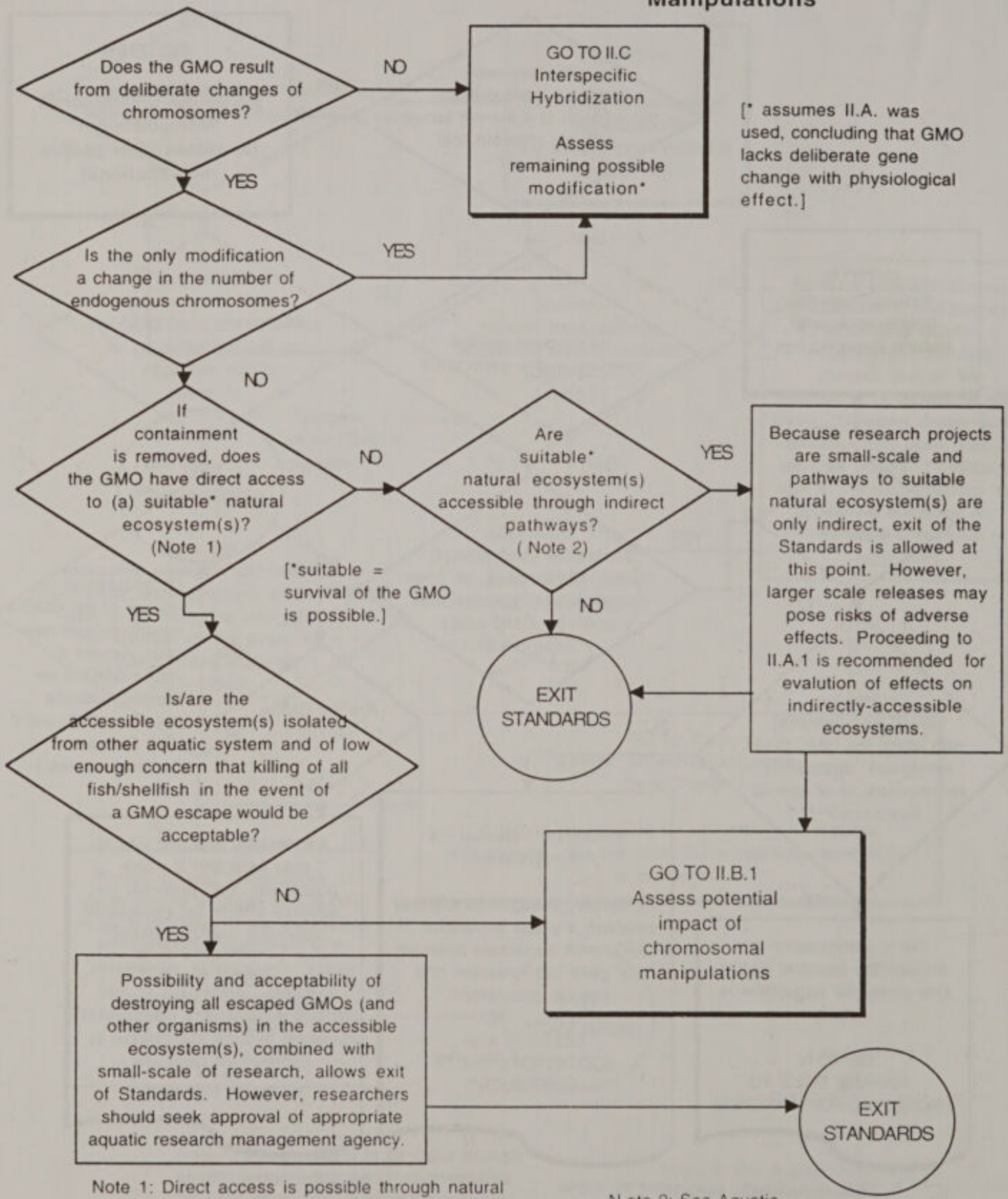
II.A.1 Impact of Deliberate Gene Changes



(**** If YES, one option is to move to a site where no protected spp. are present. However, if this is considered, other topics in the Standards must be addressed. To explore the potential implications of site relocation, answer NO here and continue.

(***Accidental escape of this GMO = introduction on new spp. with deliberate gene change. WORKING GROUP: Which is more appropriate- these Standards or ANS Protocol?

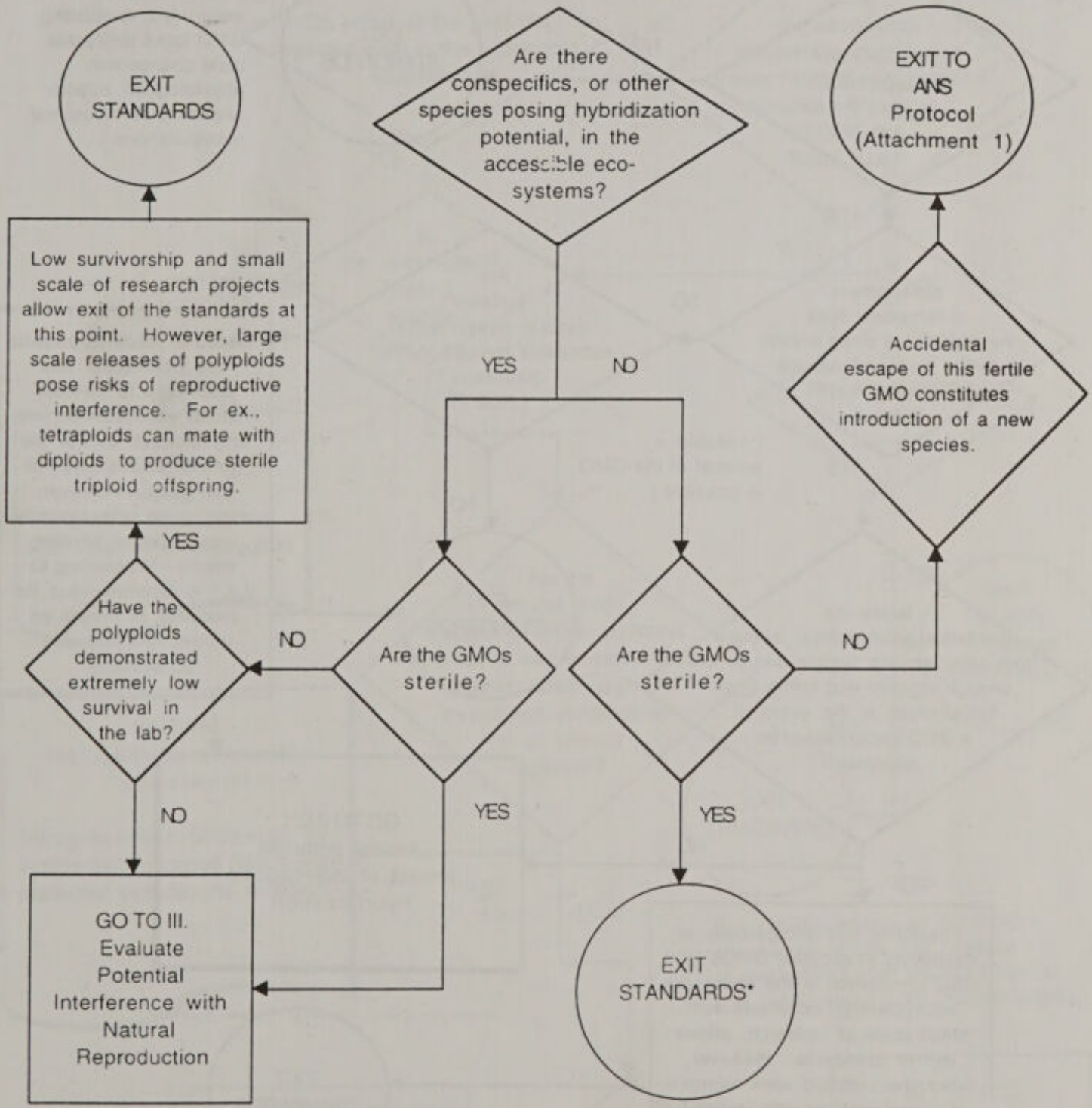
II.B. Survival and Reproduction Assessment - Deliberate Chromosomal Manipulations



Note 1: Direct access is possible through natural waterbodies and human-created physical pathways, including navigation canals, and interbasin water transfers (e.g. irrigation, municipal water supply, etc.) (ANS Protocol Table 2).

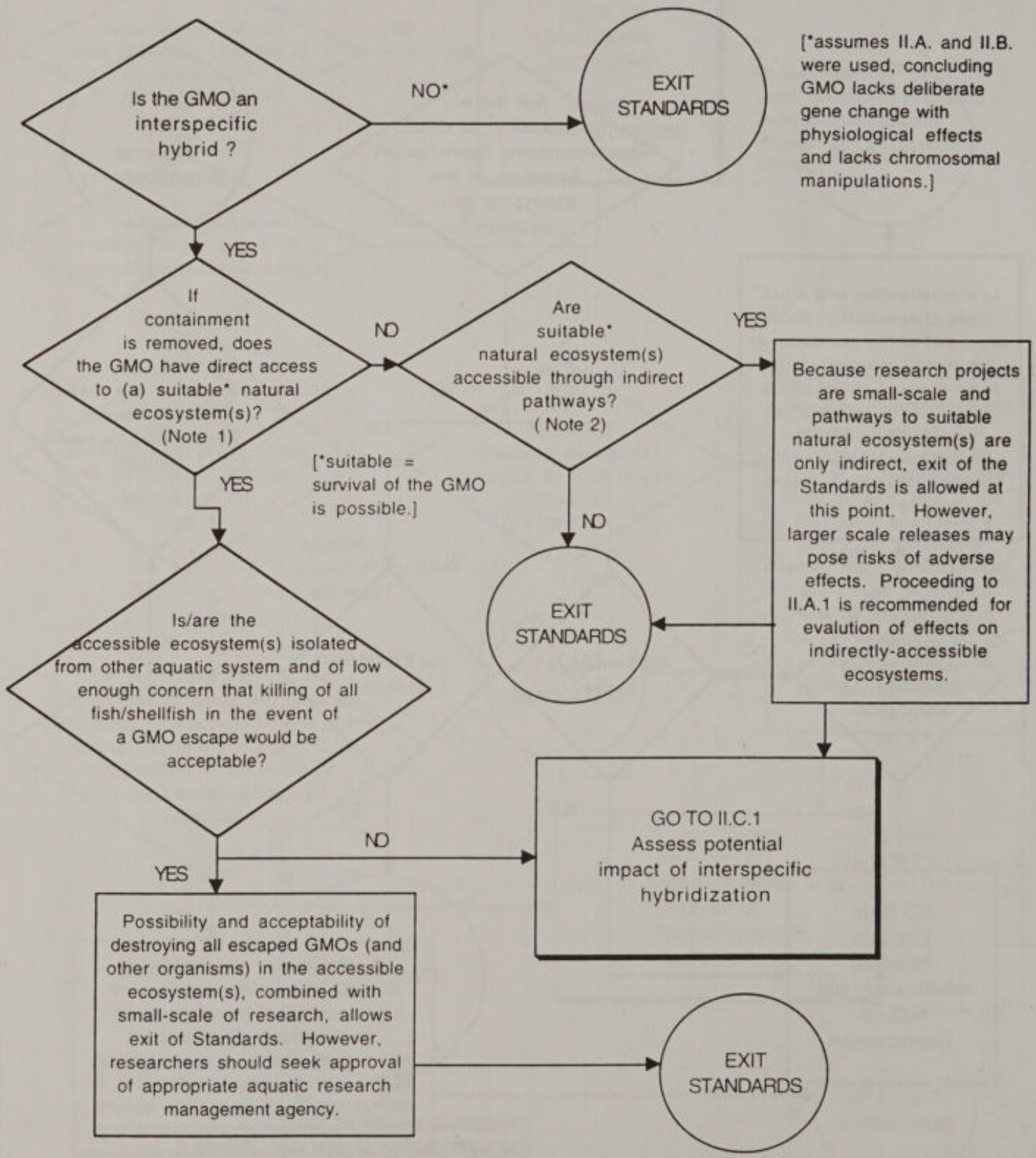
N ote 2: See Aquatic Nuisance Species (ANS) Program - Attachment 1. (Table 2) for full list of such pathways.

II.B.1 Impact of Deliberate Chromosomal Manipulations



[*Accidental escape of this GMO=introduction of new spp. Assess if sterile GMO is an aquatic nuisance species (ANS) and if ANS Protocol applies.]

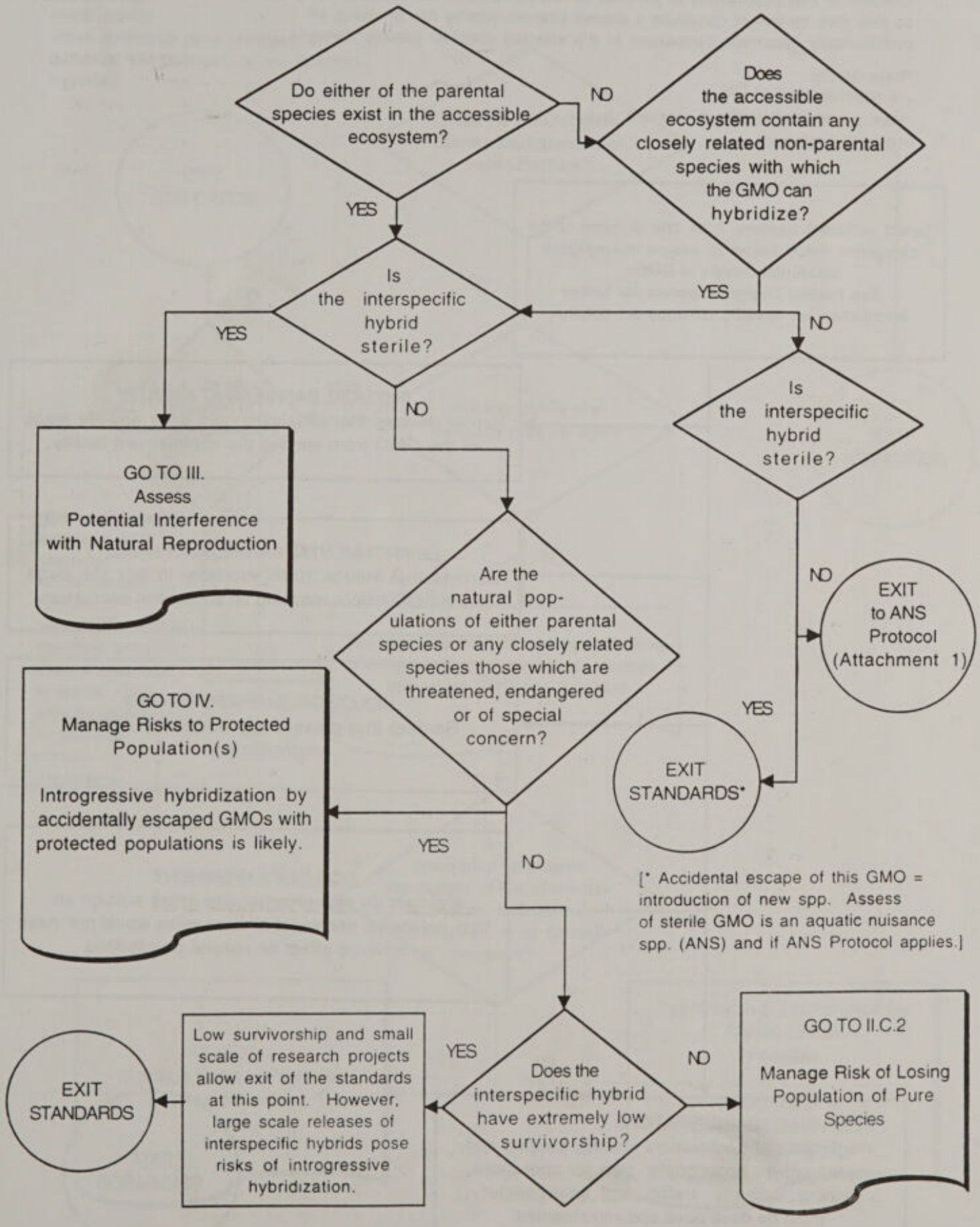
II.C. Survival and Reproduction Assessment - Interspecific Hybridization



Note 1: Direct access is possible through natural waterbodies and human-created physical pathways, including navigation canals, and interbasin water transfers (e.g. irrigation, municipal water supply, etc.) (ANS Protocol Table 2).

N ote 2: See Aquatic Nuisance Species (ANS) Program - Attachment 1. (Table 2) for full list of indirect pathways.

II.C.1 Impact of Interspecific Hybridization



II.C.2 Manage Risk of Losing Population of Pure Species

Concern is that populations of parental or related species will become introgressed, so that they no longer constitute a distinct species, posing risk of losing an evolutionarily important component of the affected species' genetic diversity.

from II.C.1

These GMOs:
are NOT sterile
-have parental/related spp. present, but none are protected.

Select sufficient barriers from one or more of the categories listed below to assure no/negligible accidental escape of GMOs.
See Facility Design Appendix for further information on specific confinement options.

PHYSICAL BARRIERS AT FACILITY
Barrier devices that physically hold back any life stage of the GMO from leaving the confinement facility.

ENVIRONMENTAL BARRIERS AT FACILITY
Barriers that induce 100% mortality in any life stage of the GMO before reaching an accessible ecosystem.

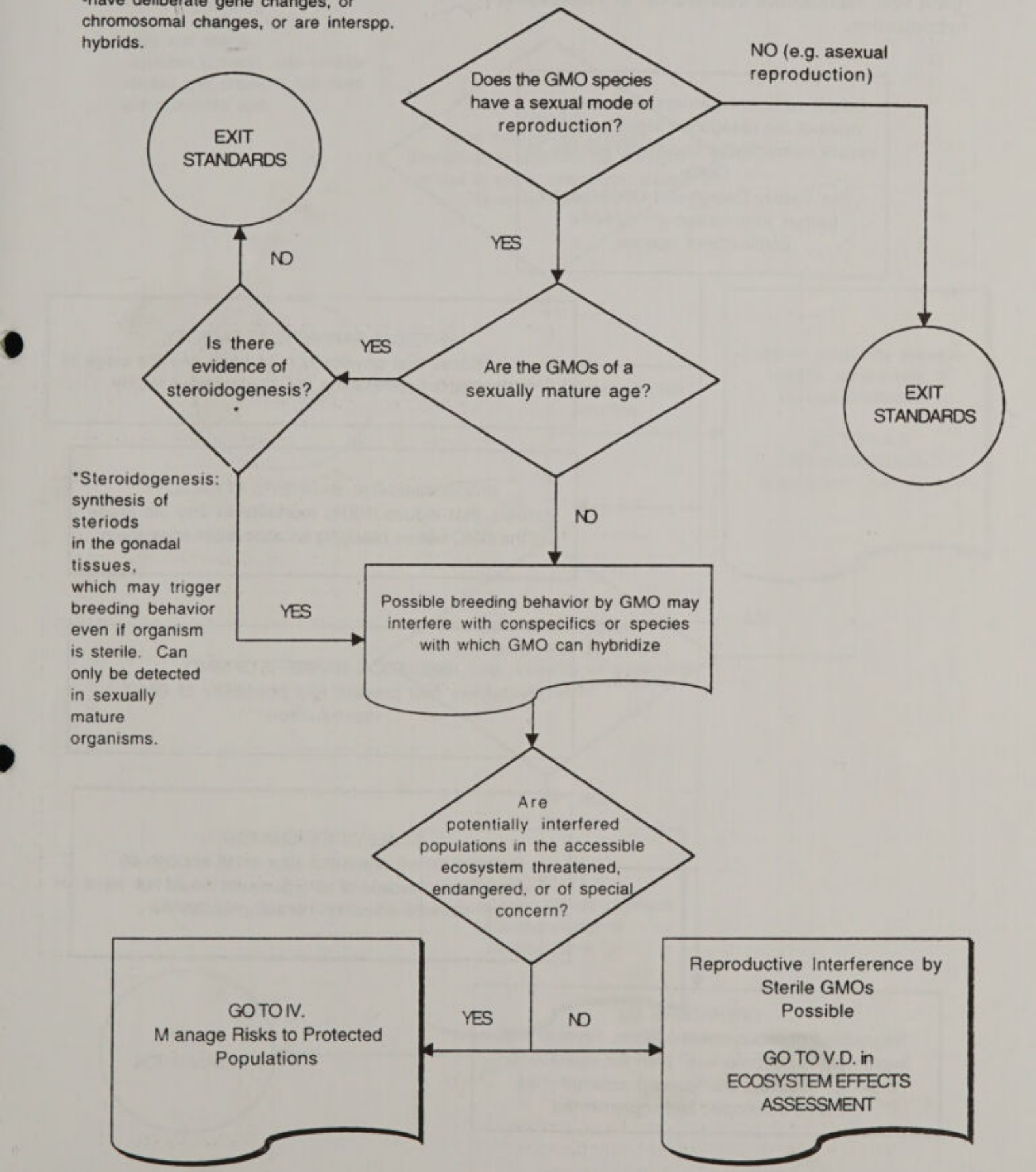
BIOLOGICAL BARRIERS OF GMO
Barriers that prevent any possibility of GMO reproduction.

SCALE OF EXPERIMENT
Maintain an experimental size small enough so that accidental escape of all organisms would not have an adverse effect on natural populations .

OPERATIONS
Regardless of confinement options, develop and implement an appropriate plan for operations, training, security, traffic, and emergencies. must be developed and implemented.

EXIT STANDARDS

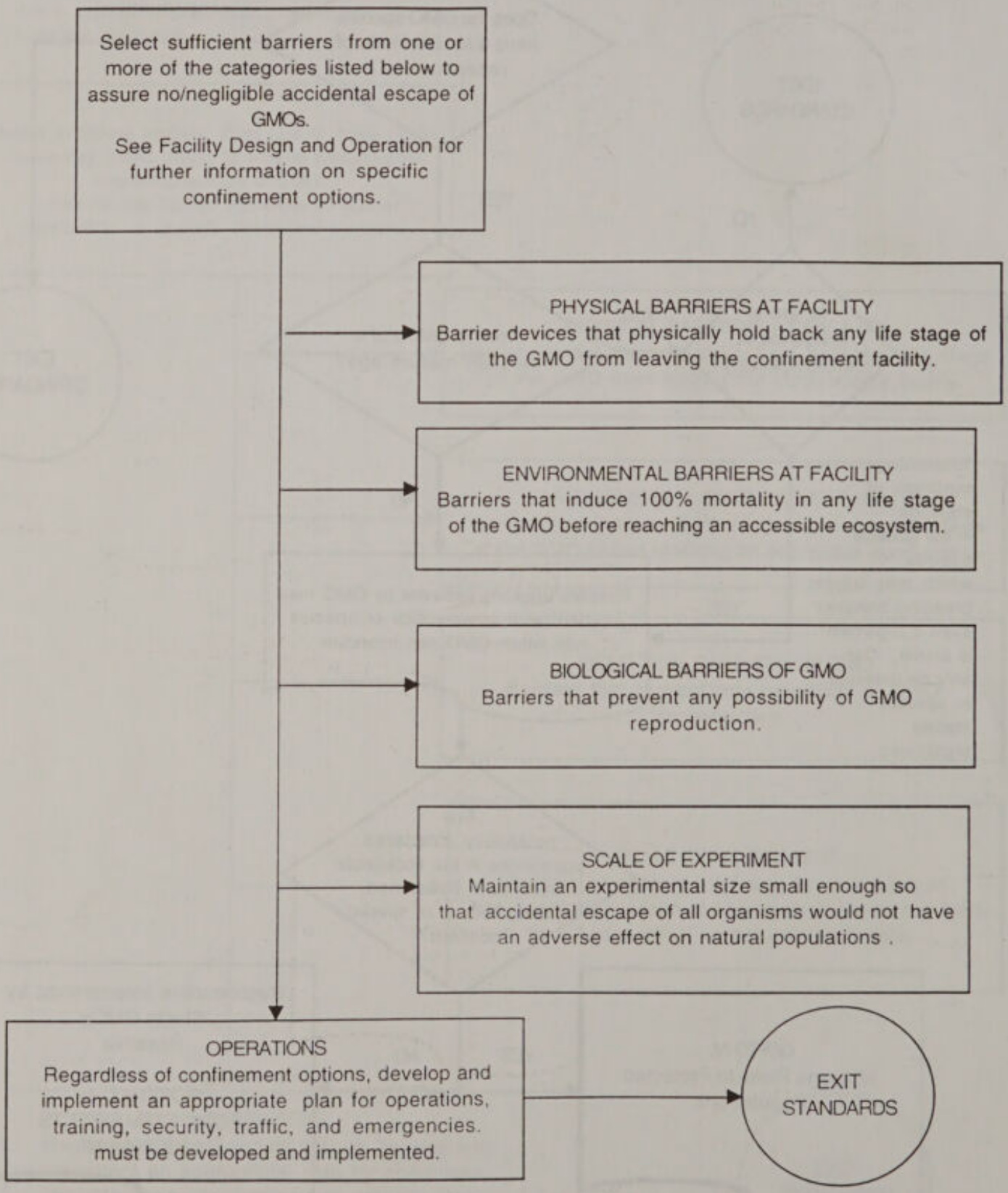
III. Potential Interference of Natural Reproduction



IV. Manage Risks to Protected Population(s)

Protected populations contain species which are threatened, endangered, or of special concern. Risks are gene flow, reproductive interference, or introgressive hybridization.

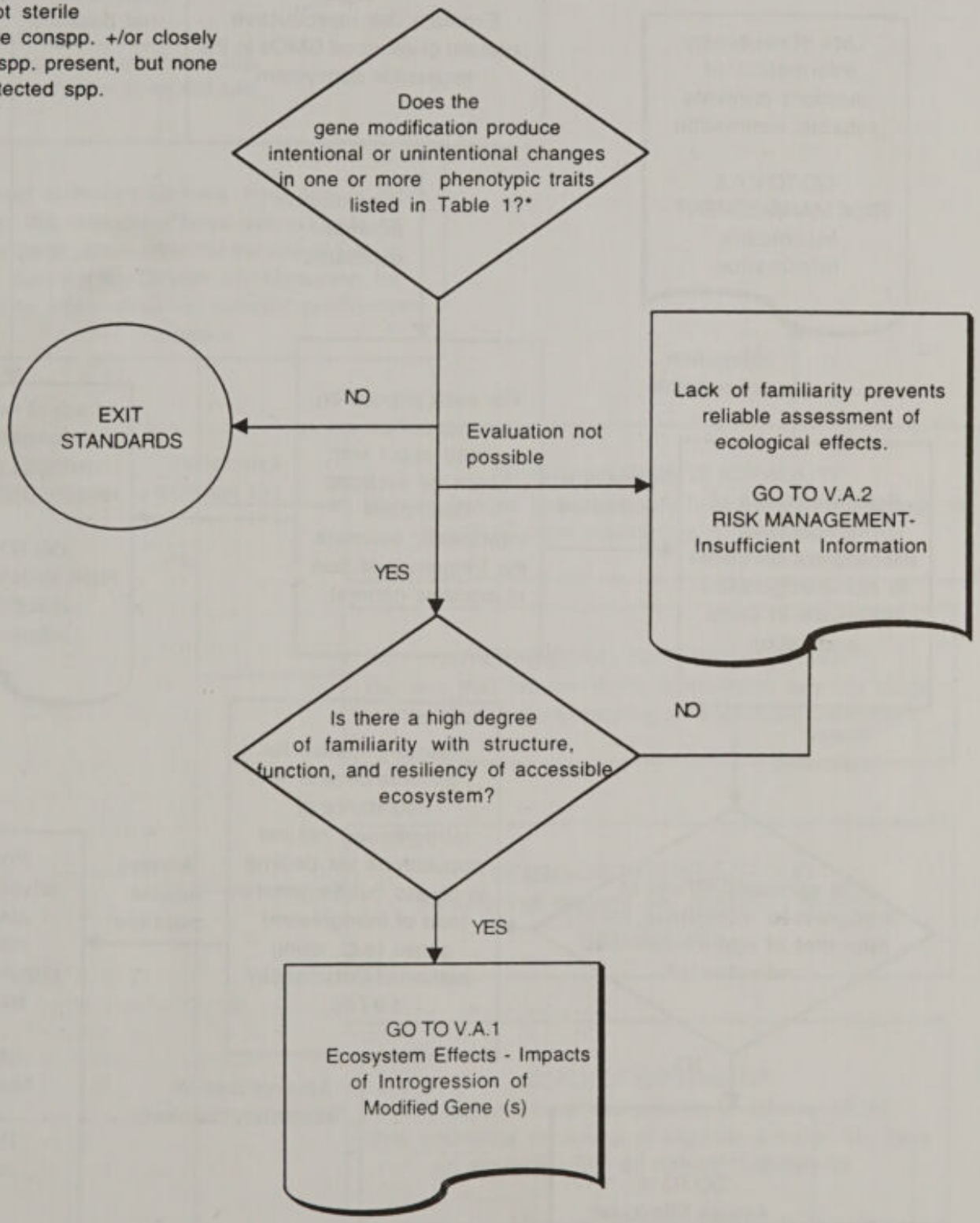
from III.
from II.A.1
from II.C.1



V.A. Ecosystem Effects - Deliberate Gene Changes

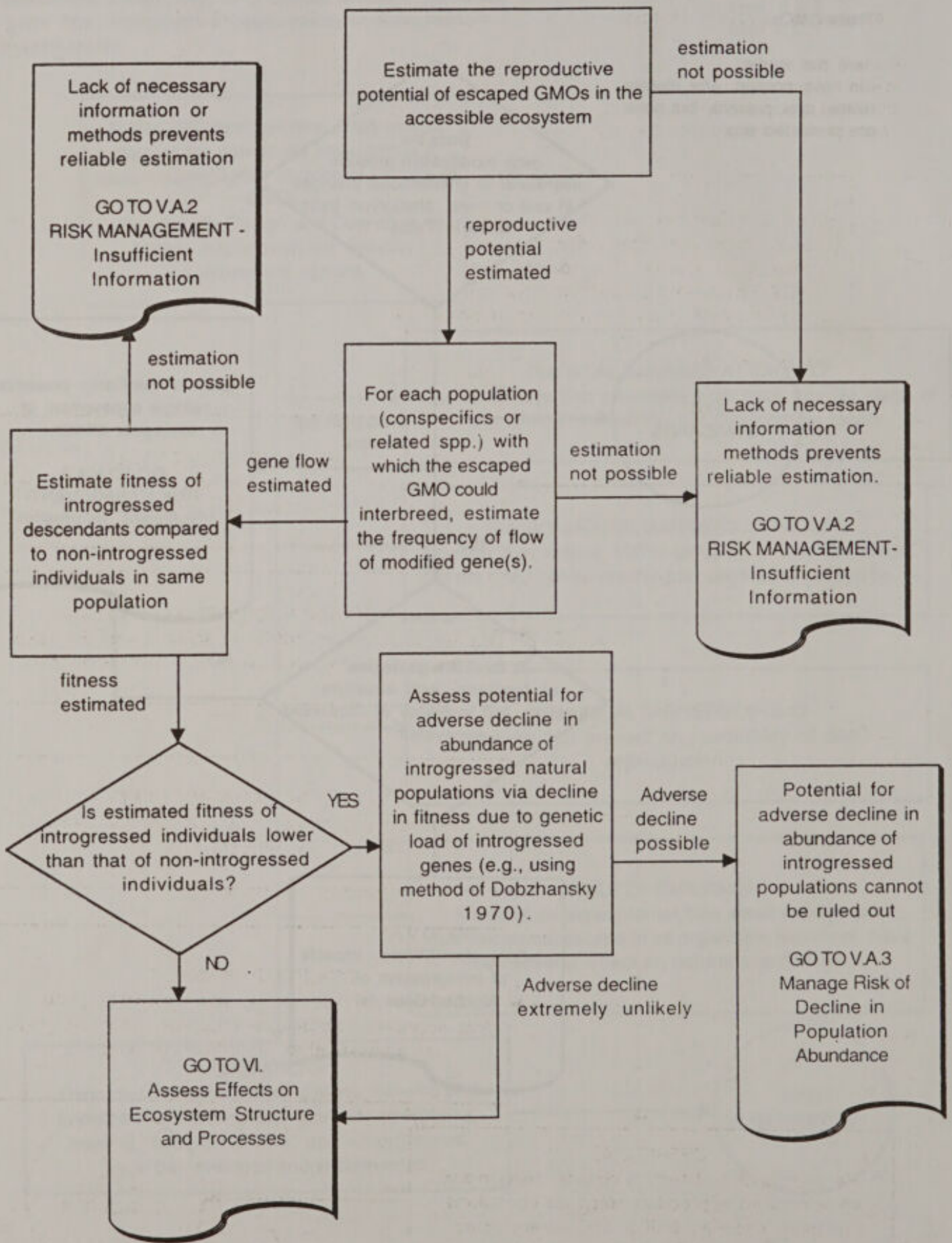
These GMOs:

-are not sterile
-do have conspp. +/or closely related spp. present, but none are protected spp.



V.A.1 Ecosystem Effects - Impacts of Introgression of Modified Gene

from V.A.



V.A.2 Risk Management - Insufficient Information

Information is insufficient to assess ecosystem effects.

from V.A.
from V.A.1

These GMOs:
-are not sterile
-do have conspp./closely related spp. present, but none are protected spp.

Select sufficient barriers from one or more of the categories listed below to assure no/negligible accidental escape of GMOs. See Facility Design and Operation for further information on specific confinement options.

PHYSICAL BARRIERS AT FACILITY
Barrier devices that physically hold back any life stage of the GMO from leaving the confinement facility.

ENVIRONMENTAL BARRIERS AT FACILITY
Barriers that induce 100% mortality in any life stage of the GMO before reaching an accessible ecosystem.

BIOLOGICAL BARRIERS OF GMO
Barriers that prevent any possibility of GMO reproduction.

SCALE OF EXPERIMENT
Maintain an experimental size small enough so that accidental escape of all organisms would not have an adverse effect on natural populations .

OPERATIONS
Regardless of confinement options, develop and implement an appropriate plan for operations, training, security, traffic, and emergencies. must be developed and implemented.

EXIT STANDARDS

V.A.3 Manage Risk of Decline in Population Abundance

from V.A.1
from V.D.

The acceptable number of accidental escapees* is one that will avoid a decline in the abundance of the affected population(s) resulting from lowered fitness or introgressed descendants (V.A.2), or from reproductive interference (V.D). Select sufficient barriers from one or more of the categories listed below to assure that accidental escapees are fewer than the acceptable number.

See Facility Design and Operation for further information on specific confinement options.

[* accidental escapes = combined outcome of scale of experiment and effectiveness of barriers.]

PHYSICAL BARRIERS AT FACILITY
Barrier devices that physically hold back any life stage of the GMO from leaving the confinement facility.

ENVIRONMENTAL BARRIERS AT FACILITY
Barriers that induce 100% mortality in any life stage of the GMO before reaching an accessible ecosystem.

BIOLOGICAL BARRIERS OF GMO
Barriers that prevent any possibility of GMO reproduction.

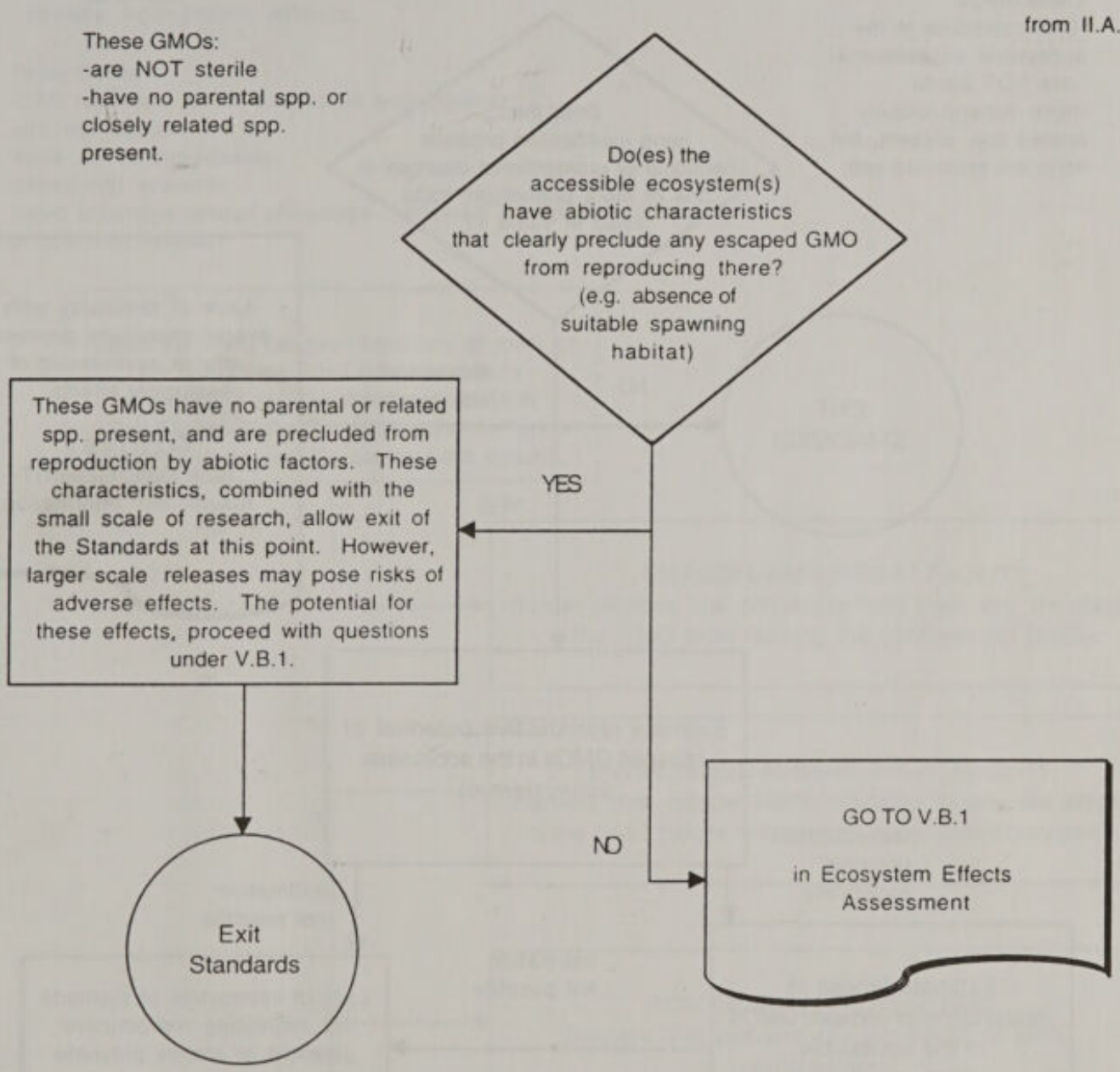
SCALE OF EXPERIMENT
Maintain an experimental size small enough so that accidental escape of all organisms would not have an adverse effect on natural populations

OPERATIONS
Regardless of confinement options, develop and implement an appropriate plan for operations, training, security, traffic, and emergencies.

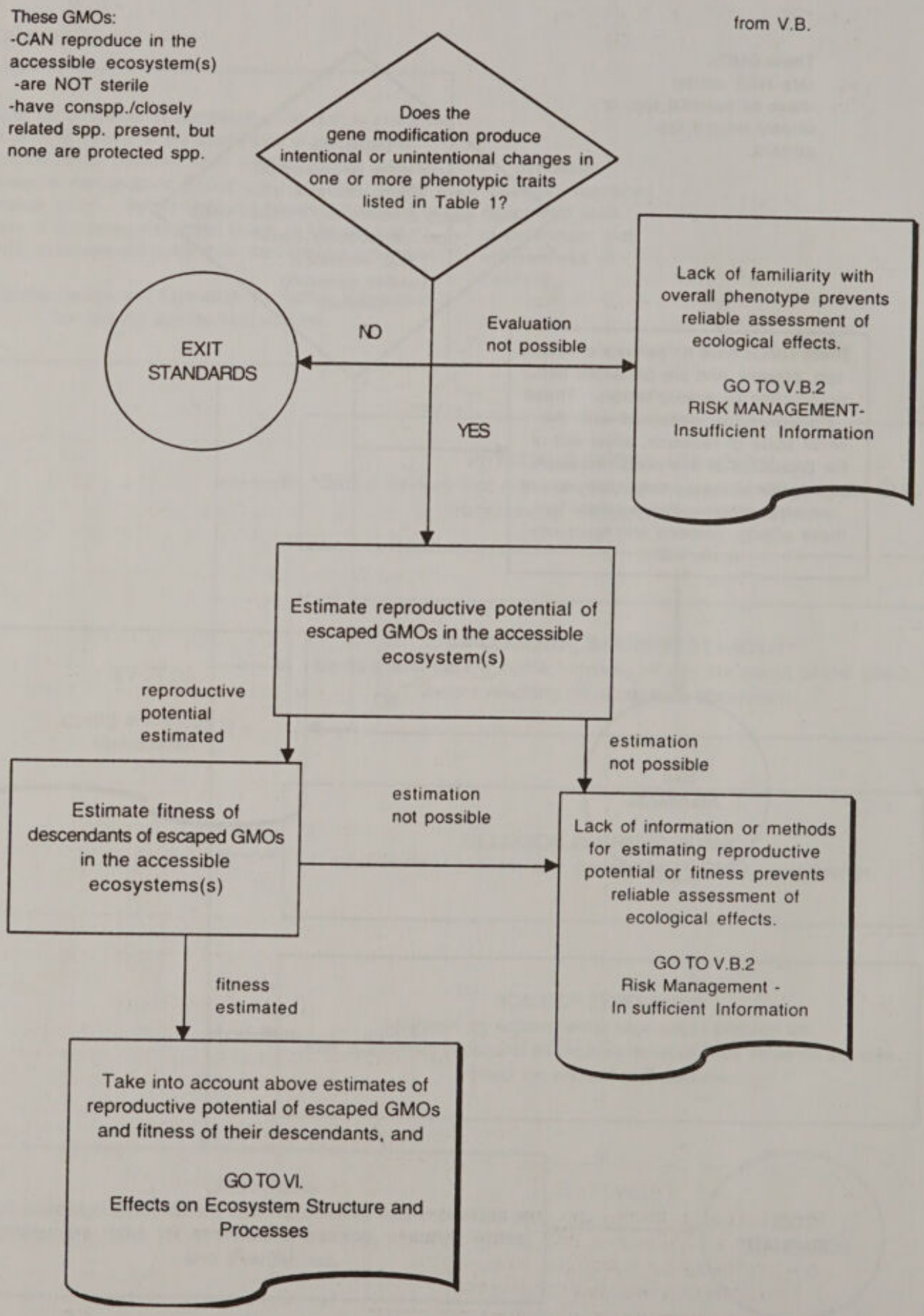
EXIT STANDARDS

V.B. Potential Barriers Associated with Accessible Ecosystem

from II.A.1.



V.B.1 Ecosystem Effects - Potential for Non-Reproductive Interaction



V.B.2 Risk Management - Insufficient Information

Information is insufficient to assess ecosystem effects.

from V.B.1

These GMOs:
-CAN reproduce in the accessible ecosystem(s)
-are not sterile
-have no conspp./closely related spp. present
-have unfamiliar overall phenotype , unknown reproductive potential or unknown fitness.

Select sufficient barriers from one or more of the categories listed below to assure no/negligible accidental escape of GMOs. See Facility Design and Operation for further information on specific confinement options.

PHYSICAL BARRIERS AT FACILITY
Barrier devices that physically hold back any life stage of the GMO from leaving the confinement facility.

ENVIRONMENTAL BARRIERS AT FACILITY
Barriers that induce 100% mortality in any life stage of the GMO before reaching an accessible ecosystem.

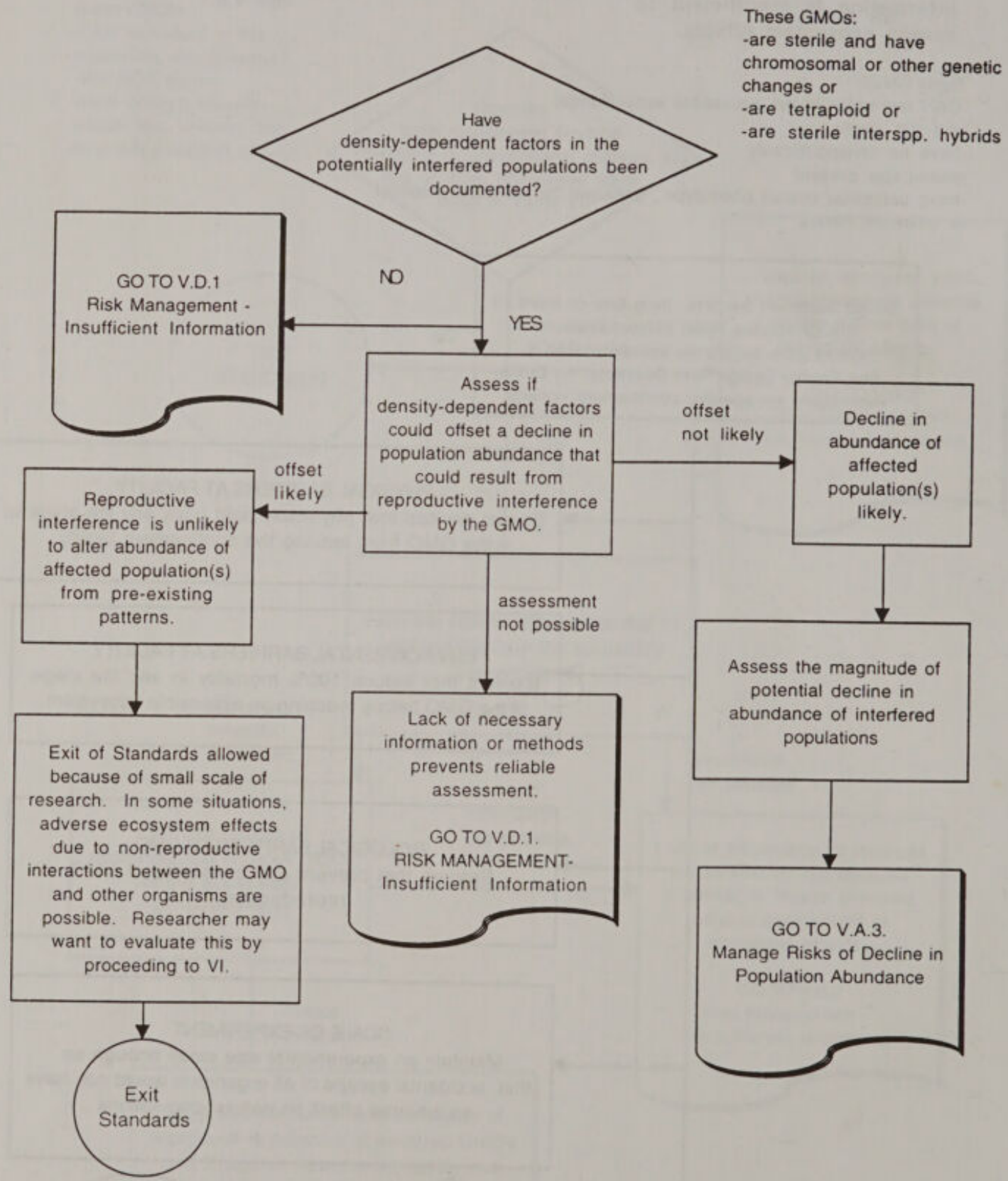
BIOLOGICAL BARRIERS OF GMO
Barriers that prevent any possibility of GMO reproduction.

SCALE OF EXPERIMENT
Maintain an experimental size small enough so that accidental escape of all organisms would not have an adverse effect on natural populations .

OPERATIONS
Regardless of confinement options, develop and implement an appropriate plan for operations, training, security, traffic, and emergencies. must be developed and implemented.

EXIT STANDARDS

V.D. Ecosystem Effects - Impacts of Reproductive Interference



V.D.1 Risk Management - Insufficient Information

Information is insufficient to assess the effect of reproductive interference on the affected population(s), or to assess the combined outcome of density-dependent factors and reproductive interference.

from V.D.

These GMOs:
-are either sterile or tetraploid
-do have conspp./closely related spp. present, but none are protected spp.

Select sufficient barriers from one or more of the categories listed below to assure no/negligible accidental escape of GMOs.

See Facility Design and Operation for further information on specific confinement options.

PHYSICAL BARRIERS AT FACILITY
Barrier devices that physically hold back any life stage of the GMO from leaving the confinement facility.

ENVIRONMENTAL BARRIERS AT FACILITY
Barriers that induce 100% mortality in any life stage of the GMO before reaching an accessible ecosystem.

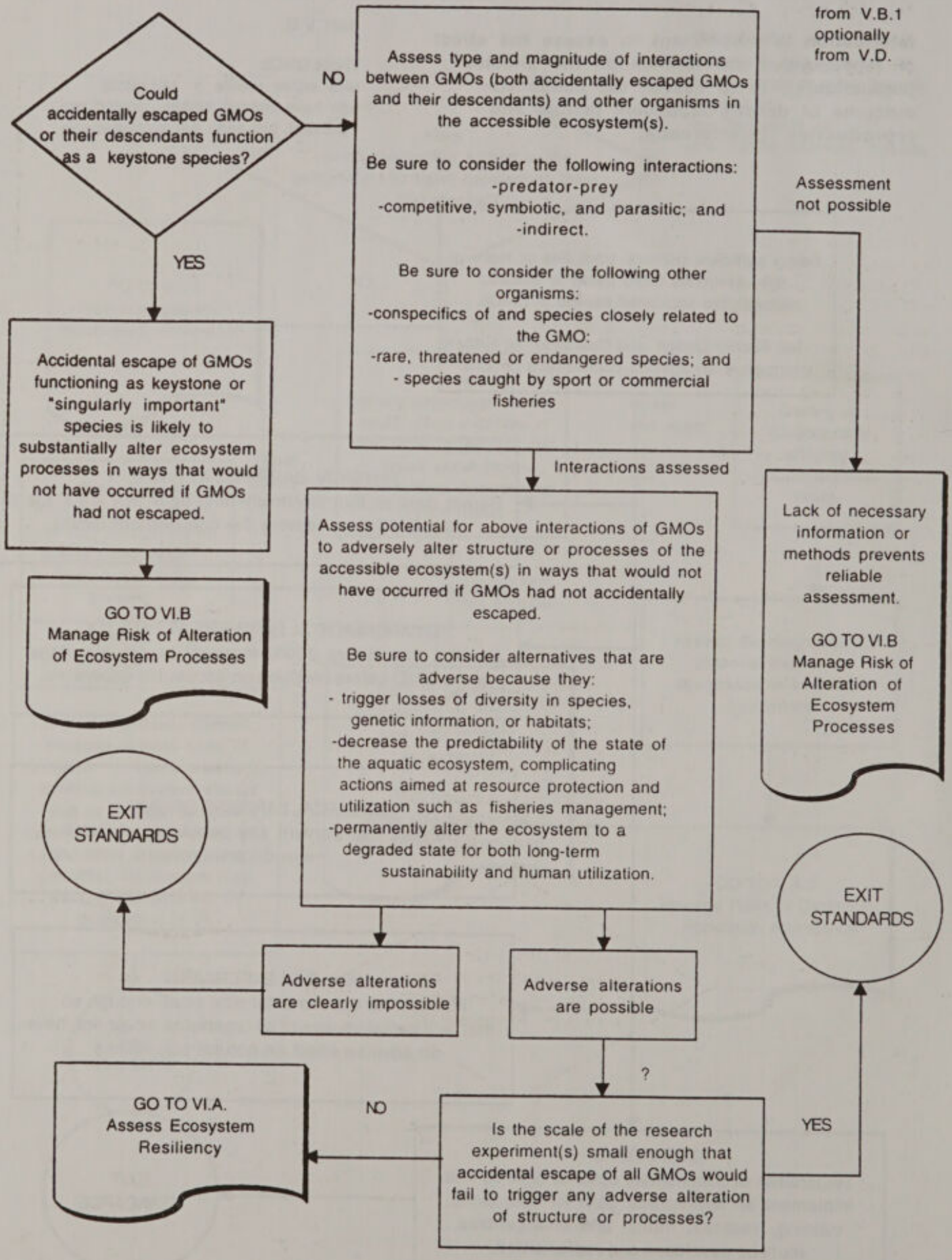
BIOLOGICAL BARRIERS OF GMO
Barriers that prevent any possibility of GMO reproduction.

SCALE OF EXPERIMENT
Maintain an experimental size small enough so that accidental escape of all organisms would not have an adverse effect on natural populations .

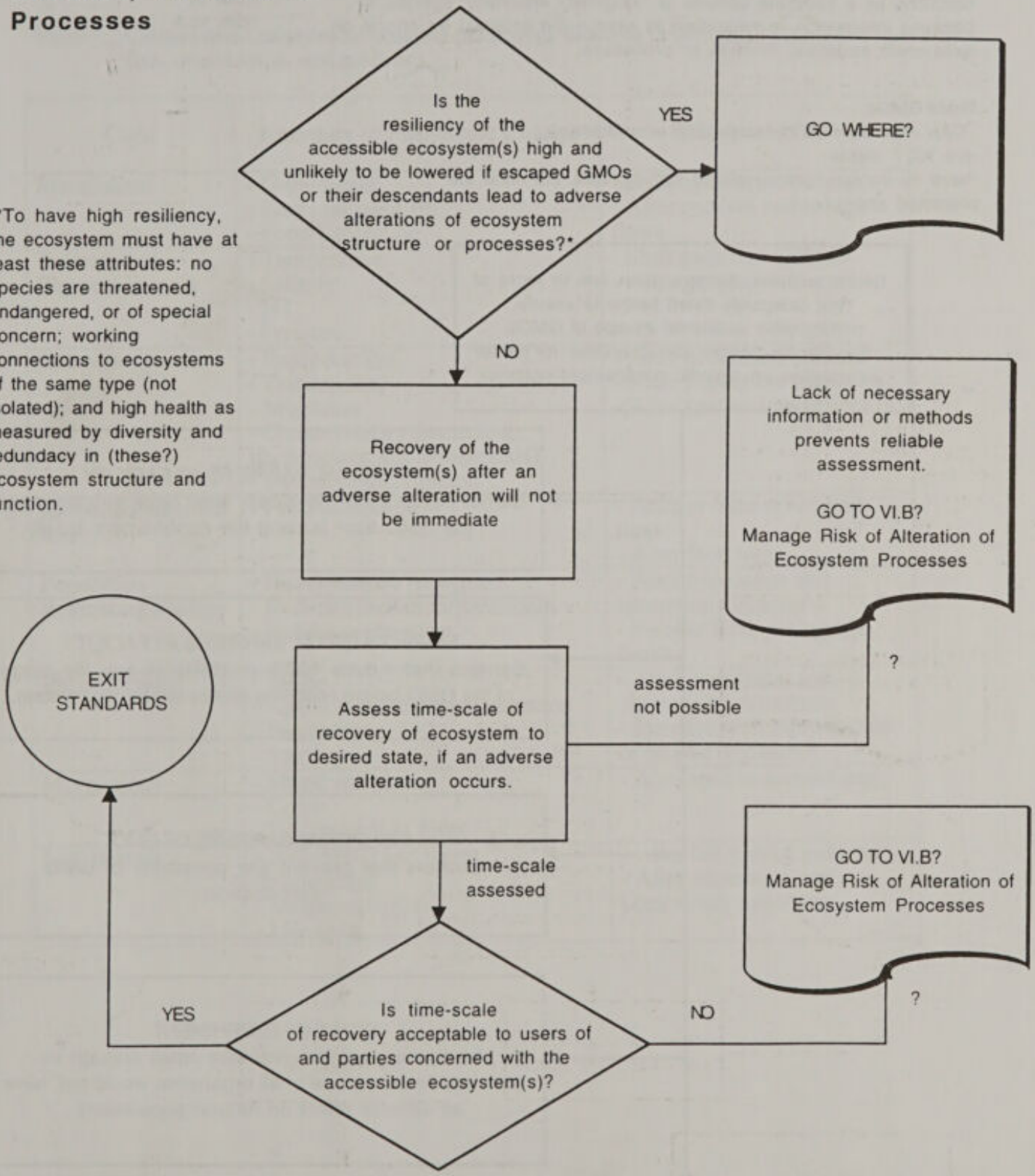
OPERATIONS
Regardless of confinement options, develop and implement an appropriate plan for operations, training, security, traffic, and emergencies. must be developed and implemented.

EXIT STANDARDS

VI. Effects on Ecosystem Structure and Processes



VI.A Assess Ecosystem Resiliency to Adverse Alterations of Structure, Function or Processes



[*To have high resiliency, the ecosystem must have at least these attributes: no species are threatened, endangered, or of special concern; working connections to ecosystems of the same type (not isolated); and high health as measured by diversity and redundancy in (these?) ecosystem structure and function.

VI.B Manage Risk of Alteration of Ecosystem Processes

Risks of alteration in ecosystem processes exist either because the GMO functions as a keystone species or "singularly important" species, or because information is insufficient to assess the potential for effects on ecosystem structure, function or processes.

from V.B.1
from VI
from VI.A

These GMOs:
-CAN reproduce in the accessible ecosystem(s)
-are NOT sterile
-have no conspp./closely related spp. present, but none are protected spp.

Select sufficient barriers from one or more of the categories listed below to assure no/negligible accidental escape of GMOs. See Facility Design and Operation for further information on specific confinement options.

PHYSICAL BARRIERS AT FACILITY
Barrier devices that physically hold back any life stage of the GMO from leaving the confinement facility.

ENVIRONMENTAL BARRIERS AT FACILITY
Barriers that induce 100% mortality in any life stage of the GMO before reaching an accessible ecosystem.

BIOLOGICAL BARRIERS OF GMO
Barriers that prevent any possibility of GMO reproduction.

SCALE OF EXPERIMENT
Maintain an experimental size small enough so that accidental escape of all organisms would not have an adverse effect on natural populations .

OPERATIONS
Regardless of confinement options, develop and implement an appropriate plan for operations, training, security, traffic, and emergencies. must be developed and implemented.

EXIT STANDARDS

Table 1. Classes and examples of possible phenotype changes in genetically modified fish, crustaceans, and molluscs.

Class	Examples of Phenotypic Change	Ecological Effect
Metabolism	- Growth rate - Enery metabolism - Food Utilization	Shift to different prey size - Alter nutrient and energy flows
Tolerance of Physical Factors	- Temperature - Salinity - pH - Pressure	- Shift preferred habitats - Alter geographic range
Behavior	- Reproduction - Territoriality - Migration - Chemosensory (including pheromones, allelochemicals) - Swimming/navigation	- Alter life history patterns - Alter population dynamics - Alter species interactions
Resource/Substrate Use	- Food utilization	- Release from ecological limits - Alter food webs
Population Regulating Factors	- Novel disease resistance - Reduced predation/parasitism - Habitat preference	- Alter population and communtiy dynamics - Release from ecological limits
Reproduction	- Mode - Age at maturation and duration - Fecundity - Sterility	- Alter population and community dynamics - Interfere with reproduction of related organisms
Morphology	- Shape and size - Color - Fin/appendage form	- Alter species interactions
Life History	- Embryonic and larval development - Metamorphosis - Life span	- Alter life history patterns - Alter population and community dynamics

Worksheet accompanying
Performance Standards for Safely Conducting Research
with Genetically Modified Finfish and Shellfish

Principal Investigator:
Proposed project:

Response Yes	No	Unk	Question	Comment
___	___	___	Do the performance standards apply to the proposed experiment?	
___	___	___	Does the GMO result from deliberate changes of genes?	
___	___	___	Are you directed to assess impact of deliberate gene changes?	
_____			Where are you directed following completion of flowchart II.A.1?	
___	___	___	Does the GMO result from deliberate changes of chromosomes?	
___	___	___	Are you directed to assess impact of chromosomal manipulations?	
_____			Where are you directed following completion of flowchart II.B.1?	
___	___	___	Is the GMO result an interspecific hybrid?	
___	___	___	Are you directed to assess the potential impact of interspecific hybridization?	
_____			Where are you directed following completion of flowchart II.C.1?	
			If you were directed to use flowchart II.C.2, what measures do you plan to adopt to manage the risk of losing a population of a pure species?	
_____			If you were directed to use flowchart III, where were you your routed?	
			If you were directed to use flowchart IV, what measures do you plan to adopt to manage risks to protected population(s)?	

_____ If you were directed to use flowchart V.A, where were you your routed?

_____ If you were directed to use flowchart V.A.1, where were you your routed?

If you were directed to use flowchart V.A.2, what measures do you plan to adopt to achieve effective confinement of the proposed research project?

_____

_____

_____

If you were directed to use flowchart V.A.2, what measures do you plan to adopt to manage the risk of decline in population abundance?

_____

_____

_____

_____ If you were directed to use flowchart V.B, where were you your routed?

_____ If you were directed to use flowchart V.B.1, where were you your routed?

If you were directed to use flowchart V.B.2, what measures do you plan to adopt to achieve effective confinement of the proposed research project?

_____

_____

_____

_____ If you were directed to use flowchart V.D, where were you your routed?

If you were directed to use flowchart V.D.1, what measures do you plan to adopt to achieve effective confinement of the proposed research project?

_____

_____

_____

_____ If you were directed to use flowchart VI, where were you your routed?

_____ If you were directed to use flowchart VI.A, where were you your routed?

If you were directed to use flowchart VI.B, what measures do you plan to adopt to manage the risk of alteration of ecosystem processes?

_____

_____

_____

_____

Signature and date:
Names of professionals with whom I consulted in making my responses: