A Compendium of Near-Miss Incidents Related to Research Integrity

(Second Edition)

Japan Agency for Medical Research and Development

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January 2024

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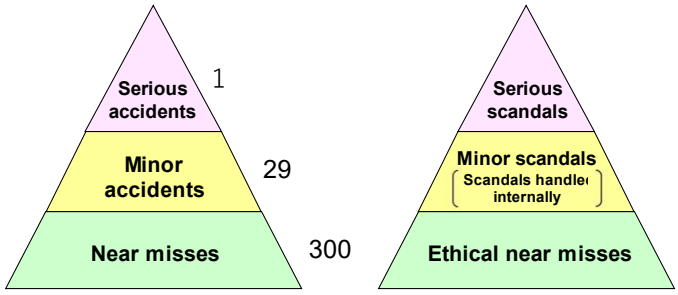
(AMED)

Introduction

Despite the fact that everyone has a conscience and seeks safety and a peace of mind, we see scandals and accidents repeatedly occurring almost every day. The fact that it is extremely important to learn from failures to prevent scandals and accidents, as exemplified by failure analysis, has been recognized widely throughout society. It has been proposed that behind each serious accident there are 29 minor accidents and 300 near-miss incidents (Heinrich's triangle). The theory of industrial accident prevention as illustrated in Heinrich's triangle posits that if you reduce the number of near misses [or minor accidents], then there will be a corresponding reduction in the number of major accidents. Various organizations share information and take measures at the near-miss level to prevent accidents.



Ethical Scandals & Heinrich's Law

Created in reference to *Practical Engineering Ethics*, New Edition p. 47 (Kagaku-Dojin Publishing) by Shuzo Nakamura

In a way perhaps similar to the theory of accident prevention, it also seems that behind serious cases of misconduct reported in the media as well as those that were handled internally within the organizations, many cases could be stopped at a stage before leading up to research misconduct. Although it is also important to be aware of the cases of serious research misconduct and their backdrop, it would be very useful for research integrity to know, in good research practices where research misconduct did not occur, how the relevant persons thought, what conversations they had with those around them, and what advice they received from those around them.

The reason why researchers slip into research misconduct may be that they were in a situation where they could not resist the devil's whisper, or where they were not even aware that the devil was whispering to them. We therefore compiled this collection in the hope that sharing information about the near-miss incidents of research misconduct will help you recognize and resist the devil's whisper.

This case collection lists quite a number of cases where research misconduct (including questionable research practices and violations of guidelines) was prevented by chance or stroke of luck. We hope that you would distribute the text summarizing the details of the case, its backdrop and factors, along with diagrams in workshops and classes, and actively use them to think about the "motives", "opportunities", and "justifying factors" that led to the person conducting research misconduct, as well as discuss the precautions and countermeasures one would need to take to prevent that from happening, chance or stroke of luck aside.

To increase the effectiveness of this compendium of incidents as a teaching material, we have revised some of the examples based on real-life cases. Where cases include inappropriate conduct by some of the individuals who appear therein, we would ask readers to bear in mind that our inclusion of this information does not mean that we endorse this behavior.

Important request

When learning from failures, it is very important to determine the cause but not pursue the responsibility. When gathering cases of failure, if the whistleblower were to be subjected to even one criticism, it would render the reporting system ineffective. We have taken great care, where possible, to ensure that no concerned

individuals or organizations are identified in this collection. However, if you happened to identify the case reporter or organization mentioned, we also ask that you do not criticize them or hold them accountable in any way.

Table of Contents

This expanded edition of the Compendium of Near-Miss Incidents contains a total of 52 examples and eight editor's columns, comprising the 31 examples and six columns contained in the first edition (issued in March 2020), plus an additional 21 examples and two editor's columns compiled in FY2022.

*: Asterisks indicate new topics, cases, and editor's columns.

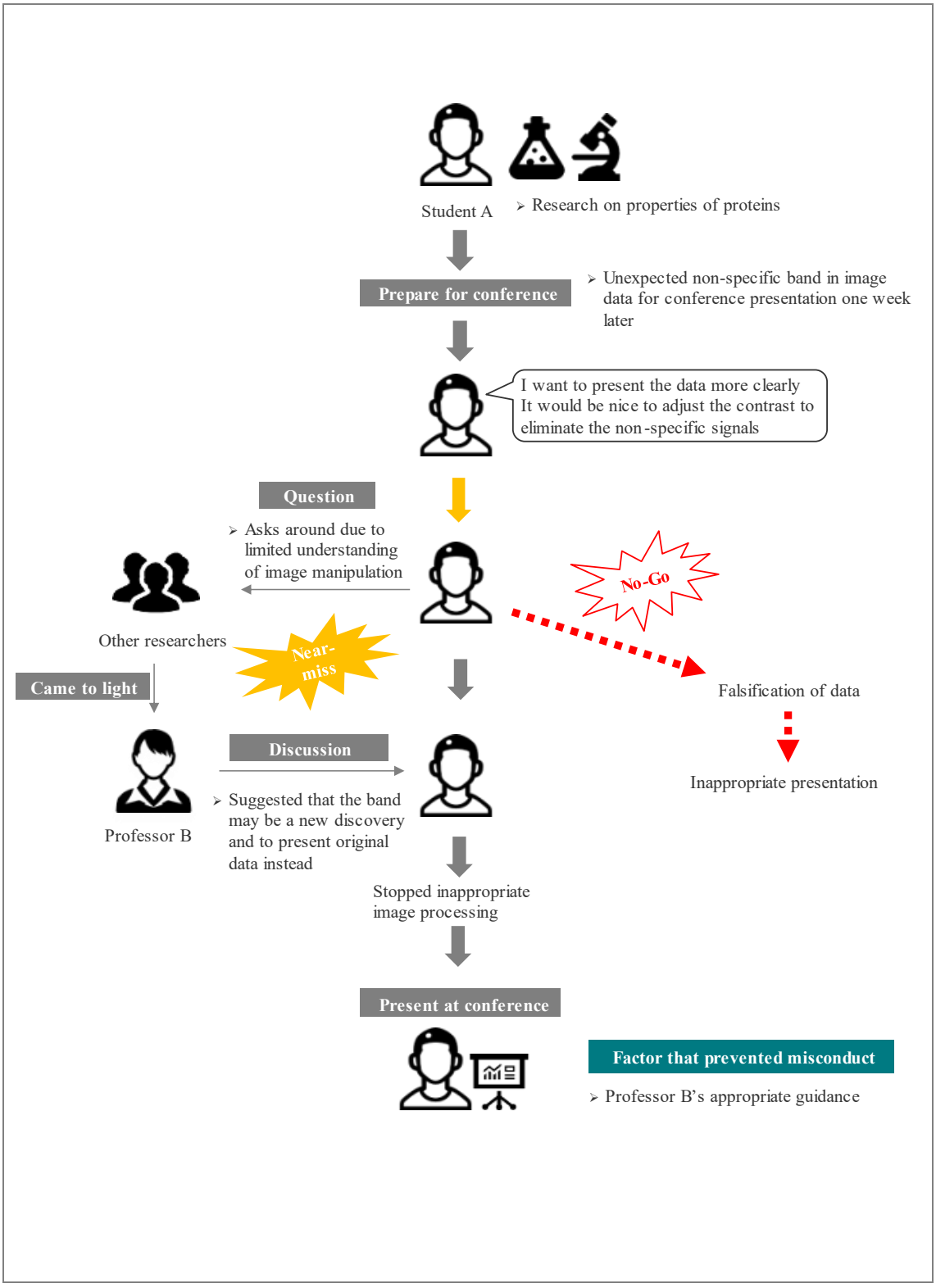
1 Fabrication, falsification, plagiarism

1. Excessive adjustment of exposure conditions during image capture
2. Data fabrication by a student in doctoral dissertation
3. Lack of verification of data submitted by a co-researcher
4. Attempted submission of falsified data to scientific journal
5. Forgetting to replace images in the manuscript for publishing
6. Prevented self-plagiarism in submission of a paper to multiple scientific journals*

Editor's column 1: Fraud triangle

1-1. Excessive adjustment of exposure conditions during image capture

Affiliated institution	University, University hospital	Field	Life sciences



1. Case details

- Student A performed western blots to visualize the type of proteins that were found in the complex mixture with a certain function, and was imaging their western blots with an optical camera.
- On one occasion, Student A observed a faint band at a position that was usually not seen, and passed it off as a nonspecific, meaningless signal. Student A planned to present the results of this experiment at a conference a week later and wanted to make the data look more "beautiful" to show off their experimental techniques.
- Student A then came up with the idea of adjusting the exposure conditions during imaging to obscure the faint, nonspecific signal by increasing the contrast of the signals. This is known as "blown-out highlights" and only an experienced researcher knows how to properly adjust the conditions for this imaging, including when it is acceptable to do so. A novice at imaging, Student A went around asking people experienced in creating "blown-out highlights", to which Professor B got to know of this. ☜ **Factor that prevented misconduct**
- When Student A discussed it with Professor B, Professor B commented that "This kind of signal is rare and it may very well be a new discovery. We might not be able to explain for it now, but in future, other researchers or we may have some ideas. How about we just show the image as it is?", to which Student A then presented the unedited images at the conference.

2. Backdrop & factors of near-miss incident

- Student A was overly confident in their experimental techniques and wanted to show off their technical skills. Student A was also an inexperienced researcher and did not think that the detected unexpected signal could be a new discovery instead.
- Student A thought that they had to eliminate the meaningless noise before even considering whether it was right or wrong to edit the image, and excused themselves by saying that it was okay because the seniors were probably doing the same thing.

3. Factors that prevented misconduct & its backdrop

- Student A merely wanted to get "beautiful" data without any ill intentions. Student A themself did not know how to adjust the conditions for blown-out highlights, so they asked around without any ill will, and eventually their behavior reached the ears of Professor B.
- After Student A got to discuss their raw data with Professor B, they were able to prevent presenting inappropriately processed images at the conference.

4. Possible research misconduct and questionable research practice

- Falsification of data.

5. Preventive countermeasures

- Provide training on appropriate image processing methods to create the awareness that excessive image processing may be considered as falsification of data.
- Implement a system that allows multiple members to conduct research together as well as check each other. In particular, do not allow anyone to handle operations on their own in which many cases of misconduct have been observed in the past, such as the handling of image data.
- The system should also provide opportunities for students to discuss with their research advisors, such as Faculty members, and inculcate a habit where they can think and discuss the entire process from checking the raw data to interpretating and discussing the data.

(Commentary)

Although it is acceptable to enhance the contrast of biological images to improve the visibility of the images, excessive processing may result in blocked-up shadows (where the parts turn completely black) and blown-out highlights (where the parts turn completely white). Any blocked-up shadow or blown-out highlight may give rise to the suspicion of image manipulation since it is impossible to distinguish whether the image was processed to merely enhance its contrast or to conceal inconvenient data[1].

It goes without saying that editing image data that would change the conclusion would construe as an act of misconduct. But there is a need to take extreme care even when editing the data to "make it clearly visible" to avoid suspicion of attempted falsification. The Japan Agency for Medical Research and Development (AMED) recommends authors to save the original images as separate files so that they can be submitted anytime upon request when editing images as well as to document the image editing techniques used[2].

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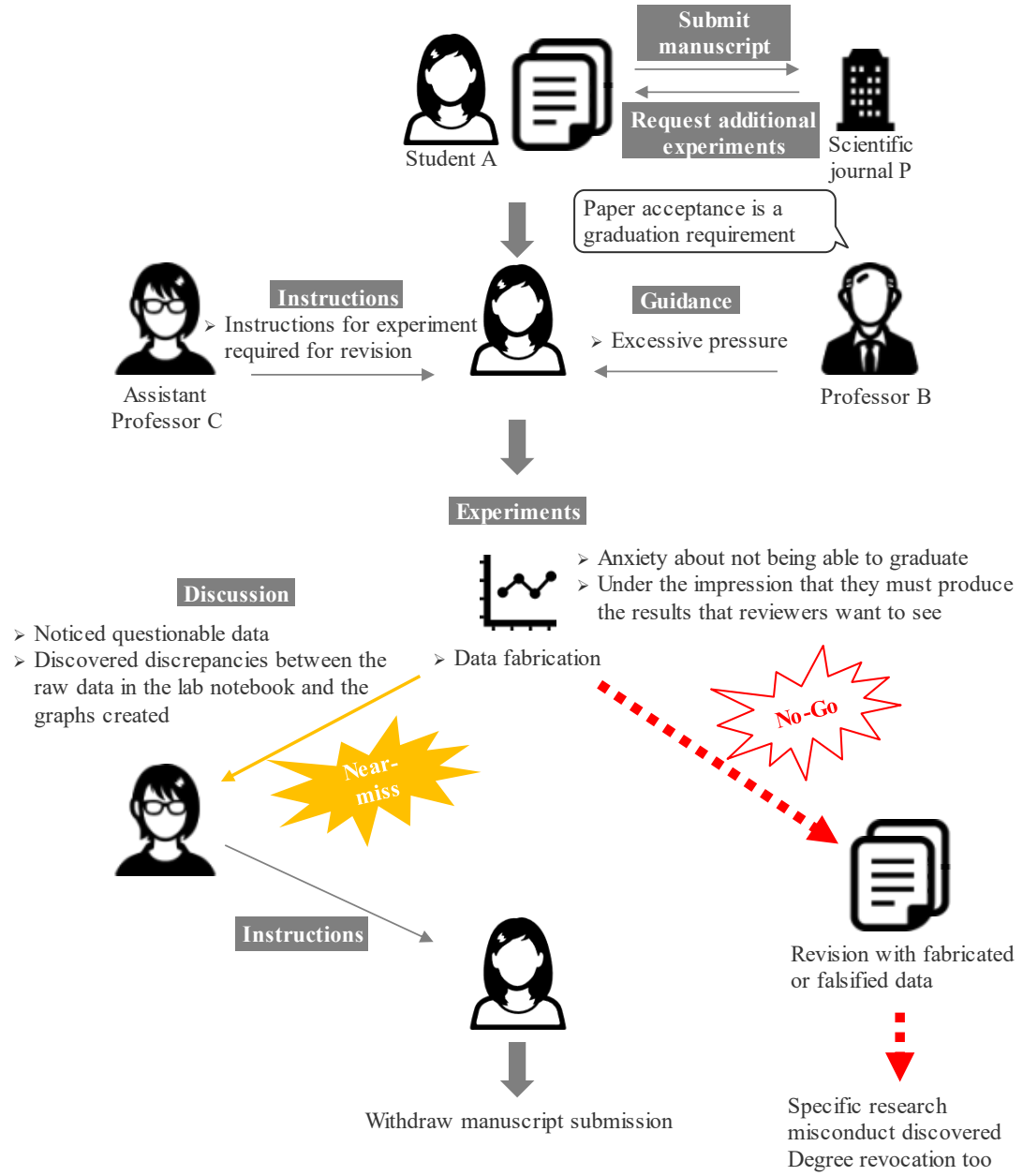
1 Japan Agency for Medical Research and Development (AMED) "Appropriate Image Processing – Explanation of Submission Guidelines of Journals" (November 2017) (Online edition: https://www.amed.go.jp/content/000078447.pdf) partially revised.

2 Japan Agency for Medical Research and Development (AMED) "Appropriate Image Processing – Explanation of Submission Guidelines of Journals" (November 2017) (Online edition: https://www.amed.go.jp/content/000078447.pdf)

1-2. Data fabrication by a student in doctoral dissertation

Affiliated institution	University, University hospital	Field	Basic medical research



Factor that prevented misconduct

- Student A had multiple research advisors
- Assistant Professor C's basic attitude & careful follow-up to check the raw data

1. Case details

- Student A, a fourth-year doctoral student, submitted their manuscript, but the reviewer pointed out a flaw in the experiments. Assistant Professor C, who was in charge of guiding Student A, instructed Student A to carry out the experiments required for the revision of the manuscript.
- Student A conducted the experiments on their own and created the graphs based on the obtained results. After Student A and Assistant Professor C discussed these graphs, Assistant Professor C noticed some questionable points in the data. When Student A showed the raw data recorded in the lab notebook to Assistant Professor C as per instructed, Assistant Professor C discovered that there were large discrepancies between the results of the raw data and the graphs.

☜ **Factor that prevented misconduct**

- Assistant Professor C instructed Student A not to submit the revised manuscript, but to withdraw the submission instead.
- It was also revealed that Professor B of the same laboratory had informed Student A that they would not be able to graduate unless the revised manuscript was accepted by the journal, despite the fact that this was not part of the requirements as stipulated by the university in question, which led to Student A assuming that that was the case.

2. Backdrop & factors of near-miss incident

- Student A believed that the manuscript would only be accepted if they produced the results as pointed out by the reviewer.
- Student A was under extreme pressure by their research advisor, Professor B, and was convinced that they would not be able to graduate unless their revised manuscript was accepted.
- Student A's research advisors did not thoroughly check their lab notebook.

3. Factors that prevented misconduct & its backdrop

- Student A had the opportunity to discuss her work with Assistant Professor C where the raw data from the lab notebook was compared with the graphs. This led to Assistant Professor C discovering the questionable data, to which Student A could withdraw the submission of the manuscript in time.
- Instead of guiding Student A, Professor B put unfair pressure that caused Student A to make wrong decisions. However, Student A had multiple research advisors who prevented the submission of the fraudulent manuscript.

4. Possible research misconduct and questionable research practice

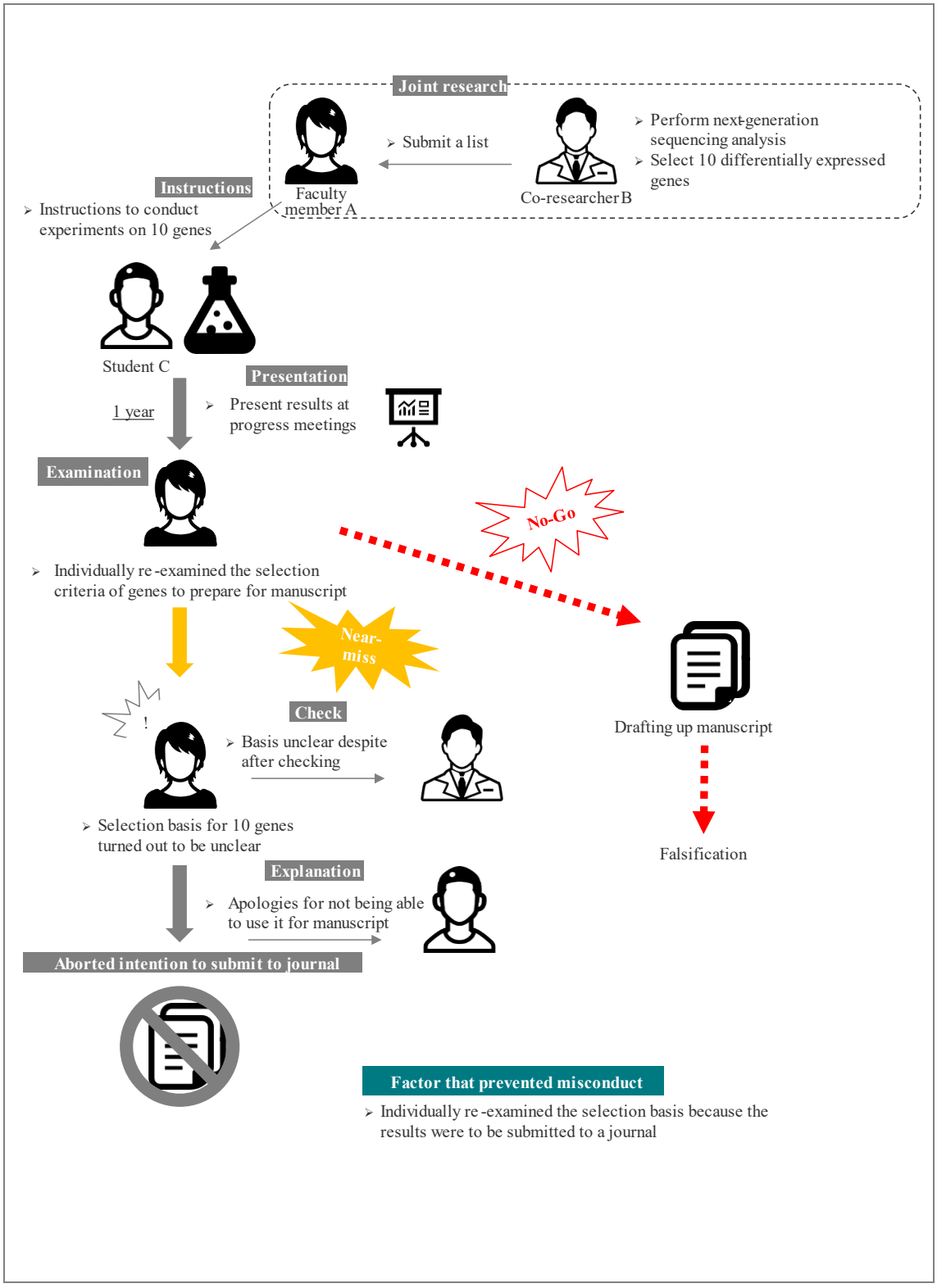
- The submission of manuscripts with fabricated or falsified results is considered as specific research misconduct.
- Credibility would be lost if the results of the manuscript cannot be reproduced by other researchers and research misconduct is discovered.
- Student A's degree might be revoked depending on the details of the misconduct.

5. Preventive countermeasures

- Ensure that the requirements for the degree are clearly stated and disclosed to public, and that students are able to obtain advice from their co-advisors from an early stage.
- Provide training on research ethics to raise awareness on the importance of fair research activities by asking participants to consider the activities that would construe as research misconduct as well as the undesirable impact it may bring to society and themselves.
- Create a framework, particularly for students, where their research advisors are able to regularly check their lab notebooks and raw data.
- Create an environment where students can easily seek advice from their research advisors on a regular basis so that students do not become isolated.

1-3. Lack of verification of data submitted by a co-researcher

Affiliated institution	University, University hospital	Field	Life sciences



1. Case details

- Faculty member A asked Co-Researcher B to generate a list of differentially expressed genes using next-generation sequencing analysis (NGS analysis).
- Based on this list, Faculty member A asked Student C to conduct experiments on 10 genes with large expression differences for about a year. During this time, Student C gave presentations of their research progress at laboratory meetings. As Student C attempted to prepare a manuscript using those results, Faculty member A re-examined the NGS analysis results from the raw data and discovered that the selection basis for the 10 genes was unclear (those genes were not selected with the method described by Co-Researcher B). No convincing explanation could be reached even after checking with Co-Researcher B. ☜ **Factor that prevented misconduct**
- It was unclear whether Co-Researcher B's inability to explain the selection basis was a simple mistake or falsification, but Faculty member A stopped Student C from further writing up the manuscript.
- Faculty member A explained to Student C that it would be difficult to submit the manuscript as it was, and convinced Student C to re-analyze this data and use it for another research instead.

2. Backdrop & factors of near-miss incident

- Since Faculty member A explained the research objectives in detail to Co-Researcher B, Co-Researcher B was able to arbitrarily select convenient genes to serve the objectives.
- Faculty member A allowed the research to proceed without verifying the data of the list of genes submitted by Co-Researcher B.

3. Factors that prevented misconduct & its backdrop

- Faculty member A personally re-examined the data when Student C was preparing the manuscript and noticed that the method of selecting genes was unclear. They then asked Student C to stop writing up the manuscript as it was.
- If any one of them had examined the selection criteria of the data and checked its reproducibility when the list was submitted, they would have noticed it at an earlier stage.
- The arbitrary interpretations could have been prevented if the information that is expected to bias the analysis results had been withheld, or if the gene extraction had been outsourced to a vendor, upon agreement with the co-researcher.
- Student C was not a doctoral student, so it was relatively easy to convince them to stop writing up the manuscript (if the degree was at stake, Student C could have encountered (financial) problems with tuition fees due to repeating a year).

4. Possible research misconduct and questionable research practice

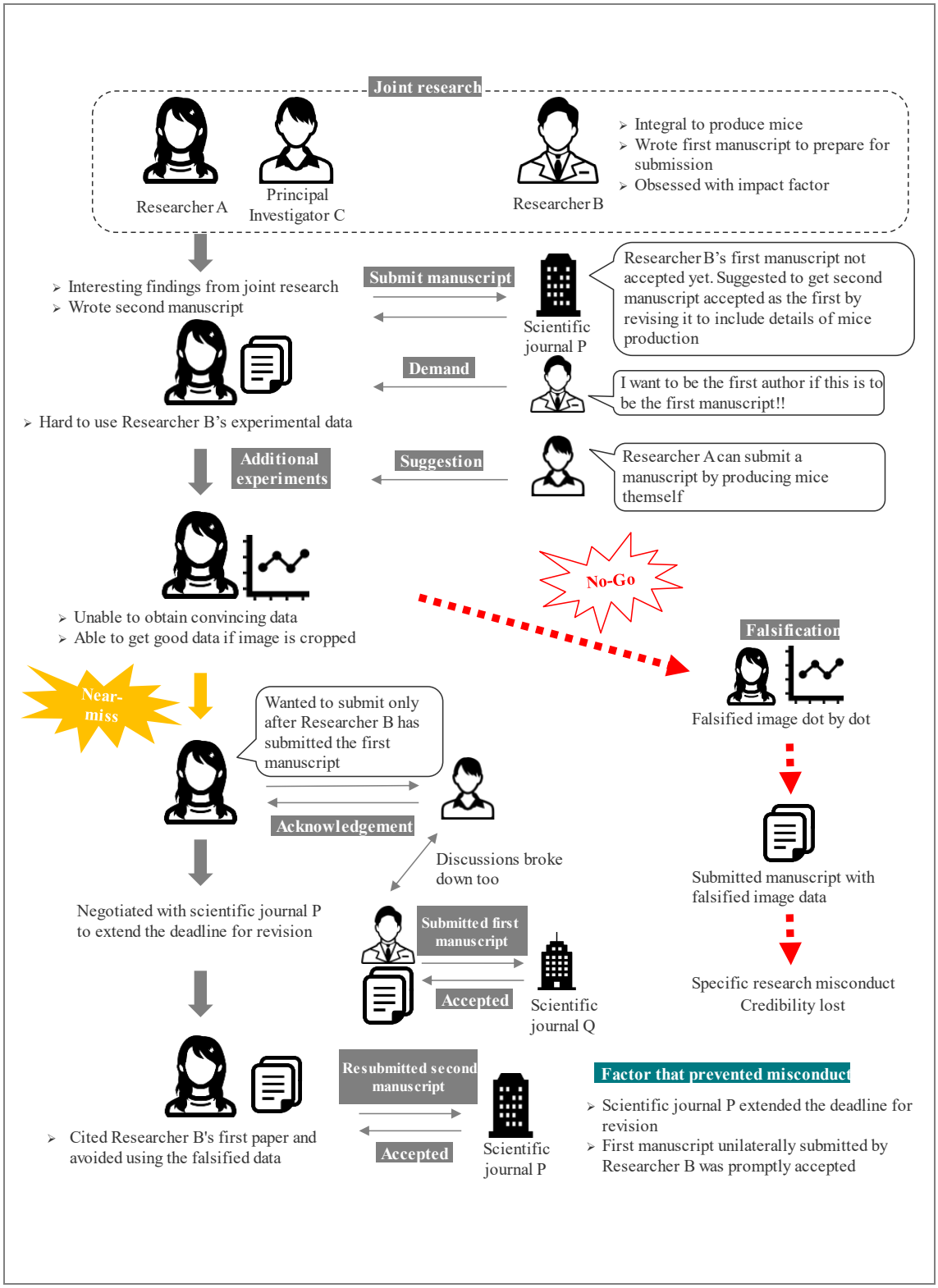
- If the manuscript had been published in its original form, they would have no grounds to deny if the reviewers pointed out the falsification of data.

5. Preventive countermeasures

- Ask the co-researcher to clarify the selection criteria in writing in advance when asking them to extract genes.
- Personally re-examine the data submitted by the co-researcher before using it in research.
- To obtain neutral data, information on matters where arbitrarily manipulation is a concern will be blinded among co-researchers or outsourced to an external vendor.

1-4. Attempted submission of falsified data to scientific journal

Affiliated institution	University, University hospital	Field	Life sciences



1. Case details

- For this international joint research, knockout mice were produced and laboratories in Japan and overseas were conducting analyses on these mice. Researcher B, who is integral to the production of these knockout mice, was working on the first manuscript, although it was repeatedly rejected due to their strong insistence on submitting it to high impact factor (IF) scientific journals.
- When Researcher A wrote the second manuscript and submitted it to scientific journal P, scientific journal P suggested that "since the first manuscript hasn't been accepted yet, Researcher A can revise their manuscript to include proof of knockout mice production so as to get it accepted as the first paper instead".
- In response, Researcher B strongly insisted to be the first author if Researcher A's manuscript was to be the first paper. As it was difficult for Researcher A to use the data from the mice experiments in the manuscript without Researcher B's permission, Principal Investigator C (Researcher A's research advisor) suggested Researcher A to conduct the same experiments to obtain data.
- Researcher A then proceeded to conduct the experiments but could not get convincing and beautiful data. While Researcher A was using imaging software to crop the unwanted parts of the images, it occurred to them that if they falsified the image dot by dot, they would be able to obtain satisfactory data. In fact, when Researcher A reduced the size of the data in the manuscript for submission, the figure was completed such that no one would be able to notice the falsification.
- However, Researcher A told Principal Investigator C that even though the manuscript was ready for submission, they would refrain from submitting it until Researcher B's first manuscript was accepted, and asked scientific journal P to extend the deadline for their revision. ☜ **Factor that prevented misconduct**
- But discussions between the Principal Investigators of the joint research broke down in the meanwhile, and Researcher B submitted the first manuscript to scientific journal Q without the consent of other co-researchers, which was immediately accepted.
- Despite the fact that the Principal Investigators of the teams other than with Researcher B were very upset, they did not ask for the published paper to be retracted. Researcher A was thus able to avoid submitting a manuscript with falsified image data by citing the Researcher B's paper accepted in scientific journal Q.

2. Backdrop & factors of near-miss incident

- As the international joint research could have crumbled upon Researcher B's strong insistence, Researcher A was under a lot of stress and mistakenly thought that there were not many options available to them.
- Although Researcher A should have found enough time to thoroughly discuss it with Principal Investigator C, both of them were aware that they were unhappy about with this project, and that opportunity was not opened to Researcher A.
- Researcher A was horrified when they realized they could produce rather beautiful images by using imaging software. But since it was already clear from numerous experiments that the results from the knockout mice were solid, Researcher A also felt that mild manipulation of the experimental results would not undermine the veracity of the research.
- Although it is not known if the editorial department of scientific journal P had any complaints about the pre-falsified image data when the manuscript was submitted, Researcher A was concerned about the low quality of the data.

3. Factors that prevented misconduct & its backdrop

- Researcher A put in a request with scientific journal P to extend the deadline for their revision.
- The first manuscript unilaterally submitted by Researcher B was promptly accepted by the journal.

4. Possible research misconduct and questionable research practice

- If Researcher A's manuscript with falsified image data was accepted by the journal, it would be considered as specific research misconduct.

5. Preventive countermeasures

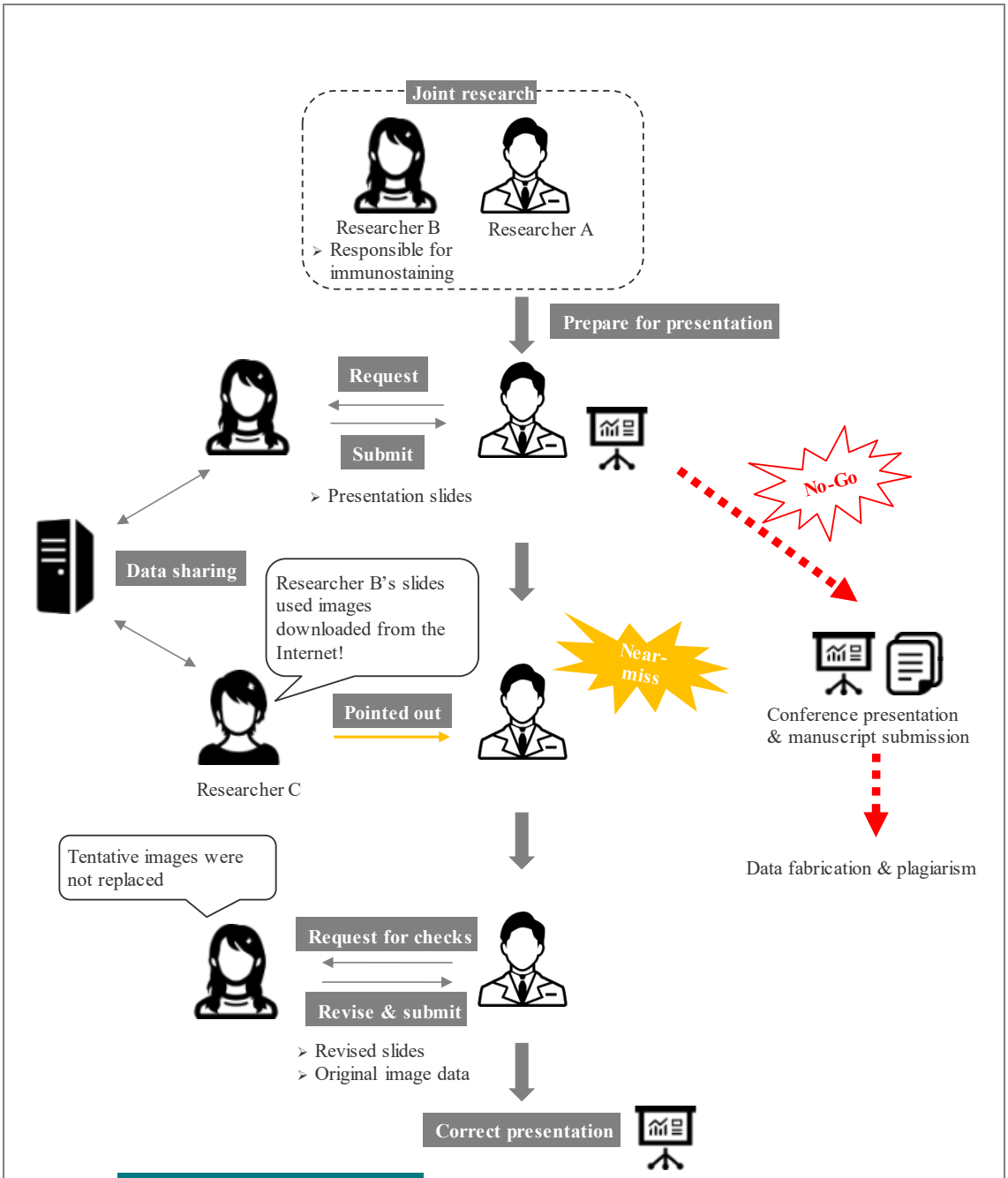
- Avoid falling into such pitfalls by understanding and keeping in mind many specific cases of misconduct.
- Although Researcher A and Principal Investigator C were on good terms, Researcher A was unable to fully consult with Principal Investigator C partly because the project was not going well. In ongoing research, it is critical to communicate well with collaborators and not try to solve problems on your own.

(Commentary)

Even if everyone in the joint research team agreed on having Researcher A to submit the first manuscript to scientific journal P, if Researcher B objected to the submission, Researcher A would have no choice but to submit data on mice that they produced themselves. If so, would Researcher A have been able to report to Principal Investigator C that they had doctored the image data? Or would Researcher A have been able to redo the experiments instead?

1-5. Forgetting to replace images in the manuscript for publishing

Affiliated institution	University, University hospital	Field	Life sciences



1. Case details

- Researcher A was conducting joint research with Researcher B and was preparing for a conference presentation.
- Researcher B was responsible for the detection of antigens from histopathological specimens using immunostaining methods. Researcher A asked Researcher B to submit presentation slides on the immunostained microscopic images and detection results.
- After Researcher B has submitted the presentation slides, Researcher A heard from Researcher C, a coworker of Researcher B, that "Researcher B used microscopic images from the Internet for the slides". Researcher C was able to notice that after seeing Researcher B's presentation slides since Researcher B was sharing data on cloud services with several researchers, including Researcher C. ☜ **Factor that prevented misconduct**
- When Researcher A checked with Researcher B, Researcher B explained that when they were preparing the presentation slides, they first searched online for microscopic images that matched their hypothesis in a bid to present the research objectives and hypothesis in an easy-to-understand manner, and decided to use these images in the slides first until the immunostaining results were out. Once the immunostaining results were out, Researcher B promptly replaced these temporary images with the actual microscopic images, but left some in the slides by mistake.
- Researcher A then asked Researcher B to resubmit presentation slides with the correctly replaced microscopic images and original image data. Subsequent presentations were not affected.

2. Backdrop & factors of near-miss incident

- To present the research objectives and hypothesis in an easy-to-understand manner, Researcher B started by searching online for microscopic images that matched their hypothesis and used them tentatively in the slides. Researcher B intended to replace the online images with actual microscopic ones but left some online images in the slides by mistake.

3. Factors that prevented misconduct & its backdrop

- As Researcher B shared data with Researcher C and other researchers in the cloud, Researcher C was able to notice the erroneous images of Researcher B.

4. Possible research misconduct and questionable research practice

- If no one had noticed the erroneous images and they were used for conference presentation or manuscript for submission to journals, the authors would be alleged of fabrication and plagiarism of data.
- If the original image data were not kept, the authors would also not be able to deny such allegations.

5. Preventive countermeasures

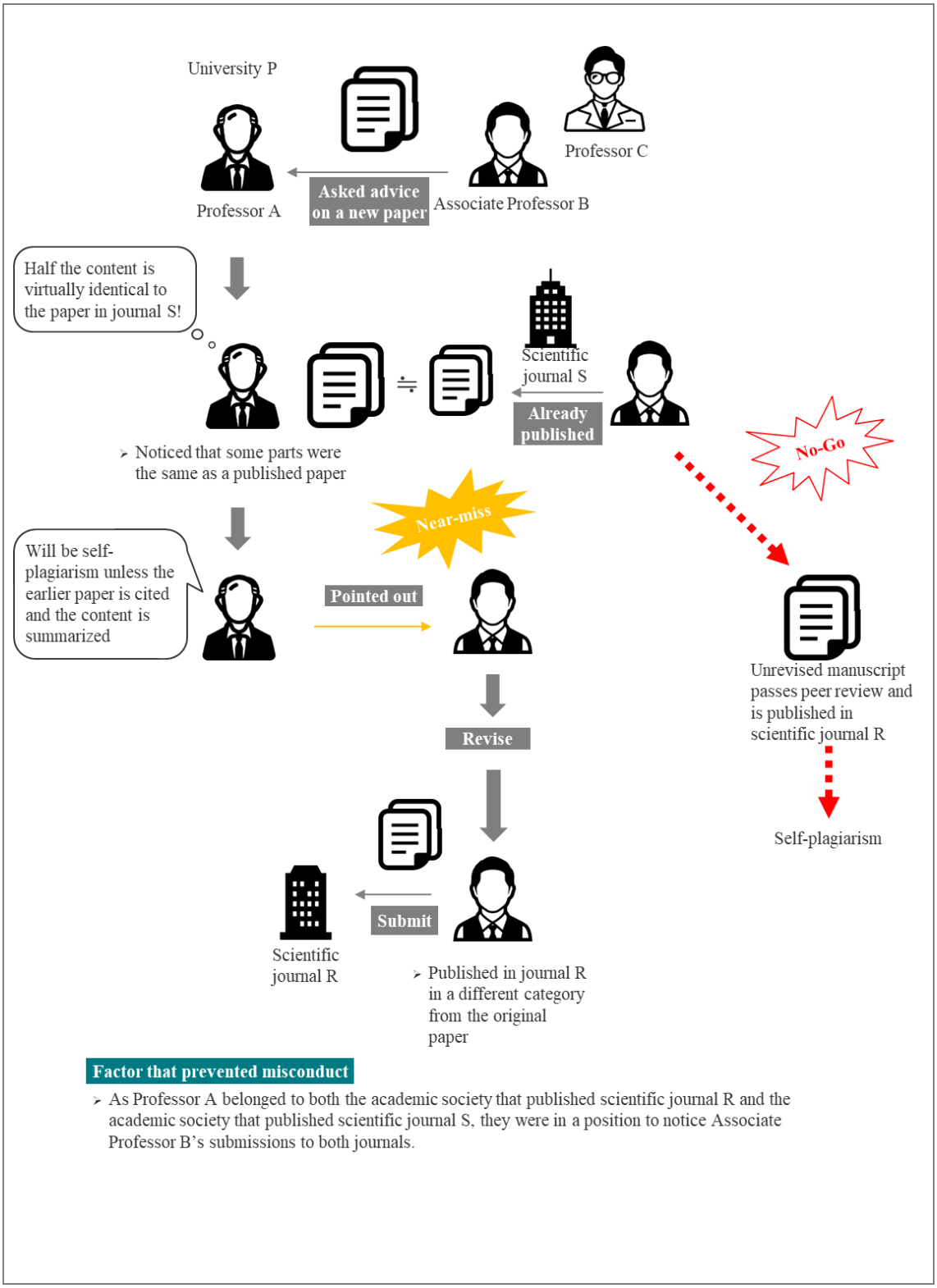
- Materials compiled by co-researchers should be provided along with the original data for checking of discrepancies.
- When using tentative images of expected results, the figures should be diagrams (e.g., hand-drawn) that cannot be mistaken for the actual image, or clearly indicated accordingly.

(Commentary)

While it is common practice to tentatively state the expected results in the conceptual stage of preparing the manuscript and figures, this case has clearly shown us that one small mistake can perilously lead to the termination of a researcher's career and the loss of the laboratory's credibility. The more realistic-looking the result is, the more likely it will be overlooked if you neglect to go over it. It is best to clearly indicate such tentatively placed results. When a tentative image is used, the more similar the image is to the original data, the more likely it is to be misidentified as an actual image if a check is insufficient. If a tentative image is required, it should be clearly indicated that it is a tentatively placed image.

1-6. Prevented self-plagiarism in submission of a paper to multiple scientific journals

Affiliated institution	University, University hospital	Field	Medicine, humanities and social sciences



Factor that prevented misconduct

- As Professor A belonged to both the academic society that published scientific journal R and the academic society that published scientific journal S, they were in a position to notice Associate Professor B's submissions to both journals.

1. Case details

- Professor A at University P is a humanities and social sciences researcher whose research focuses on healthcare.
- One day, Professor A was asked by Associate Professor B for their opinion on the final draft of a manuscript that Associate Professor B planned to submit. Associate Professor B belongs to the laboratory of Professor C, who routinely exchanges opinions with Professor A.
- Professor A was aware to some extent of the content of Associate Professor B's research via discussions with Professor C.
- The manuscript was due to be submitted to scientific journal R with Associate Professor B as the corresponding author.
- When Professor A checked the content of the manuscript, they noticed that half of the content was virtually identical to a paper Associate Professor B had recently published in the scientific journal S, which is the journal of an academic society in an adjacent field. The paper published in scientific journal S was not cited or referenced in the manuscript due to be submitted.
- Professor A told Associate Professor B that the paper could be considered self-plagiarism. Professor A recommended that Associate Professor B should clearly show the citation of the earlier paper published in scientific journal S if it was necessary, keep quotations to the minimum necessary, and summarize the quoted content. ☚ **Factor that prevented misconduct**
- As a result, Associate Professor B made substantial changes to the manuscript and their paper was, following peer review, ultimately published in scientific journal R, in a different category from the original paper.

2. Backdrop & factors of near-miss incident

- Associate Professor B lacked adequate awareness and understanding of the appropriate method of referencing their own research achievements.
- In interdisciplinary research and research involving multiple different fields, such as the natural sciences and humanities and social sciences, researchers may face differences in customs and diverse ways of thinking in regard to writing and presenting papers.
- In particular, as there are few open access papers in Japanese humanities and social sciences journals, opportunities to learn about the content of the paper in scientific journal S and the content of the other articles published by Associate Professor B in the past were limited. Accordingly, it was also difficult for the paper's co-authors to spot the self-plagiarism when checking the manuscript before submission.

3. Factors that prevented misconduct & its backdrop

- As Professor A belonged to both the academic society that published scientific journal R and the academic society that published scientific journal S, they were in a position to notice Associate Professor B's submissions to both journals.

4. Possible research misconduct and questionable research practice

- As Associate Professor B used their own earlier paper in their manuscript without citing it appropriately, they would have committed self-plagiarism if their manuscript had been published in scientific journal R in its original state.

5. Preventive countermeasures

- Universities and research institutions should provide thorough training on research ethics with specific examples, to identify differences between the natural sciences, the humanities and social sciences, and interdisciplinary fields in terms of rules on the submission of manuscripts and the like. In addition, encourage the formulation of clear rules, while respecting the traditions and approaches in each field, rather than requiring other research fields to comply with standard practice in a specific research field.
- If the university or research institution can provide a plagiarism checking tool, the development of a system enabling researchers themselves to check their own papers before submission could be an option.
- Another possibility is to put in place a system for checking manuscripts for plagiarism in advance, such as by having the editorial committees of scientific journals use plagiarism checking tools.
- A highly effective means of addressing this issue is for the editorial committees of scientific journals to establish peer review guidelines and to compile a list of points to which attention should be paid in the peer review process, as well as to provide specific standards in the submission rules that detail the criteria for determining duplicate publication and self-plagiarism, based on the attributes of the individual field.
- Encouraging efforts to make papers open access can be an effective deterrent against plagiarism.

(Commentary)

Reviewers have a duty to maintain confidentiality. What action would it be desirable for a reviewer to take if they received two separate peer review requests from two different journals and noticed that the content of both manuscripts was largely the same?

Editor's column 1: Fraud triangle

Accounting fraud such as embezzlement is said to occur when the perpetrator is motivated, able to perceive that opportunity as well as rationalize one's behavior[1]. In research misconduct as well[2], there are motivation factors (such as a required number of publications, approaching deadlines) and opportunities for misconduct (such as violator's sole access to primary data, lack of monitoring). Violators may commit research misconduct by coming up with excuses to justify their actions, such as "the conclusion is not going to change", or "there is large enough margin of safety". Eliminating any one of motivation, opportunity, and rationalization can prevent research misconduct. However, our social systems are such that motivation cannot be eliminated in many cases. While sharing of primary data is desirable whenever possible, there are limitations as well. While it may seem difficult to stop oneself from rationalizing, in reality, it is entirely possible to do so if you ever find yourself unable to justify (see columns on "Boiling frog syndrome" and "The process of developing ethical awareness").

Factor	Accounting fraud	Research misconduct
Motivation	• Financial difficulties	• Required number of publications • Approaching deadlines
Perceived opportunity	• Entrusted with accounts	• Sole access to primary data
Rationalization	• Yet the President is living it up...	• Conclusion is not going to change • Large enough margin of safety

1 Donald R. Cressey, "Other People's Money: A study in the social psychology of embezzlement", Wadsworth Publishing Company, 1971.

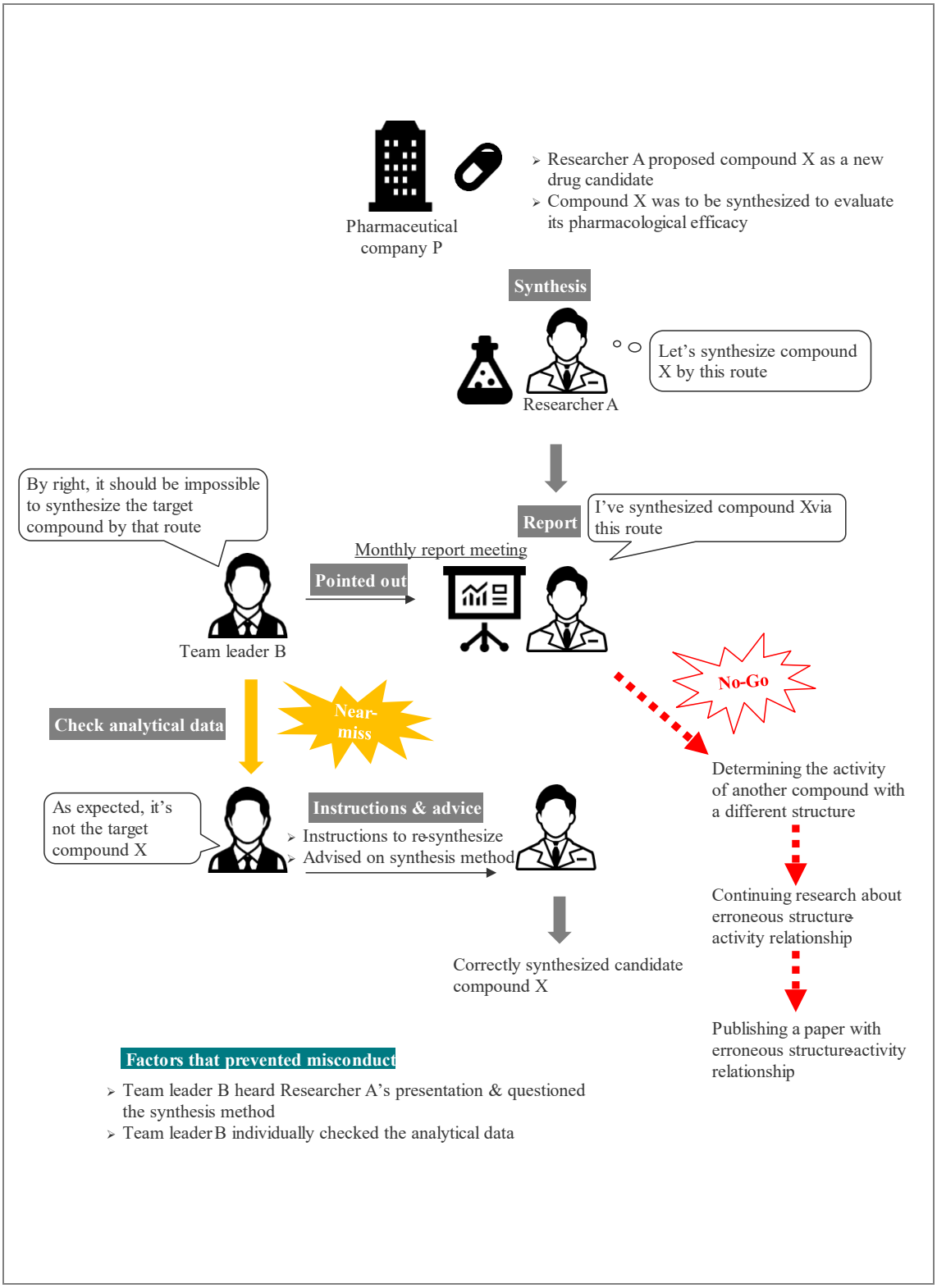
2 Takahisa Kawai, Kensuke Inai, Rei Nouchi, "Proposal of Ethic Education System to Inhibit Scientist's Misconduct in Research", pp.1-7, vol.31, no.5(2017-1), JSiSE Research Report, 2017
https://www.jsise.org/society/committee/2016/5th/TR-031-05-A-001.pdf

2 Collection, management, and processing of data

1. Errors in the structural formula of synthetic compound
2. Discovery of errors in the first draft's figure during manuscript revision
3. Prevented the publication of a manuscript with the wrong image
4. Prevented copyright infringement from inappropriate use of well-known survey
5. Deficiency in the procedure for obtaining consent due to an error in the construction of a system for an online survey*
6. Request for deletion of research data registered before conclusion of a joint research agreement*
7. Avoidance of out-of-scope patients' medical records being viewed by an external EDC data entry operator*
8. Concern about the provision of data to a third party by company managing research data*

2-1. Errors in the structural formula of synthetic compound

Affiliated institution	Corporate	Field	Medicinal chemistry (synthesis)



1. Case details

- Researcher A was conducting experimental synthesis of new drug candidate compounds in the laboratory of pharmaceutical company P. Researcher A designed the candidate compound X and proceeded to synthesize it in their own synthetic route.
- In a monthly report meeting where all researchers in the group to which Researcher A belongs had to make presentations about the things they have done for that month, Researcher A reported that they had synthesized candidate compound X via such a route. Using common sense in organic synthetic chemistry, Team leader B thought that it was not possible to synthesize the target compound using that route and pointed it out.
- After the monthly report meeting ended, Team leader B looked up the analytical data and checked the structure, and found out that it was indeed not the target compound as claimed by Researcher A. ☜ **Factor that prevented misconduct**
- This blunder happened by reasons that Researcher A did not carefully examine the analytical results; they merely conducted a superficial analysis and assumed that they had successfully synthesized the compound. Fortunately, they had not yet submitted compound X to the pharmacology group, so no one was asked to determine the biological activity of a compound that did not have the intended structure.

2. Backdrop & factors of near-miss incident

- Researcher A's lack of knowledge in synthetic organic chemistry and mistakes in checking the analytical data.
- Although Researcher A's team often discussed the design of the compound, they proceeded with the synthesis on the assumption that it could be done by known methods, and rarely discussed about how to go about synthesizing it. Team leader B, who knew that Researcher A had about 10 years of experience in organic synthesis research, did not expect Researcher A to attempt to synthesize candidate compound X by an impossible route.

3. Factors that prevented misconduct & its backdrop

- Team leader B noticed the problem at the monthly report meeting and personally checked the analytical data.

4. Possible research misconduct and questionable research practice

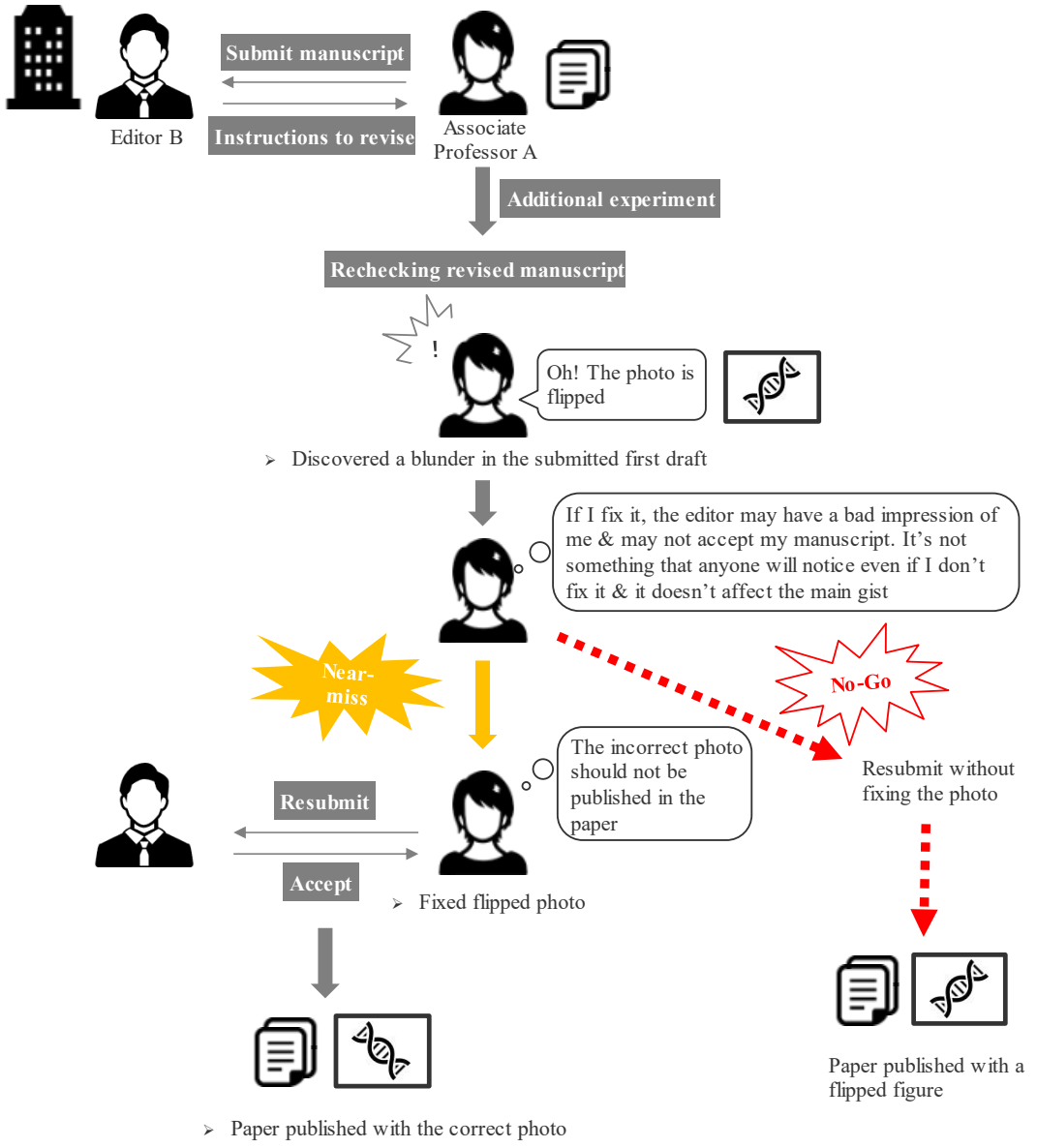
- Publication of a paper with erroneous structure-activity relationship.
- Researchers may start to study the relationship between biological activity and structure (structure-activity relationship) of a compound that does not have the intended structure. If promising results are obtained, much time and effort would have been wasted focusing on experimental synthesis in the wrong direction.

5. Preventive countermeasures

- Share all cases of compound synthesis, including failed ones, with researchers at regular meetings and other opportunities.
- Do not hesitate to check the raw data when in doubt about the reported details.

2-2. Discovery of errors in the first draft's figure during manuscript revision

Affiliated institution	University, University hospital	Field	Life sciences



Factors that prevented misconduct

- During revision, Associate Professor A went through the entire manuscript instead of just the parts pointed out by Editor B
- Associate Professor A insisted on submitting an accurate manuscript

1. Case details

- Associate Professor A conducted an additional experiment upon Editor B's request to revise the submitted manuscript.
- When Associate Professor A went through the manuscript again in a bid to resubmit the revised version, they noticed that there was a figure with a flipped photo in another part that they were supposed to revise under Editor B's instructions.
- While Associate Professor A did not think that a flipped photo would affect the gist of the manuscript, they thought that correcting the photo error in the resubmitted manuscript might negatively impact the acceptance of the manuscript. Associate Professor A therefore hesitated to report the error.
- Although no one would have noticed anything even if the photo was not corrected, Associate Professor A did not think that it was a good idea to use an incorrect photo in the manuscript. ☜ **Factor that prevented misconduct**
- Associate Professor A informed Editor B that the photo was flipped and submitted a revised manuscript. The resubmitted manuscript was accepted and no issues were taken with the flipped image.

2. Backdrop & factors of near-miss incident

- When Associate Professor A submitted the first draft, they were more focused on polishing up the text.
- While it is possible that Associate Professor A did not go through the first draft carefully during submission since the flipped photo would not affect the interpretation of the data, they lacked confirmation of all the figures prior to submission.

3. Factors that prevented misconduct & its backdrop

- During the revision of the manuscript, Associate Professor A went through all the data again, including the parts that were not pointed out by the editor.
- Associate Professor A insisted on submitting an accurate manuscript.

4. Possible research misconduct and questionable research practice.

- Since the uncorrected image did not affect the gist of the manuscript – which was a trivial detail that no one might have noticed anyway – the incorrect photo could have ended up being used in the finalized draft

5. Preventive countermeasures

- Before submitting a manuscript to a publisher of journals or periodicals, be sure to check for unexpected mistakes in figures and photographs.

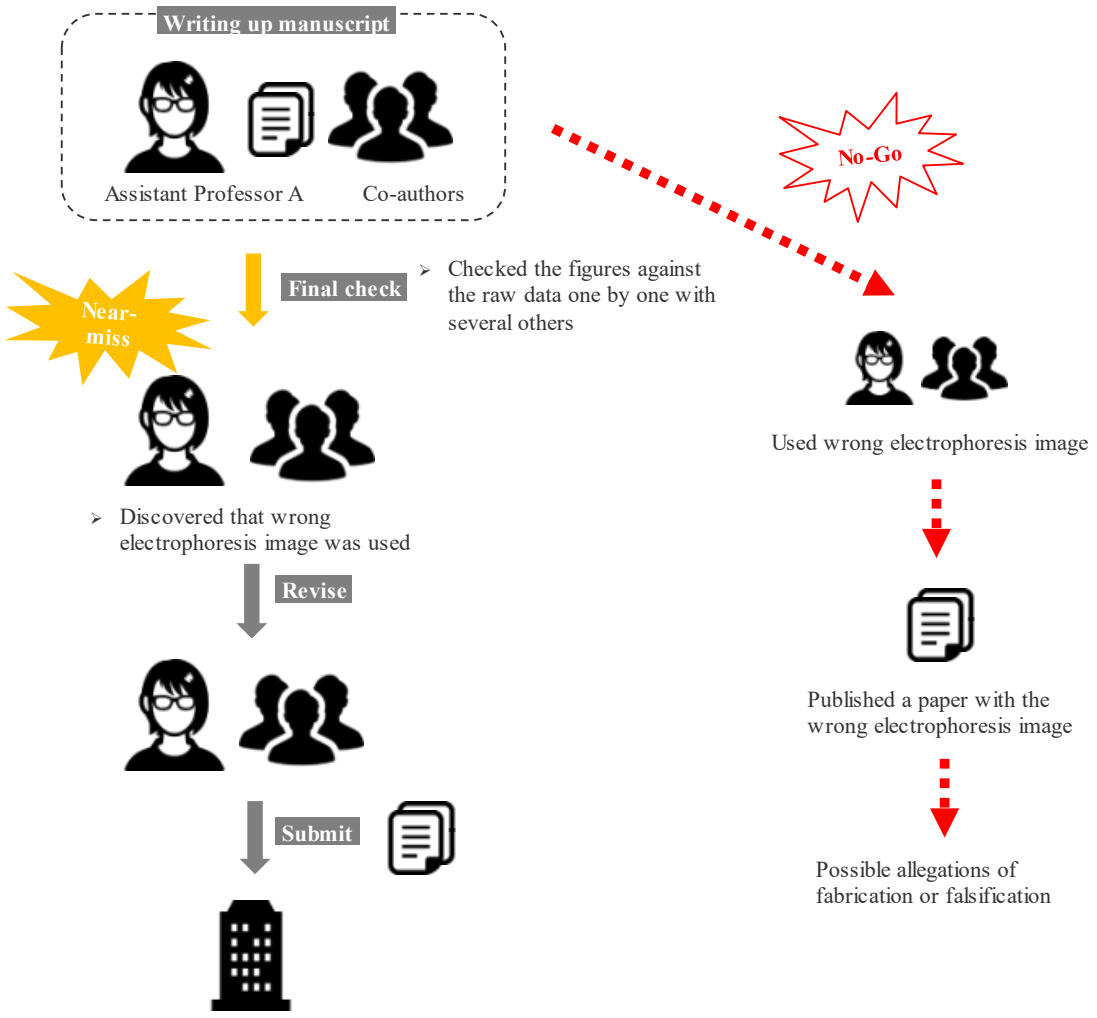
(Commentary)

To the researcher who submitted a manuscript, responding to the outcomes of the peer review by editors and referees after the submission is an important process that will determine its acceptance for publication. Particularly in the case of revision, under a situation where the manuscript will be accepted for publication as long as the author properly answers the referee's comments, the author is inclined to avoid making a bad impression on the editors or referees as much as possible.

Above all, researchers are required to properly handle the data, as well as to present data that can be properly substantiated in an appropriate manner in the manuscript. If you are alerted to any errors – even if it does not affect the substance of the argument – it is best to be upfront with the publisher of the journals or periodicals. Although everyone is liable to make mistakes, as a researcher, please be reminded of the importance of reviewing all the data in your manuscript in detail before submission.

2-3. Prevented the publication of a manuscript with the wrong image

Affiliated institution	University, University hospital	Field	Life sciences



Factors that prevented misconduct

- Assistant Professor A carefully checked the data against the raw data with several others and confirmed that the wrong image was used

1. Case details

- Assistant Professor A was about to submit a manuscript with several co-authors. As a final check before submission, Assistant Professor A checked the figures against the raw data one by one with the co-authors. ☜ **Factor that prevented misconduct**
- Assistant Professor A then discovered that they had mixed up the photos of the (gel) electrophoresis image in one of the figures; they replaced it with the correct photo and submitted the manuscript.

2. Backdrop & factors of near-miss incident

- Photos of electrophoresis gels all look the same at first glance, and it is often difficult to distinguish different samples.
- Since cropped photos are usually combined to create figures, operational errors in file management or workflow may cause the photos to get mixed up.

3. Factors that prevented misconduct & its backdrop

- As Assistant Professor A carefully checked the data in each figure against the original data one by one with several others, they were able to notice that the wrong photo was used.

4. Possible research misconduct and questionable research practice.

- Publication of a paper with incorrect photos may lead to allegations of fabrication or falsification of data.

5. Preventive countermeasures

- Careless mistakes can be prevented by checking figures against raw data with several people before submitting the manuscript.

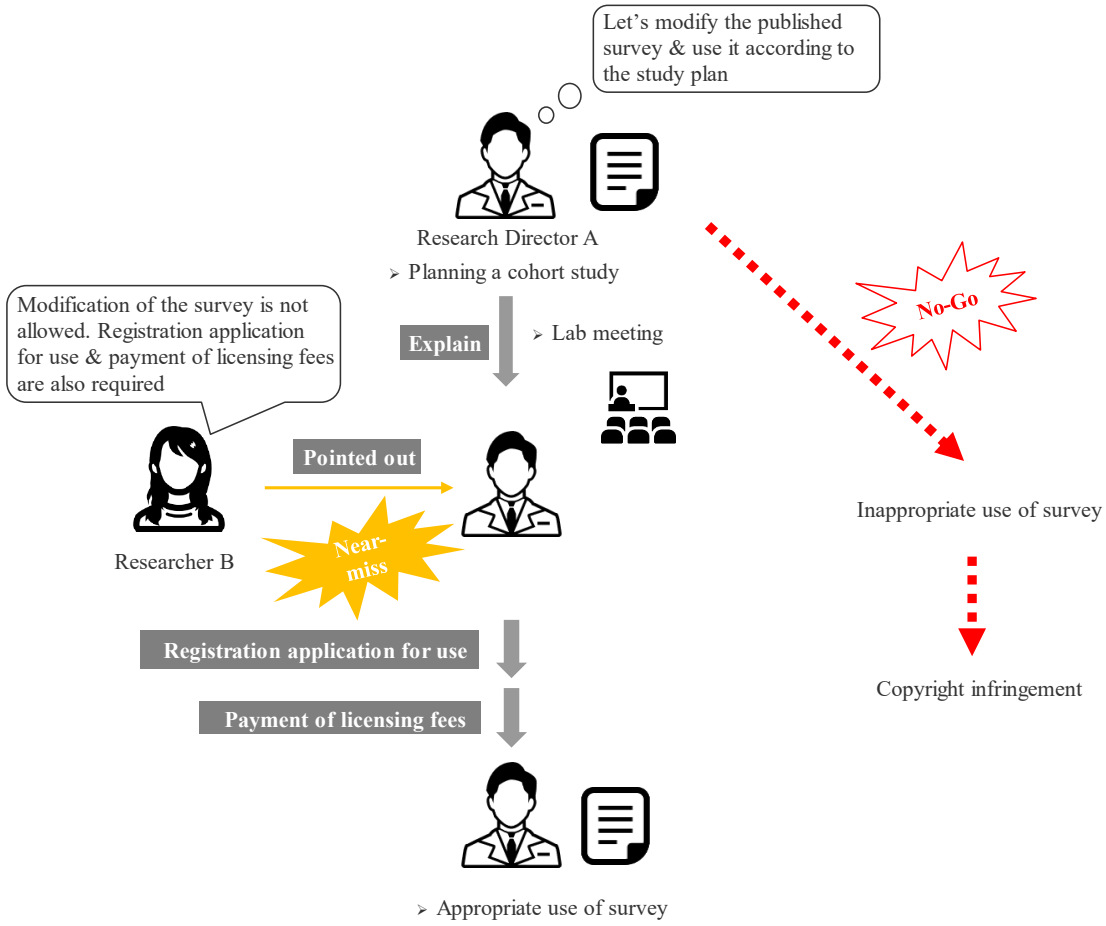
(Commentary)

How electrophoresis images of nucleic acids and proteins are presented in papers is changing as the amount of data to be published in papers increases. After the 2000s especially, many created figures where a large number of electrophoresis images with cut-out bands of interest are lined up. If the bands of an electrophoresis image are cut out from the original photograph of the entire gel, it is difficult to distinguish what the data is from the cut-out itself. Inadequate data management coupled with the performing of many experiments may therefore cause the researcher to mix up the cut-out bands. Researchers need to be reminded of the importance of data storage method and experimental environment put in place so as to allow for the appropriate verification of data.

In addition, a student without sufficient knowledge may accidentally arrange or line up cut-out bands together where they should be presented separately, or they may paste the images of different bands or flip images due to mistakes made when creating figures. Researchers should be well aware that even if a photo is mistakenly used due to a careless mistake, they may be alleged of fabrication or falsification by a third party if pointed out. It is therefore advisable to check all data against the original data, compare them with the lab notebooks or pre-processed photos, before submitting the manuscript.

2-4. Prevented copyright infringement from inappropriate use of well-known survey

Affiliated institution	National/local government agency	Field	Clinical medicine



Factors that prevented misconduct

- When Research Director A explained their study plan at a lab meeting, Researcher B pointed out the terms and conditions for using the survey

1. Case details

- Research Director A was considering using a survey called SF-36® (MOS 36-Item Short-Form Health Survey)[1] to conduct a cohort study[2]. They thought of modifying some of the question items to fit the context of the cohort study they were planning to conduct.
- When Research Director A explained their intention to use this survey at a lab meeting, Researcher B pointed out that modification of the survey was not allowed and that prior registration and payment of licensing fees were required to use it. ☜ **Factor that prevented misconduct**
- Research Director A completed the necessary paperwork, such as registration application for use and payment of licensing fees, and used the survey form appropriately without altering its contents to conduct the cohort study.

2. Backdrop & factors of near-miss incident

- Research Director A had only read the papers on the survey and considered using it, but was unaware that the company controlled the copyrights and so on to the survey.
- As Research Director A did not check the terms and conditions for using the survey, they were not aware that modification of the survey was not allowed and that prior registration and payment of licensing fees were required to use it.

3. Factors that prevented misconduct & its backdrop

- When Research Director A explained their intention to use this survey at a meeting of the laboratory to which they belonged to, Researcher B pointed out the terms and conditions for using the survey.

4. Possible research misconduct and questionable research practice.

- Copyright infringement from inappropriate use of the survey.

5. Preventive countermeasures

- When using a third-party program or software, be sure to check the legal rights such as copyrights by carefully reading the terms and conditions regarding its use.
- Provide opportunities like meetings for researchers to exchange opinions about their study plans so that they can point out issues to each other.

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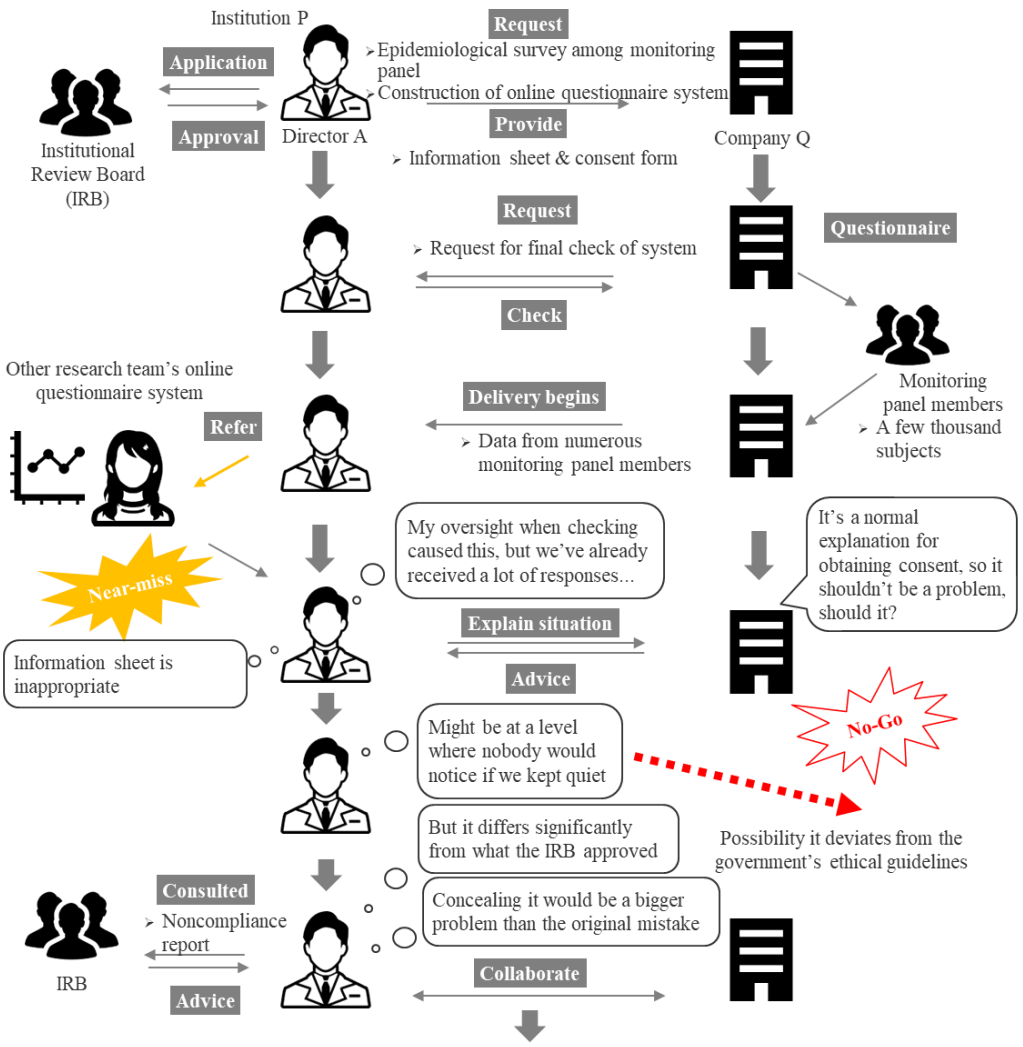
1 https://www.rand.org/health-care/surveys_tools/mos/36-item-short-form.html#:~:text=As%20part%20of%20the%20Medical%20Outcomes%20Study%20%28MOS%29%2C,upon%20patient%20self-reporting%20and%20have%20been%20widely%20used.

2 A cohort study is a type of longitudinal study that follows and observes a large number of research participants who do not have the outcome of interest to begin with, from the present time (or some timepoint in the past) over a long period of time to determine whether the presence or absence of certain factors is associated with the development or prevention of disease.

2-5. Deficiency in the procedure for obtaining consent due to an error in the construction of a system for an online survey

Affiliated institution	National/local government agency	Field	Social epidemiology, public health



Director A and Company Q obtained subjects' consent again and redid the survey

Factor that prevented misconduct

- Director A was in a position in which they could readily communicate with the IRB secretariat on a day-to-day basis, so they were able to be frank in seeking the IRB's advice about the situation
- Moreover, as Director A is a departmental director and also a member of an IRB subcommittee (member of the first-stage review board in the two-stage review process), they thought their position demanded that they take the correct course of action
- Director A had seen media reports of press conferences by companies and Diet members involved in scandals and misconduct, and had felt skeptical about those who sought to conceal their mistakes and make excuses for them, rather than admitting them. As such, Director A did not want to do the same thing

1. Case details

- Director A at Institution P requested that Company Q, which undertakes online surveys, conduct an epidemiological survey using an online questionnaire among several thousand members of Company Q's monitoring panel who met the criteria.
- Director A also provided Company Q with the information sheet, consent form, and other documents approved by the Institutional Review Board (IRB) and asked them to build an online questionnaire system.
- Immediately after the data gathered from numerous subjects had been delivered, Director A looked at the screen for a similar online questionnaire system built by a different research team and realized that the information sheet for Director A's project might not have been worded properly. ☚ **Factor that prevented misconduct**
- Director A checked again and determined that, when Company Q had asked Director A to carry out a final check of the system, Director A had failed to notice that the content of the information sheet page was not appropriate. Although this did not disadvantage participants, it meant that consent from subjects had been obtained based only on the presentation of an inadequate information sheet.
- At this point, as numerous responses had already been obtained, it had not been possible to point out the oversight at the time of the final check, and none of the respondents had made any comments or asked any questions by that stage, it crossed Director A's mind that nobody would notice if they said nothing about the issue. In addition, Company Q took the view that the information sheet in question was a normal explanation for obtaining consent, so there were no problems from their perspective as a business operator.
- However, Director A considered the situation again from the perspective of a conscientious researcher, taking into account such matters as the fact that consent had been obtained using an information sheet whose content differed considerably from that approved by the IRB, and that concealing the mistake would be a bigger problem than the original error. Accordingly, Director A contacted the IRB to report the noncompliance with the Ethical Guidelines for Medical and Biological Research Involving Human Subjects[1] and to seek its advice.
- Ultimately, Director A and Company Q conducted the survey once more after obtaining consent afresh from all subjects based on the appropriate information sheet, in order to carry out the study properly.

2. Backdrop & factors of near-miss incident

- Director A did not conduct adequate checks on the system that had been built, due in part to their heavy workload.
- Due in part to the fact that Company Q's procedure and explanation did not differ much from the way in which most other survey companies work, the likelihood of questions or complaints from subjects was envisaged to be low. Consequently, Director A thought that nobody would notice if they kept quiet.

3. Factors that prevented misconduct & its backdrop

- Director A was in a position in which they could readily communicate with the IRB secretariat on a day-to-day basis, so they were able to be frank in seeking the IRB's advice about the situation.
- Moreover, as Director A is a departmental director and also a member of an IRB subcommittee (member of the first-stage review board in the two-stage review process), they thought their position demanded that they take the correct course of action.
- Director A had seen media reports of press conferences by companies and Diet members involved in scandals and misconduct, and had felt skeptical about those who sought to conceal their mistakes and make excuses for them, rather than admitting them. As such, Director A did not want to do the same thing.

4. Possible research misconduct and questionable research practice

- There was a possibility that this might fall under "Deficiency in procedures for obtaining informed consent," which is explained in Chapter 6, No. 11, Section 1. (3) 2. of the Guidance on Ethical Guidelines for Medical and Biological Research Involving Human Subjects[2] as something that undermines the ethical validity of research.

5. Preventive countermeasures

- In the case of situations involving documents sent to subjects and other matters relating to obtaining consent and fundamentals of research integrity, consult a superior colleague, rather than trying to solve the problem singlehandedly.
- When adopting a comparatively new method, such as an online survey, check the points regarding which care should be taken beforehand and then share information within your department regarding such matters as the specific approach to conducting the survey.

(Commentary)

In this case, the researcher, who was in a position of responsibility, noticed the issue themself and succeeded in addressing it. Imagine how you would respond to a similar problem if this had been a mistake in checking by someone you manage or your superior, thinking about how you could address it and at what stage.

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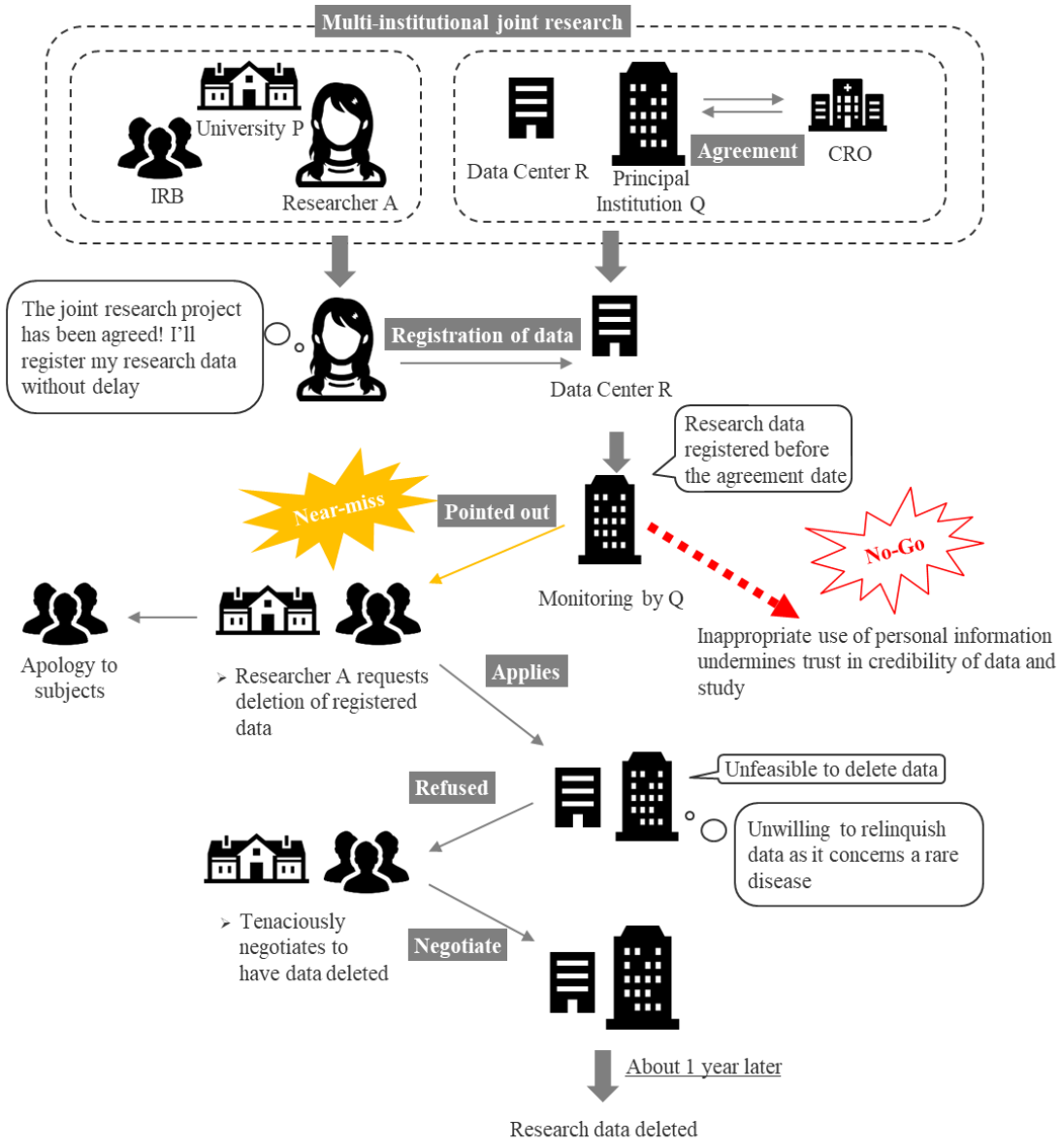
1 https://www.mhlw.go.jp/content/000909926.pdf
2 https://www.mhlw.go.jp/content/000946358.pdf

2-6. Request for deletion of research data registered before conclusion of a joint research agreement

Affiliated institution	University, University hospital	Field	Life sciences



Factor that prevented misconduct

- After the discovery that the research data had been registered before the date of the agreement, University P swiftly applied for the deletion of the data and also explained the situation to the research subjects and apologized to them
- Principal Institution Q initially made no effort to delete the research data from Data Center R, but University P tenaciously negotiated with Principal Institution Q via the CRO

1. Case details

- At Data Center R, which is designated by Principal Institution Q, Researcher A from University P recorded research data from a multi-institutional joint research project in which University P was participating.
- When Q, as principal institution, carried out monitoring, it discovered that the date on which Researcher A registered the research data was before the date of the multi-institutional joint research agreement in question. Accordingly, Principal Institution Q pointed out Researcher A's error in handling the data to the Institutional Review Board (IRB) at University P. ☜ **Factor that prevented misconduct**
- University P submitted a formal written request to Principal Institution Q for the deletion of the data registered by Researcher A, and then explained the situation to the research subjects who had cooperated in the acquisition of the data, apologized to them, and informed them that the data in question would not be used in the study.
- However, Principal Institution Q subsequently informed University P that it was not feasible to delete the data. Following negotiations between the IRB secretariat at University P, Principal Institution Q, and the CRO[1] commissioned by Q, it took about a year for the data in question to be deleted from Data Center R.
- It is presumed that the reason why Principal Institution Q did not readily respond to the request to delete the data was that it offered invaluable data about a rare condition, so there may well have been a reluctance to delete it, even if it could not be used in research.

2. Backdrop & factors of near-miss incident

- There was a lack of awareness of the fact that the start date of the study, including the acquisition and use of research data, needed to be after the date on which the multi-institutional joint research agreement took effect.

3. Factors that prevented misconduct & its backdrop

- After the discovery that the research data had been registered before the date of the agreement, University P swiftly applied for the deletion of the data and also explained the situation to the research subjects and apologized to them.
- Principal Institution Q initially made no effort to delete the research data from Data Center R, but University P tenaciously negotiated with Principal Institution Q via the CRO.

4. Possible research misconduct and questionable research practice

- Deviating from laws and guidelines concerning the acquisition and use of personal information undermines the credibility of not only the research data, but also the research itself and the institutions conducting it.

5. Preventive countermeasures

- Ensure that ethics training for researchers covers the fact that, when conducting joint research with other institutions, the study – including data gathering – must not begin until a joint research agreement has been concluded, even if the IRB has granted approval.
- In concluding agreements on data management and distribution, researchers and administrative staff must check beforehand that there are no problems, giving full consideration to such matters as the data management system, access rights, and specific matters relating to data handling and circulation.
- Ensure that all institutions participating in multi-institutional joint research agree in advance on the timing of the conclusion of the joint research agreement and the start date of the study.

(Commentary)

Decisions on whether or not to use the data should be made not on the basis of whether or not subjects were actually harmed, but rather based on whether the prescribed procedure was complied with. Permitting exceptions to the principle of prior consent could lead to the undermining of trust in scientists.

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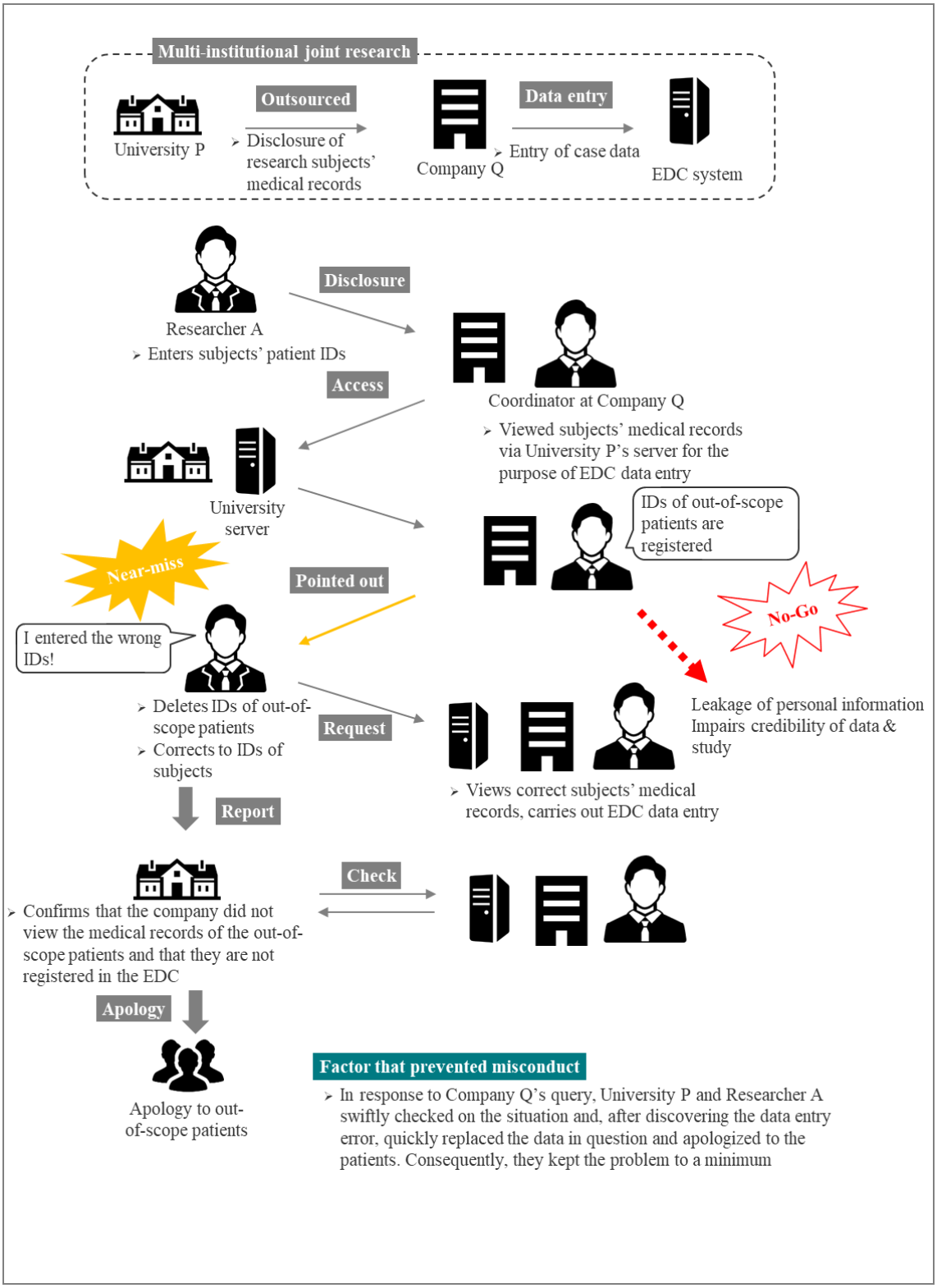
1 CRO: Contract research organization. CROs are contracted to carry out and support various tasks in clinical studies and postmarketing surveillance in order to increase the efficiency of pharmaceutical development and produce new drugs more quickly.
https://www.jcroa.or.jp/customers/service.html

2-7. Avoidance of out-of-scope patients' medical records being viewed by an external EDC data entry operator

Affiliated institution	University, University hospital	Field	Life sciences



1. Case details

- University P was participating in multi-institutional joint research and was using an EDC[1] system to manage the clinical trial data.
- The entry of case data from research subjects' medical records into the EDC had been outsourced to Company Q. To ensure that Company Q could view the research subjects' medical records alone, University P extracted the medical records that could be viewed by Company Q by linking the patient ID to the unique study ID in the system. The medical records had not been anonymized and contained personal information.
- Company Q commented that the IDs of patients who were not research subjects might be included in the list of patients whose records could be viewed. When University P checked, it discovered that Researcher A had mistakenly entered the IDs of patients who were not research subjects. This meant that University P had enabled the external organization Company Q to view the medical records of patients not involved in the study in question. **☚ Factor that prevented misconduct**
- University P swiftly entered the correct ID and took steps to ensure that Company Q could not view the medical record associated with the mistakenly entered patient ID. In addition, Researcher A apologized to the patient whose medical record had erroneously been made accessible.
- University P apologized to Company Q, which confirmed that it had checked only the ID of the patient who was not a research subject, and had neither viewed the content of the medical record containing personal information, nor entered the case data into the EDC.

2. Backdrop & factors of near-miss incident

- Researcher A mistakenly entered the ID of a patient who was not a research subject because they were pressed for time. Furthermore, University P was unable to spot the data entry error until Company Q pointed it out.

3. Factors that prevented misconduct & its backdrop

- In response to Company Q's query, University P and Researcher A swiftly checked on the situation and, after discovering the data entry error, quickly replaced the data in question and apologized to the patient. Consequently, they kept the problem to a minimum.

4. Possible research misconduct and questionable research practice

- If a violation of relevant laws and guidelines in the form of the leakage of personal information is suspected, it could undermine the credibility of the research and cause a loss of trust in the institution implementing the study.

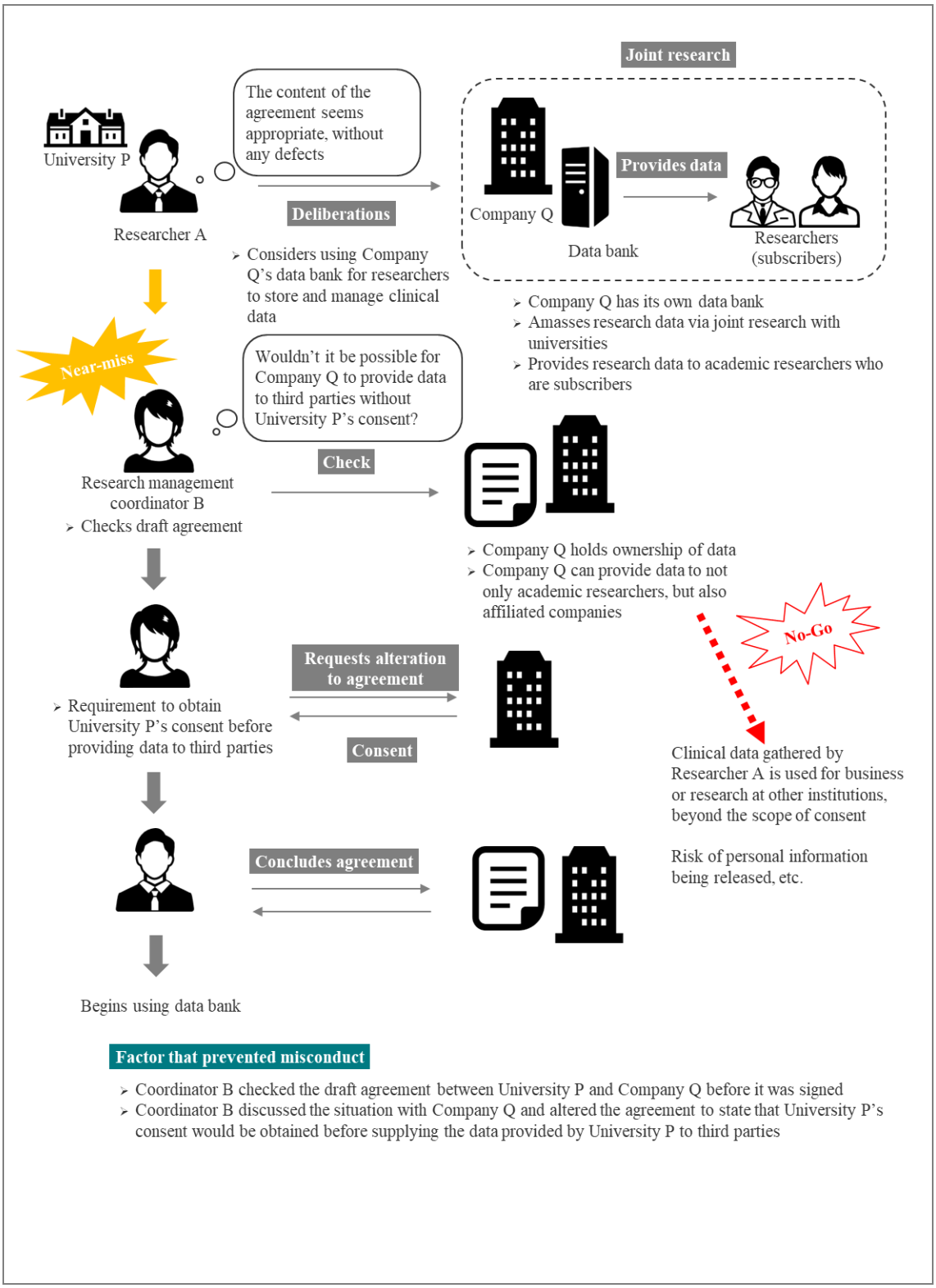
5. Preventive countermeasures

- Gain a renewed understanding of the serious implications of making information from the medical records of third parties who are not research subjects accessible.
- Build a system capable of detecting when an incorrect ID has been entered.
- Take steps to ensure that personal information cannot be leaked outside the institution even if a patient ID is entered incorrectly, by ensuring that EDC entry is managed within the institution only by the minimum necessary relevant parties who have received permission to do so, and that any outsourcing of work to external parties is also kept to the minimum level necessary.
- Rather than having the coordinator alone compare the entered IDs with the research subjects, have another researcher or other staff member carry out double-checks.
- Ensure that the head of the institution provides guidance to the effect that researchers who are too busy to be able to conduct appropriate research should refrain from participation.
- Ensure that an individual in a supervisory position stays abreast of the situation and coordinates duties, so as to ensure that mistakes caused by researchers having a heavy workload do not occur.

1 EDC: Electronic data capture. EDC refers to the process of acquiring case data in clinical studies electronically or the system used to do so. Built in order to increase the efficiency of clinical trials and studies, these systems electronically import to a server the data entered on computers by the principal investigator and clinical trial staff.

2-8. Concern about the provision of data to a third party by company managing research data

Affiliated institution	University, University hospital	Field	Clinical medicine, computer science



Factor that prevented misconduct

- Coordinator B checked the draft agreement between University P and Company Q before it was signed
- Coordinator B discussed the situation with Company Q and altered the agreement to state that University P's consent would be obtained before supplying the data provided by University P to third parties

1. Case details

- When conducting clinical research, Researcher A at University P was thinking about concluding an agreement with Company Q for the storage and management of clinical data. Company Q has its own data bank and has established a business based on amassing research data gained through joint research with universities, which it then shares with academic researchers who subscribe to its service.
- However, in the process of concluding the joint research agreement, when University P's research management coordinator B checked the draft agreement, they found provisions stating that the data would be shared with not only academic researchers, but also companies affiliated to Company Q, and that ownership of the data would be retained by Company Q.
- Aside from the concerns about the extent of data provision, there were no particular shortcomings in the draft agreement, and the content of the agreement fell within the appropriate extent. However, as Researcher A did not appear to understand the reality of Company Q's activities or be particularly aware of data ownership, B discussed the situation with Company Q and altered the agreement to state that Company Q would obtain University P's consent before supplying the data provided by University P to third parties. ☚ **Factor that prevented misconduct**

2. Backdrop & factors of near-miss incident

- Researcher A failed to properly check the actual activities undertaken by Company Q, which manages clinical data, and to the content of the agreement with Company Q.
- The original draft of the agreement would have readily allowed the data to be widely used via Company Q, with the possibility that the data could have been provided to and used by third parties, without asking University P.

3. Factors that prevented misconduct & its backdrop

- Coordinator B checked the draft agreement between University P and Company Q before it was signed.
- Coordinator B discussed the situation with Company Q and altered the agreement to state that University P's consent would be obtained before supplying the data provided by University P to third parties.

4. Possible research misconduct and questionable research practice

- The clinical data gathered by Researcher A would have been shared with third parties via Company Q, and risked being used for business or research at other institutions, beyond the scope of the study objectives and research method based on which University P had gained informed consent. There was also a risk that personal information might have been released as a result.

5. Preventive countermeasures

- For clinical research likely to involve data sharing or making data available as open data, establish a system that requires checks to be carried out and advice given by a body such as the data management committee responsible for monitoring compliance with the data policy at University P.
- Provide researchers with lectures and training courses on data management and data security.

(Commentary)

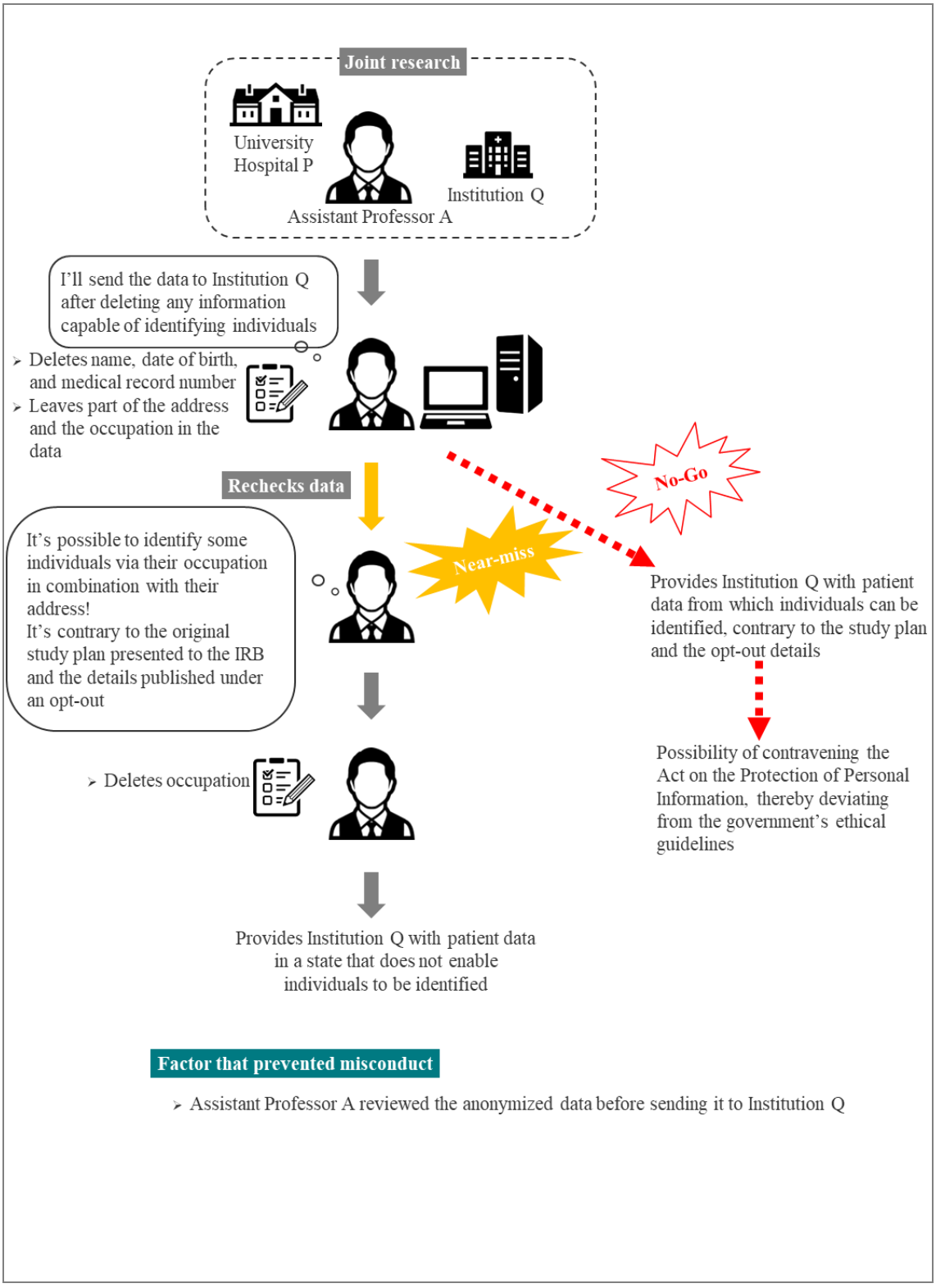
It is necessary to formulate measures that give full consideration to the risk of being unable to recover information once it has been released externally. In addition to the perspective of the protection of personal information, it is also necessary to give full consideration to the security, economic, and social risks of carelessly releasing information to institutions and universities, etc. in other countries. This applies to all kinds of information, not just technical information. It is vital for researchers to understand the need to clearly identify where data ownership lies under any agreements, specify the usage rights and conditions to which the data is subject, and strive to protect the data.

3. Protection and management of personal information

1. Presence in data provided to an external party of information that could identify an individual*
2. Release of data from a contract research organization*

3-1. Presence in data provided to an external party of information that could identify an individual

Affiliated institution	University, University hospital	Field	Clinical study



1. Case details

- Assistant Professor A at University Hospital P was conducting joint research with Institution Q.
- Patient data from University Hospital P was to be provided to Institution Q and the plan was that University Hospital P would process the patient data in accordance with the Act on the Protection of Personal Information[1] and then send it to Institution Q in a state in which individuals could not be identified.
- In carrying this out, Assistant Professor A deleted the patients' names, dates of birth, and medical record numbers, but left the details for patients' place of residence (after deleting part of the address) and occupation as they were.
- When Assistant Professor A was reviewing the anonymized data before sending it to Institution Q, they noticed that it was possible to identify[2] some individual patients from two items of data, namely their place of residence and occupation. ☚ **Factor that prevented misconduct**
- As place of residence data was required under the study plan, Assistant Professor A deleted the occupation item from the data.

2. Backdrop & factors of near-miss incident

- Assistant Professor A assumed that place of residence and occupation did not count as information capable of identifying individuals.

3. Factors that prevented misconduct & its backdrop

- Assistant Professor A reviewed the anonymized data before sending it to Institution Q.

4. Possible research misconduct and questionable research practice

- Data containing information capable of identifying individuals would have been shared externally, contrary to the original study plan presented to the Institutional Review Board (IRB) and details published under an opt-out.

5. Preventive countermeasures

- When using patient data or other personal information in research, ensure that only the items necessary are kept and that everything else is deleted.
- If there is a possibility that specific individuals could be identified by comparing multiple pieces of information, process the data after giving full consideration to information capable of identifying an individual.
- It may be possible to avoid identifying individuals by providing drop-down menus or similar for necessary data items rather than entering full details (for example, prefecture or the like, in the case of place of residence).
- At institutions handling personal information, provide researchers with sufficient training on the handling of personal information.

(Commentary)

If the number of people employed in an occupation is low, it may be possible to identify an individual from their occupation when combined with information about the prefecture in which they live. In this case, the researcher was able to delete the information about patients' occupations, but another conceivable method is to classify research subjects by the attributes of occupations necessary for the study. It is vital to describe the anonymization method and other matters relating to the handling of personal information in the study plan, have it screened by the IRB, and comply with the approved details.

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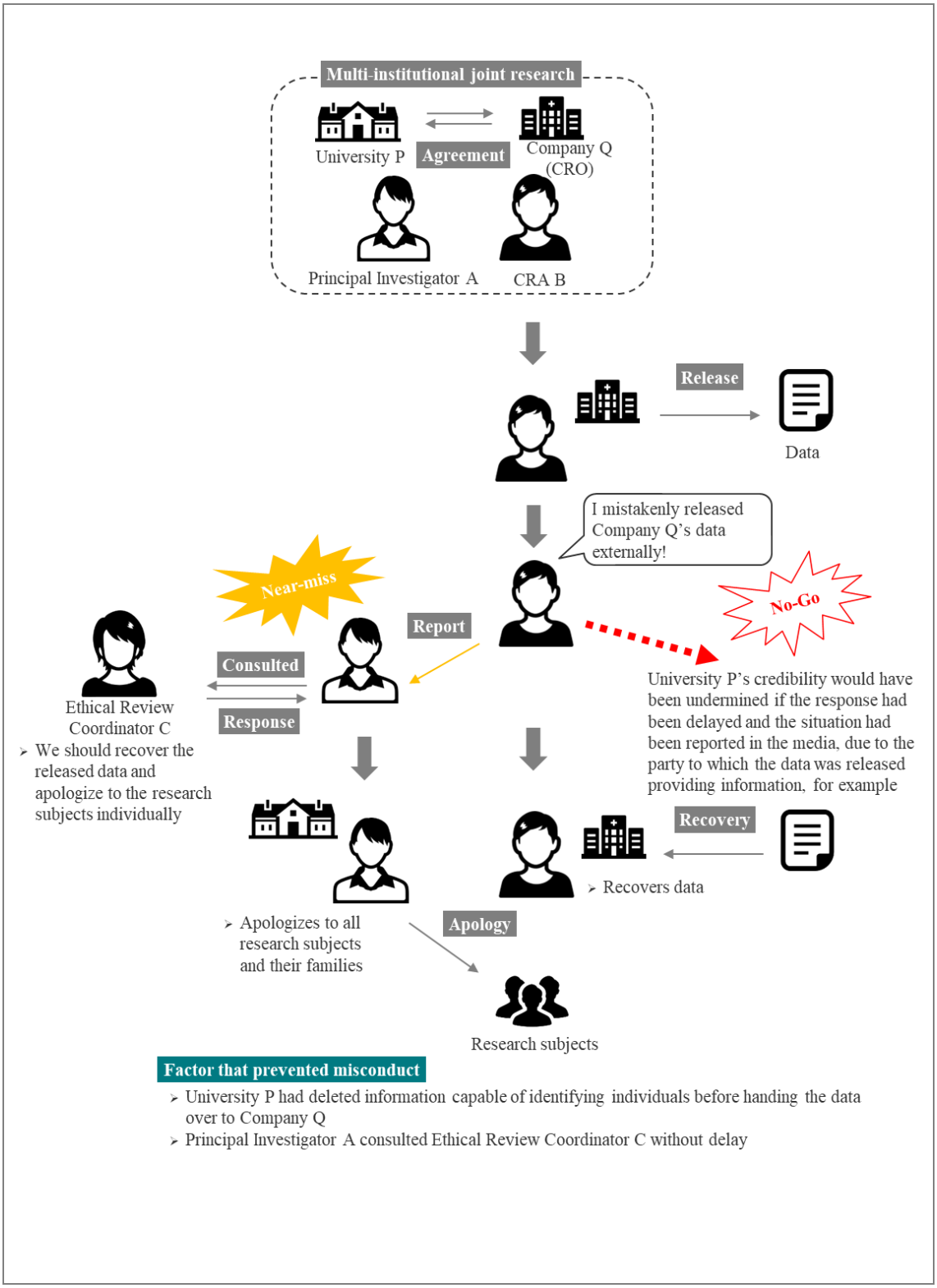
1 https://elaws.e-gov.go.jp/document?lawid=415AC0000000057

2 While place of residence and occupation are not in themselves personal information, if a specific individual can easily be identified when these items are compared with other information, they are classed as personal information in combination with the other information.
(Q&A on the Guidelines on the Act on the Protection of Personal Information, A1-3)
https://www.ppc.go.jp/personalinfo/faq/APPI_QA/#q1-1

3-2. Release of data from a contract research organization

Affiliated institution	University, University hospital	Field	Life sciences



1. Case details

- University P was participating in multi-institutional joint research and Researcher A was serving as the principal investigator.
- Part of the study was outsourced to Company Q, an organization specializing in supporting pharmaceutical development (CRO[1]), and the coordinator for the work was clinical development monitor (CRA[2]) B.
- One day, Principal Investigator A received a report from CRA B regarding the work outsourced to Company Q by University P, stating that they had released data externally in error. However, as University P had removed information capable of identifying individuals from the data before handing it over to Company Q, they avoided the release of personal information.
- Principal Investigator A consulted Ethical Review Coordinator C without delay. They decided to recover the externally released data and, although no personal information had been released, to apologize to each research subject individually from a moral standpoint. ☚ **Factor that prevented misconduct**
- As the scope of the data release was minimal and the response swift, they were able to apologize to all the research subjects and their family members, and secure their understanding.

2. Backdrop & factors of near-miss incident

- CRA B released Company Q's data in error.
- There were defects in Company Q's data management.

3. Factors that prevented misconduct & its backdrop

- University P had deleted information capable of identifying individuals before handing the data over to Company Q.
- Principal Investigator A consulted Ethical Review Coordinator C without delay.

4. Possible research misconduct and questionable research practice

- University P's credibility would have been undermined if the response had been delayed and the situation had been reported in the media, due to the party to which the data was released providing information, for example.

5. Preventive countermeasures

- Check that not only your own institution, but also the party to which you outsource any tasks has put in place a data management system.
- Provide opportunities for training and the like, at which researchers and other staff can acquire the latest knowledge about laws and regulations.
- When selecting a CRO for outsourcing tasks, carry out all possible checks of their management system governing the handling of data and the content of internal rules and work instructions, among other matters.

(Commentary)

While the release of data is unacceptable, in the event that data is accidentally released, you must minimize the harm by means of swift intervention after the fact, as in this example.

In this case, it was possible to contact all the research subjects and their families to explain the situation to them and apologize face-to-face. However, what kind of response would be necessary if there were people who could not be contacted?

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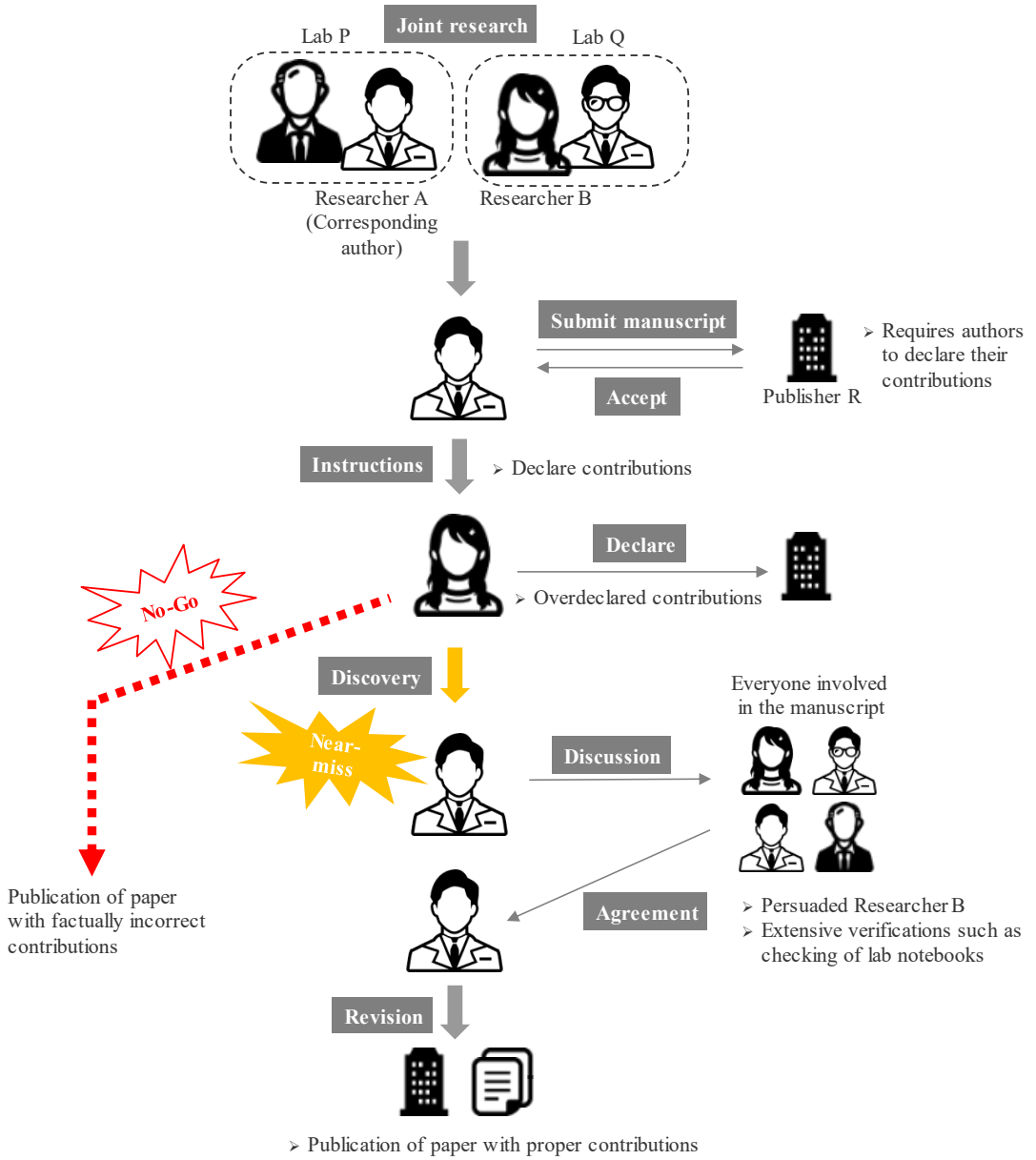
1 CRO: Contract research organization. CROs are contracted to carry out and support various tasks in clinical studies and postmarketing surveillance in order to increase the efficiency of pharmaceutical development and produce new drugs more quickly.
https://www.jcroa.or.jp/customers/service.html

2 CRA: Clinical research associate. CRAs monitor whether clinical studies are being conducted in accordance with the rules.

4 Authorship

4-1. Self-reporting of improper contribution

Affiliated institution	University, University hospital	Field	Life sciences



Factors that prevented misconduct

- Researcher A discussed with Researcher B and the Principal Investigators, and persuaded them to amend the contributions to an appropriate one
- To verify their contributions, they conducted extensive investigations including repeated discussions & retrieval of lab notebooks

1. Case details

- As the corresponding author, Researcher A summarized the results of the joint research conducted at several institutions in a manuscript and submitted it to the journal of the Publisher R, to which it was accepted. That journal required each co-author to declare their contributions to the manuscript.
- Researcher A then instructed the co-authors to declare their contributions to Publisher R.
- Later on, Researcher A noticed that their co-author, Researcher B, had overdeclared their contributions. When Researcher A contacted Publisher R in a bid to revise it, Publisher R asked that the approval of all co-authors was required for revision, which led to a discussion between all parties involved in the manuscript after it was accepted.

  ☜ **Factor that prevented misconduct**
- Although Researcher B was not really convinced, they eventually agreed to the appropriate revision.
- Since that incident, joint research between the laboratories to which Researcher A and Researcher B respectively belonged came to cease.

2. Backdrop & factors of near-miss incident

- As Researcher B also exaggerated their contributions even in their own laboratory, the Principal Investigator of Researcher B's laboratory was unable to recognize the inappropriate self-declaration.

3. Factors that prevented misconduct & its backdrop

- After Researcher A discussed with their Principal Investigator and Researcher B discussed with their Principal Investigator separately, Researcher A persuaded Researcher B to appropriately amend their contributions. To verify their contributions, they conducted extensive investigations including repeated discussions and retrieval of lab notebooks.

4. Possible research misconduct and questionable research practice

- Publication of a paper with improper contributions.

5. Preventive countermeasures

- Clarify the roles and responsibilities of each institution involved in the joint research in writing and communicate among researchers, including the Principal Investigators of each institution, on a regular basis about the progress of the research.
- Clarify the authorship and contributions of all co-authors and get their approval in writing before writing up the manuscript.

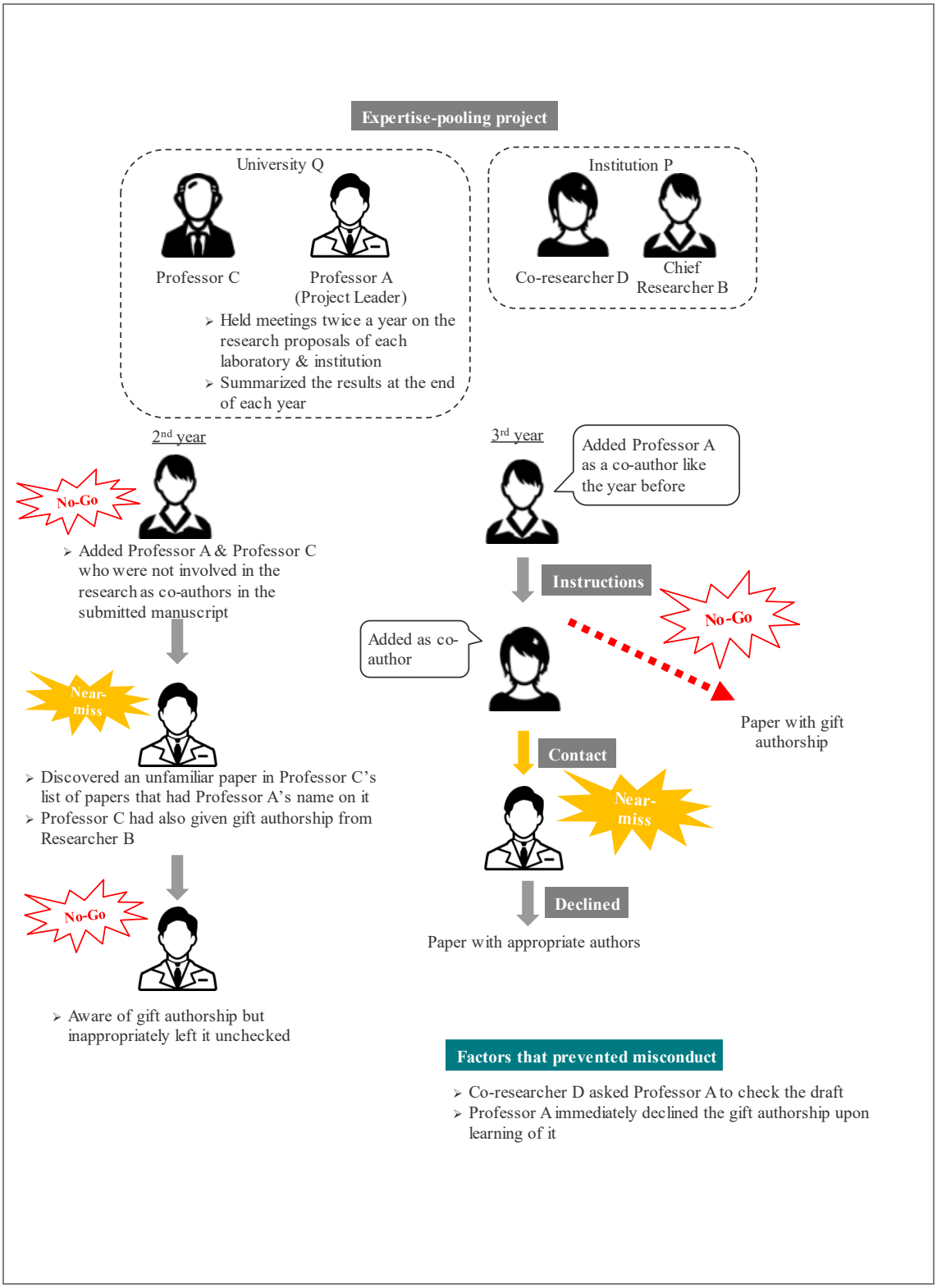
(Commentary)

The credit for research results is the "recognition of a scientist's contribution to research", which "becomes a criterion for evaluating individual scientists, and can make a significant difference in their careers (e.g., getting jobs or promotions) and in securing research funding"[1]. Accurate descriptions reflecting each researcher's contribution are thus required.

1 Japan Society for the Promotion of Science, Editing Committee "For the Sound Development of Science", "For the Sound Development of Science – The Attitude of a Conscientious Scientist –", p.49
Online edition (English): https://www.jsps.go.jp/j-kousei/data/rinri_e.pdf

4-2. Gift authorship

Affiliated institution	University, University hospital	Field	Life sciences



1. Case details

- Several universities (laboratories) and public research institutions participated in the "expertise-pooling project".
- As the Project Leader, Professor A held meetings twice a year on the research proposals of each laboratory and institution, and was responsible for summarizing the results at the end of each year. Professor A was not involved in the individual research of the members, and left the submission of manuscripts and patent applications to each laboratory and institution.
- In the second year of the project, Senior Researcher B of Public Research Institution P submitted a manuscript that listed Professor A as a co-author, which was subsequently accepted. After the paper was published, Professor A chanced upon an unfamiliar paper in Professor C's (from the same university) list of papers that had Professor A's name on it. Although Professor C had reviewed the final draft of the manuscript in question, like Professor A, Professor C was not directly involved in the research of Senior Researcher B.
- At that time, rules concerning authorship were not thoroughly enforced at research institutions and publishers. Senior Researcher B added the name of Professor A, who was the project leader, to the list of authors without obtaining Professor A's prior consent, as per custom.
- Senior Researcher B also submitted a manuscript in the third year of the project. During which Co-researcher D, another researcher who worked with Senior Researcher B, sent an e-mail to Professor A with a draft of the manuscript to be submitted, informing that Professor A would be added as to the manuscript's list of authors. ☜ **Factor that prevented misconduct**
- Professor A politely declined the gift authorship.

2. Backdrop & factors of near-miss incident

- Originally, a researcher needs to make significant contribution to the research in order to be listed as an author of the paper. However, Senior Researcher B added the name of Professor A, who was not directly involved in the research in question, to the list of authors, as it was conventional then to add project leaders to the list of co-authors.
- The lack of communication between Professor A and Senior Researcher B may be the reason why the gift authorship could not be avoided for the paper submitted in the second year of the project.
- Professor A was busy when he discovered the published paper in the second year of the project, so they could not immediately tell Senior Researcher B that it would not be necessary to add Professor A as an author in future papers.

3. Factors that prevented misconduct & its backdrop

- Co-researcher D sent an e-mail to check with Professor A about adding Professor A's name as a co-author to the manuscript to be submitted in the third year of the project.
- Professor A was tempted since they did not manage to garner enough publications that year, but declined the gift authorship from Senior Researcher B in light that it was a violation of research ethics.

4. Possible research misconduct and questionable research practice

- Publication of a paper with inappropriate authorship.

5. Preventive countermeasures

- The corresponding author should check the authorship when submitting a manuscript.
- The corresponding author should also get the manuscript for submission looked over by several people to ensure appropriate authorship and contributions.

(Commentary)[1]

"Gift authorship" is a term referring to a practice in which a true author, out of kindness, gives authorship to someone not deserving it. Since the authors are held accountable for the research, it is not permissible to list someone as an author who did not actually contribute to the research.

1 Japan Society for the Promotion of Science, Editing Committee "For the Sound Development of Science", "For the Sound Development of Science – The Attitude of a Conscientious Scientist –", pp.51-52
Online edition (English): https://www.jsps.go.jp/j-kousei/data/rinri_e.pdf

Editor's column 2: Gift authorship

Adding someone who is not qualified as an author to the list of authors is an act of misconduct called gift authorship. As an instance of the rules for manuscript submission, "For the Sound Development of Science" (Green Book)[1] introduces the uniform requirements for manuscript submission established by the International Committee of Medical Journal Editors (ICMJE). According to that, **all** of the following conditions must be satisfied in order for one to be listed as an author of a paper:

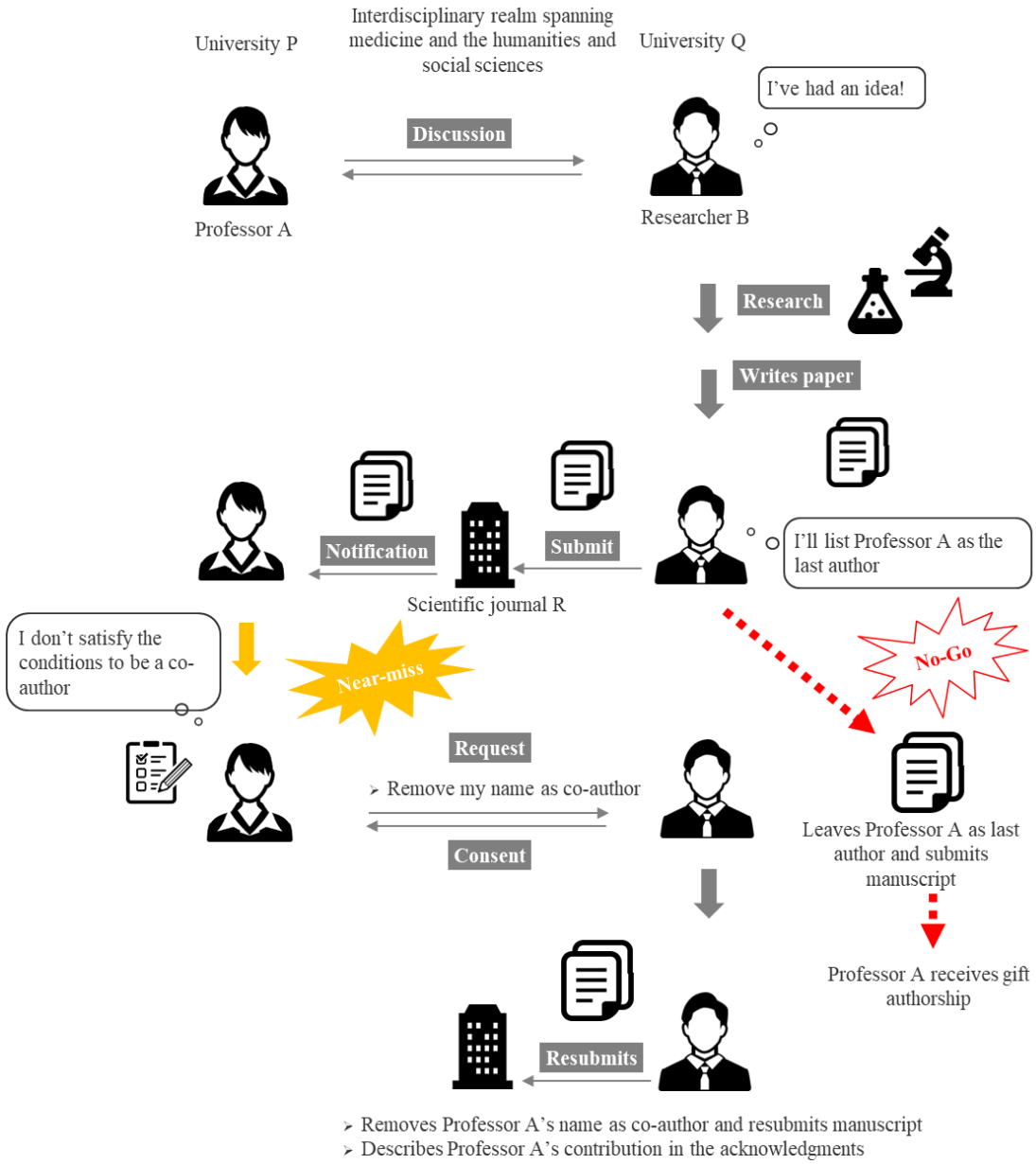
1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work;
2. Drafting the work or revising it critically for important intellectual content;
3. Final approval of the version to be published;
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

If we are to follow these submission rules, the act of automatically adding the head of an institution or the head of a project as an author, for instance, would be considered gift authorship. While it may be customarily acceptable that not all conditions need to be met in some fields of research, we have to be aware that these requirements are fast becoming a global standard. For joint research that spans across different fields, there is a need to be extremely careful when it comes to the handling of authorship.

1 Japan Society for the Promotion of Science Editing Committee, "For the Sound Development of Science", "For the Sound Development of Science – The Attitude of a Conscientious Scientist –", pp.50-51
Online edition (English): https://www.jsps.go.jp/j-kousei/data/rinri_e.pdf

4-3. Authorship by faculty members

Affiliated institution	University, University hospital	Field	Medicine, humanities and social sciences



Factor that prevented misconduct

- It is not customary to list the principal investigator (PI) as the last author in the humanities and social sciences, so Professor A realized before publication that their name must not be listed as the co-author of a paper for which they could not take overall responsibility

1. Case details

- The specialist field of Professor A at University P was the humanities and social sciences, but their research focused on an interdisciplinary realm spanning medicine and the humanities and social sciences. For some time, Professor A had had interactions with a laboratory at University Q working in a similar realm.
- One day, Professor A received notification via the manuscript submission system of scientific journal R that a manuscript had been submitted by e-mail. The manuscript in question was a paper whose corresponding author was Researcher B, whose employment at University Q was financed by external research funding. The manuscript listed Professor A as the last author.
- Researcher B had embarked on their study after being inspired by a conversation with Professor A and had initially conducted their research together with Professor A, but subsequently ceased to provide Professor A with any reports on the progress of the study and wrote the paper independently.
- Until receiving the e-mail, Professor A had forgotten about this, and had not been able to check such details of Researcher B's paper as the research data and wording. Professor A also noticed that the submitted manuscript described a different research process from that which they had envisaged. ☚ **Factor that prevented misconduct**
- Deciding that they could not take responsibility for the entirety of Researcher B's paper, Professor A told Researcher B to remove their name from the list of co-authors. Researcher B complied with this request and revised the paper by adding an acknowledgment of Professor A's contribution.

2. Backdrop & factors of near-miss incident

- In medical and life science research fields, it is often customary to list the senior lecturer, principal investigator (PI), or other senior researcher as the last author of papers in which members of the laboratory or project are involved. As Researcher B worked in the field of medicine and life science, they did not harbor any particular doubts about listing Professor A as a co-author on the paper they had written.

3. Factors that prevented misconduct & its backdrop

- It is not customary to list the PI as the last author in the humanities and social sciences, so Professor A realized before publication that their name must not be listed as the co-author of a paper for which they could not take overall responsibility.

4. Possible research misconduct and questionable research practice

- Publication of a paper listing Professor A as a co-author despite their being unable to take overall responsibility for it would constitute gift authorship.
- On the other hand, if Professor A had been removed from the list of co-authors and their contribution had then not been appropriately cited, referenced, or noted in the paper as an acknowledgment, there is also a possibility it could have constituted ghost authorship.

5. Preventive countermeasures

- While there is a tendency in the field of medicine to list as diverse an array of contributors as possible as authors, sole-authored papers and books tend to be regarded as more important in the humanities and social sciences. In interdisciplinary fields, where differing academic cultures intersect, discuss and agree on the approach to authorship at the laboratory or project level before writing the paper.
- In research ethics training for early-career scientists, too, review the authorship rules that serve as basic assumptions for the specific academic field or laboratory and examine them anew.

(Commentary)

As an instance of the rules for manuscript submission, "For the Sound Development of Science" (Green Book) introduces the uniform requirements for manuscript submission established by the International Committee of Medical Journal Editors (ICMJE).[1] Under these rules, **all** of the following conditions must be satisfied in order for one to be listed as an author of a paper:

1. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work;

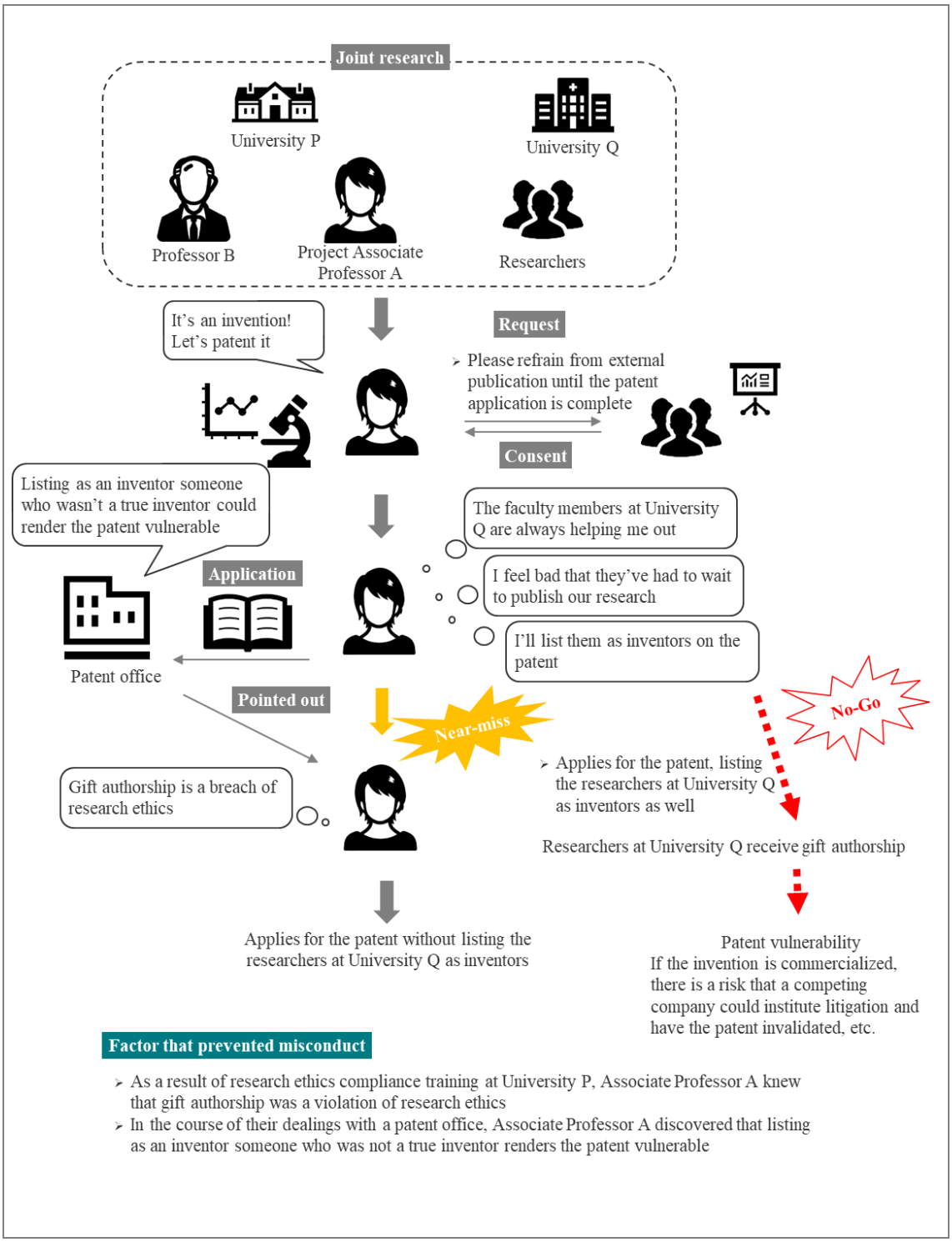
1 Japan Society for the Promotion of Science Editing Committee, "For the Sound Development of Science", "For the Sound Development of Science – The Attitude of a Conscientious Scientist –", p. 66, Maruzen Publishing, 2015
Online edition: https://www.jsps.go.jp/j-kousei/data/rinri.pdf, pp.66-67

2. Drafting the work or revising it critically for important intellectual content;
3. Final approval of the version to be published;
4. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Particularly in the case of papers concerning joint research with other fields, it is desirable to pay full attention to the handling of authorship and establish a shared understanding with the others involved concerning this matter before writing or submitting the manuscript.

4-4. Gift authorship of patents

Affiliated institution	University, University hospital	Field	Life sciences



Factor that prevented misconduct

- As a result of research ethics compliance training at University P, Associate Professor A knew that gift authorship was a violation of research ethics
- In the course of their dealings with a patent office, Associate Professor A discovered that listing as an inventor someone who was not a true inventor renders the patent vulnerable

1. Case details

- Project Associate Professor A at University P was conducting joint research with a laboratory at University Q under the supervision of Professor B.
- Among the outcomes of the research, the part for which Associate Professor A was responsible included something that constituted an invention, which Associate Professor A decided to patent.
- Associate Professor A needed to ensure that not only Professor B, but also other faculty members at University Q who were not directly associated with the part involving the invention refrained from publishing papers or giving conference presentations about the research until the patent procedure was completed.
- Article 30 of the Japanese Patent Act provides for an exception to the lack of novelty of invention; under this provision, if a patent application is filed after the publication of an invention and certain conditions are met, the invention is not treated as lacking novelty on the grounds of prior publication. While the application of this exception was considered, it turned out to be unfeasible, as it was difficult to provide an idea of the timing of the application, due to the time required for coordinating views among those involved and other matters relating to the coordination involved in finalizing the patent scope and conditions for patentability in regard to the application.
- As it had taken time to patent the invention, Associate Professor A decided to add the names of the faculty members at University Q from whose assistance they routinely benefited as inventors on the patent, out of a spirit of gratitude and desire to compensate them for having had to wait to publish their research.
- However, Associate Professor A remembered that adding individuals who did not directly contribute to an invention to the list of inventors on a patent constitutes gift authorship[1] and could also provide grounds for invalidating the patent, so they abandoned their plan to add the faculty members at University Q to the list of inventors. ☚ **Factor that prevented misconduct**

2. Backdrop & factors of near-miss incident

- It took time to patent Associate Professor A's invention.
- The faculty members at University Q did not directly contribute to the invention, but had to refrain from publishing papers and giving conference presentations about the associated research output while the patent application process was underway.
- Associate Professor A wanted to add the names of the faculty members at University Q as inventors on the patent, out of a spirit of gratitude and desire to compensate them for having had to wait to publish their research.

3. Factors that prevented misconduct & its backdrop

- As a result of research ethics compliance training at University P, Associate Professor A knew that gift authorship was a violation of research ethics.
- In the course of their dealings with a patent office, Associate Professor A discovered that listing as an inventor someone who was not a true inventor could render the patent vulnerable.

4. Possible research misconduct and questionable research practice

- If a patent with gift authorship is commercialized, there is a risk that a competing company could institute litigation and have the patent invalidated.

5. Preventive countermeasures

- In addition to compliance training, universities should provide opportunities to receive training in risk management when undertaking commercialization, in order to communicate and raise awareness of the risks of research misconduct from the perspectives of both ethics and practice.
- When patenting inventions, researchers should liaise carefully with the intellectual property department of their institution from the preparatory stage and have the department check the format and content of the requisite documentation, among other matters.

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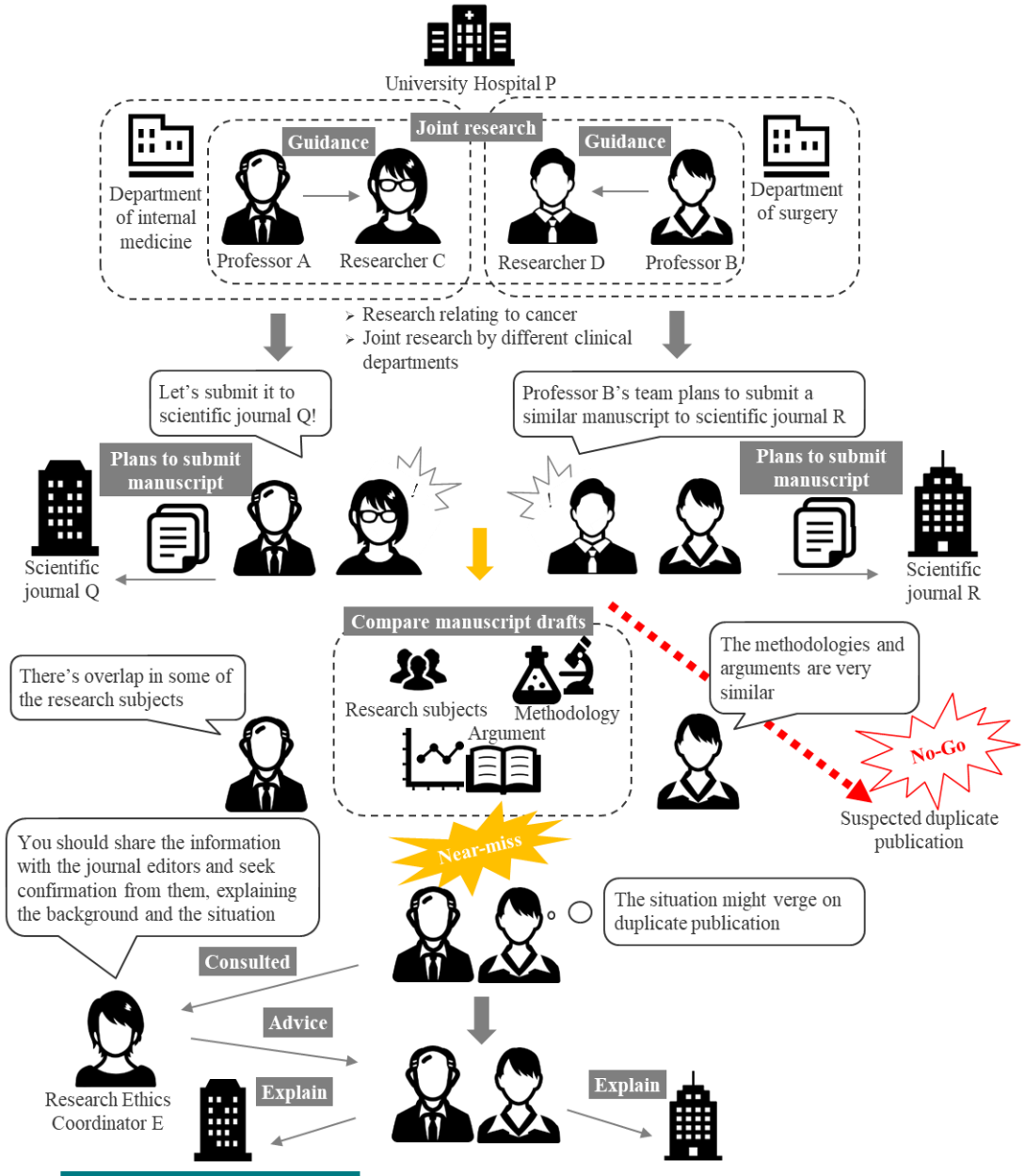
1 Japan Society for the Promotion of Science Editing Committee, "For the Sound Development of Science", "For the Sound Development of Science – The Attitude of a Conscientious Scientist –", pp. 67-68, Maruzen Publishing, 2015 Online edition: https://www.jsps.go.jp/j-kousei/data/rinri.pdf, p.68

4-5. Example that could have coincidentally resulted in duplicate publication

Affiliated institution	University, University hospital	Field	Medicine



Factor that prevented misconduct

- Researchers C and D, who were working on papers under the supervision of Professor A and Professor B respectively, found that their two papers closely resembled each other and, realizing the possibility that this could constitute duplicate publication if left unaddressed, sought advice from the professors

1. Case details

- The department of internal medicine and the department of surgery at University Hospital P were conducting joint research into cancer using data on the hospital's patients.
- While Professor A, the chair of the department of internal medicine, was preparing to submit a manuscript to scientific journal Q with Researcher C and others, they received a report from Researcher D in the department of surgery and discovered that a group led by Professor B, who was the chair of Researcher D's laboratory, intended to submit a similar research paper to scientific journal R. ☚ **Factor that prevented misconduct**
- Accordingly, Professor A from the department of internal medicine and Professor B from the department of surgery compared the drafts of their manuscripts and found that there was considerable overlap in the research subjects, as both studies dealt with cancer patients at the same hospital. They also discovered that their methodologies and arguments were very similar.
- While this situation did not constitute duplicate publication, in which the same researchers submit papers with identical content, Professor A and Professor B felt uncomfortable about a situation so close to duplicate publication, however unintentional, so they sought advice from Research Ethics Coordinator E.
- Research Ethics Coordinator E told them the researchers should share the information with the journal editors and seek confirmation from them, explaining the background and the situation. Accordingly, Professor A and Professor B respectively contacted the editors of scientific journals Q and R, and sought their judgment on whether the situation constituted duplicate publication.

2. Backdrop & factors of near-miss incident

- As it turned out, even though the laboratories of Professor A from the department of internal medicine and Professor B from the department of surgery had been conducting the study as a joint research project, Professor A and Professor B did not consult each other when writing their papers about the study, nor did the researchers participating in the joint research share information with each other across the boundaries of their departments when writing these papers.

3. Factors that prevented misconduct & its backdrop

- Researchers C and D, who were working on papers under the supervision of Professor A and Professor B respectively, found that their two papers closely resembled each other and, realizing the possibility that this could constitute duplicate publication if left unaddressed, sought advice from the professors.

4. Possible research misconduct and questionable research practice

- Duplicate publication in scientific journals.

5. Preventive countermeasures

- When conducting research spanning multiple laboratories, it is desirable for the principal investigator (PI) to take responsibility for ensuring opportunities for coordination regarding the scope of the joint research to be published and the handling of each other's contributions, at least before starting to write the papers.
- When conducting research activities based on loose collaboration with the involvement of multiple laboratories at a university, seek to ensure open two-way communication to avoid excessive duplication of the content of papers for publication, by such means as establishing a forum within the university for presenting and reporting research content to each other, and considering altering topics or conducting joint research if similar studies are being undertaken.

(Commentary)

Submitting manuscripts is the most important aspect of research activities for researchers. However, as a result of concentrating on their research and devoting all their energies to the immediate concerns of experiments and manuscript writing due to pressure of time, researchers can become careless about maintaining objective viewpoints and judgments regarding manuscript submission itself. In particular, think about a situation in which individuals from different institutions conduct joint research that unexpectedly leads to the emergence of competition as a result of their efforts in good faith, and consider what the conceivably valid standards for solving this problem might depend upon. In solving problems relating to manuscript submission, there are cases in which the judgment of the journal publisher or editor is of more critical importance than the understanding or judgment of the researchers themselves.

Editor's column 3: The line-drawing method

When compelled to make an ethical decision, one approach that can be used to make decisions that you will not regret is the line-drawing method. When making judgments on a situation, first think of several similar cases, including one in which there is clearly an ethical issue and another in which there is not. Next, list them in order, starting from the one with the biggest ethical issue and think about where the problematic case is positioned. Then compare it with the adjacent cases and judge whether those cases would be socially acceptable.

For example, let us say you happened to bump into A from a supplier at a coffee shop on a day off work and made small talk for a while, but A then tried to pick up the bill and get a receipt when leaving. There are six conceivable similar situations, as follows.

(1) You received cash in return for favors.
(2) You received hospitality at a high-class restaurant in expectation of favors.
(3) You were treated to lunch.
(4) During a factory tour, the office paid for coffee to be delivered from a coffee shop.
(5) During a factory tour, the office served you coffee made by one of the staff members*.
(6) During a factory tour, a staff member brought your coat from where it was hanging up.

*In Japan, visitors to offices and the like are customarily served tea or coffee made by staff members.

The scenarios here are already arranged in descending order of the magnitude of the ethical issue. Let us say that the aforementioned scenario of being treated to coffee during free time outside of work falls between (4) and (5), and think about the extent to which this is ethically acceptable.

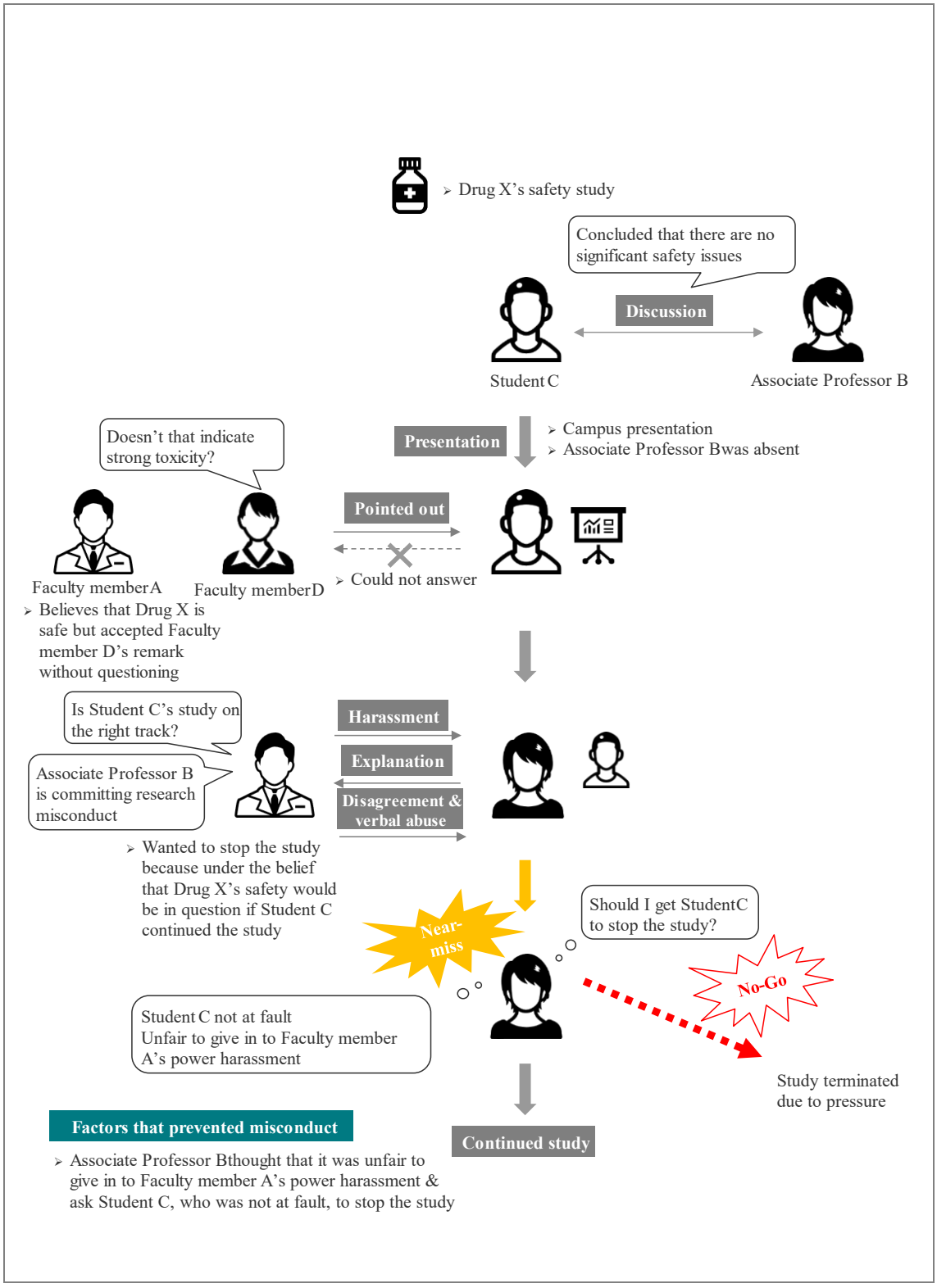
Under the National Public Service Ethics Act, public officials are prohibited from receiving not only money, goods, and hospitality from interested parties, but also the provision of services. Accordingly, there may well be some people who would consider scenario (6) to correspond to the provision of a service, strictly speaking. On the other hand, if you were working at a private sector company, quite a few people would likely say that anything up to scenario (2) would be safe, as you would not be accused of a crime as long as you did not cause any loss to the company. However, if the parts supplied by A's company served as the heart of a safety function, some people would probably say that everything down to scenario (4) was bad, even if you were working at a private sector company. On the other hand, even if you were a public official, some people might change their mind if you had given A some helpful advice and A had been moved by it to pay for your coffee out of their pocket money.

Where people draw the line depends on their individual value judgments and every situation is different, so it is tricky to draw a hard and fast line. However, thinking about the issues in this way and asking a third party for their views on the pros and cons of your judgment is likely to enable you to make decisions that you will not regret.

5 Laboratory management, research guidance, harassment

5-1. Power harassment due to misinterpretation of research data

Affiliated institution	University, University hospital	Field	Basic medical research



1. Case details

- Associate Professor B was supervising Drug X's safety study conducted by Student C.
- Associate Professor B discussed the data obtained from the study with Student C and came to the conclusion that there did not appear to be any significant safety issues with Drug X.
- Student C reported the study results at a small presentation on campus (Associate Professor B did not attend), to which Faculty member D pointed out that some of the data presented "may indicate strong toxicity". From a scientific perspective, the association of the data in question to toxicity was unclear. However, Student C could not provide a satisfactory answer and gave the presentation attendees the impression that Drug X might be toxic.
- After the presentation, rumors began to spread inside and outside the university that the contents of Student C's presentation were questionable. Tracking down the source of the rumors revealed that Faculty member A, who believes that Drug X is safe, has been spreading unsubstantiated rumors to other researchers alleging that "Associate Professor B is committing research misconduct and making false reports". Based on Faculty member D's question of "Is Drug X highly toxic?" in response to Student C's presentation, Faculty member A surmised that "the safety of Drug X is questionable if Student C continues with this study", and proceeded to harass Associate Professor B and Student C, and tried to get them to terminate their safety study of Drug X.
- Associate Professor B explained the legitimacy of their study to Faculty member A, including the fact that the results obtained in Student C's study indicated that there were no significant safety issues with Drug X, but Faculty member A was not convinced at all. In fact, Faculty member A verbally abused Associate Professor B in front of several people.
- Associate Professor B did not think they could continue to be subjected to such pressure from Faculty member A, and thought that it would be easier to just terminate the study. Associate Professor B considered telling Student C to stop the study, but changed their mind since Student C did not do anything wrong and felt that it was unfair to give in to Faculty member A's power harassment. ☜ **Factor that prevented misconduct**
- Associate Professor B did not tell Student C about the series of events that happened and allowed the experiments to continue.

2. Backdrop & factors of near-miss incident

- Faculty member D made a one-sided remark despite the fact that they did not have an accurate understanding of the research data.
- Student C's failure to adequately answer Faculty member D's question left the presentation attendees with the impression that Drug X might be toxic.
- As drug safety studies have a significant impact on the efficacy of a drug, they receive an extremely high level of attention from interested parties.

3. Factors that prevented misconduct & its backdrop

- Associate Professor B changed their mind of "asking Student C to terminate the study since it is unfair and would mean that we are giving in to Faculty member A's power harassment".

4. Possible research misconduct and questionable research practice

- Despite the fact Student C was not at fault, Associate Professor B could have given in to Faculty member A's power harassment and unfairly stopped Student C's study.
- Terminating the drug safety study could be detrimental to society.

5. Preventive countermeasures

- When students present their research, even in a small presentation, a supervising faculty member should be present to ensure that there are no misunderstandings, especially on sensitive matters, during the Q&A session.

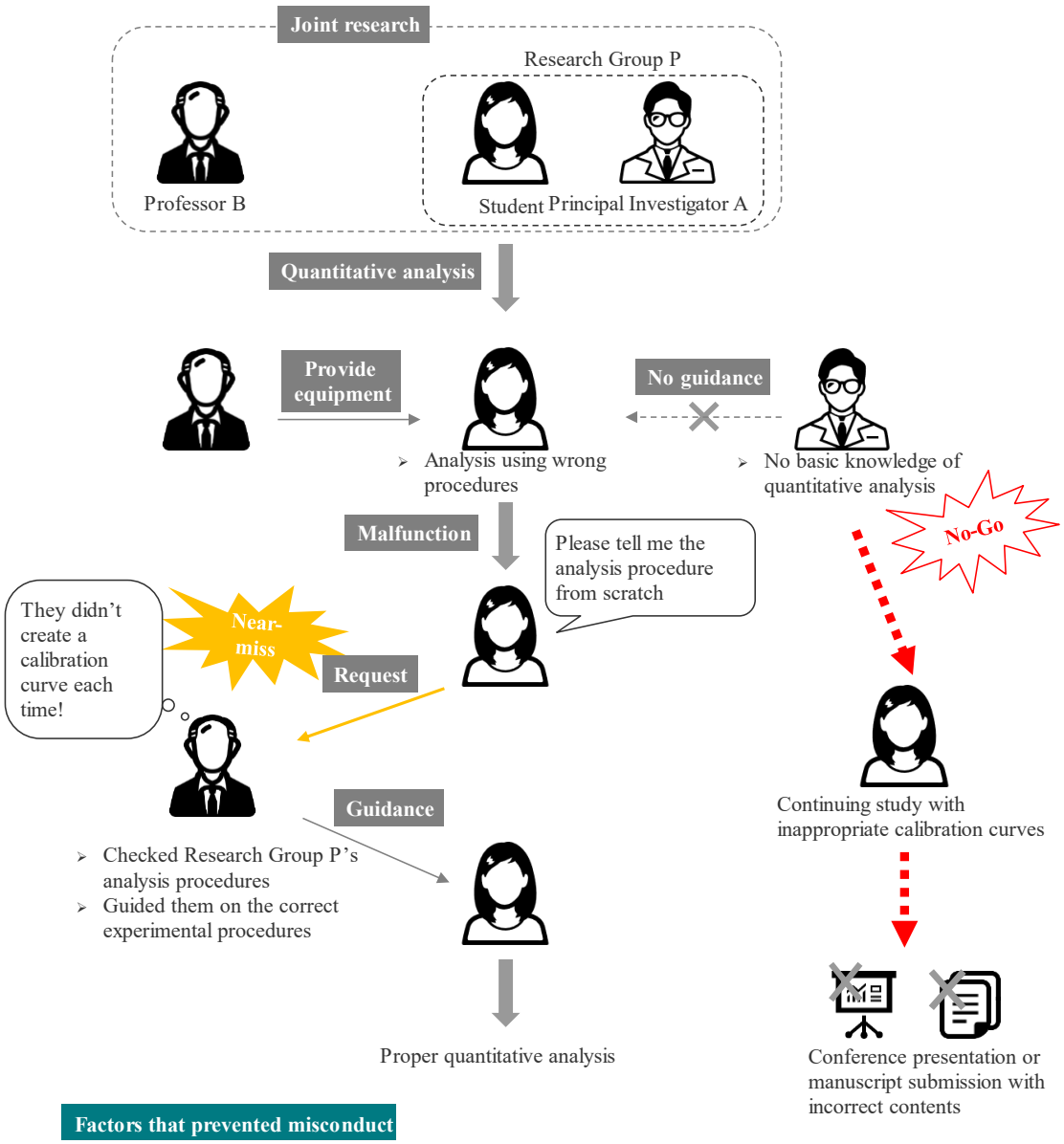
(Commentary)

When flaws or deficiencies are pointed out in one's theory or views, a scientist must face it in a calm and earnest manner. Obviously, we should refrain from making counterarguments based on non-objective facts or emotional rebuttals. It also goes without saying that slanders against the person pointing out the flaws are also unacceptable.

In this case, the other faculty members are expected to verify the facts and admonish Faculty member A for taking an emotional stance.

5-2. Prevented incorrect quantitative analysis

Affiliated institution	University, University hospital	Field	Analytical chemistry



Factors that prevented misconduct

- The malfunctioning of the equipment prompted the graduates & undergraduates in Research Group P to ask Professor B to teach them the procedures for quantitative analysis from scratch
- Professor B confirmed with the students the quantitative analysis procedures performed in Research Group P & provided appropriate guidance

1. Case details

- Professor B was conducting joint research with Research Group P led by Principal Investigator A.
- Professor B provided Research Group P with the quantitative analysis equipment under Professor B's supervision.
- When a student in Research Group P was using this analysis equipment in Professor B's laboratory, the equipment malfunctioned. The troubled student asked Professor B to teach them how to use equipment from scratch, including the procedures for quantitative analysis.
- For this quantitative analysis, it is necessary to create a calibration curve using reference samples[1] for each experiment in order to take into account the effects of contaminants and interfering substances present in the samples. When Professor B confirmed with the students the analysis procedures, they found that the students in Research Group P did not create a calibration curve for each experiment, but instead, performed quantitative analyses using standard calibration curves found in textbooks or calibration curves created by researchers in the same research group who had performed similar measurements in the past. ☜ **Factor that prevented misconduct**
- Professor B guided the students on the correct procedures to perform quantitative analysis, to which they subsequently continued to perform the analyses in the right way.

2. Backdrop & factors of near-miss incident

- Principal Investigator A, who should have guided the students in Research Group P, did not provide appropriate guidance to the students because they did not have a fundamental understanding of the procedures of quantitative analysis and was unable to differentiate between procedures that could be simplified and those that were essential.

3. Factors that prevented misconduct & its backdrop

- The malfunctioning of the equipment prompted a student in Research Group P to ask Professor B to teach them the procedures for quantitative analysis from scratch.
- Professor B confirmed with the students the analysis procedures performed in Research Group P, and provided appropriate guidance.

4. Possible research misconduct and questionable research practice

- Dissertations, conference reports, and academic papers based on the improper quantitative analysis data could have been prepared and published.

5. Preventive countermeasures

- Students who are unfamiliar with research should be guided by researchers who have comprehensive knowledge of correct experimental techniques, correct use of equipment and instruments, and appropriate handling of samples.
- Provide opportunities for external researchers, such as those from joint research partnering institutions, to check experimental methods as they might be able to point out errors that have been overlooked.

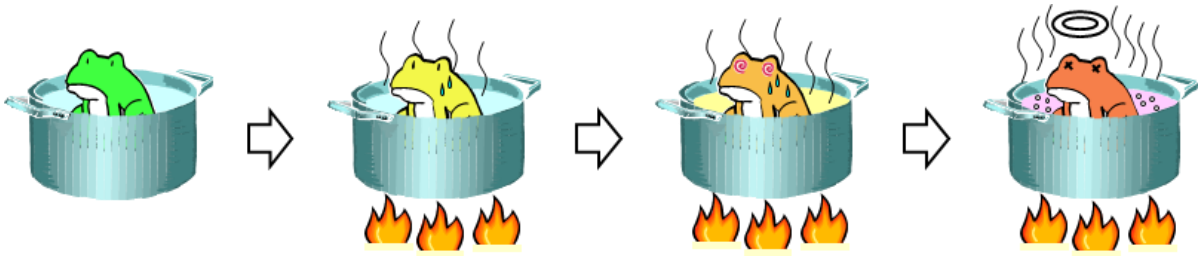
(Commentary)

Without proper guidance, many students think that calibration curves can be reused with no issues. In addition, to determine whether the effects of interfering substances are negligible, the standard addition method (where a known amount of standard is added to a sample in stages and analyzed to cancel the effects of interfering substances) should be used at least for the initial analysis.

1 A sample of known purity used as a reference material in quantitative analysis.

Editor’s column 4: Boiling frog syndrome

Have you ever heard of the term “boiling frog syndrome”? If we attempt to put a frog into a pot of boiling water, it will not want to go in, but if we put the frog into a pot of cool water, the frog will jump in. And if we slowly bring this pot of water to boil, the frog will not perceive the danger and will be cooked to death. When you first started a club activity or a part-time job, or joined a laboratory or a new academic society, have you ever thought, “Huh? So that’s how they think here”, or, in some cases, “This way of thinking is not normal”. But after a year or so, you started to think in the same way and even imposed your way of thinking or doing on junior members and newcomers? All of us belong to some organization. But organizations are simply groups of people who work together to achieve a certain goal, and in many cases, the values of the organization deviate from the average values in the world. If we are not aware of this gap, we will be under the illusion that our organization’s values are the norm in the world as well. We often see reports of scandals at companies, universities, and government agencies in the media, and many of the comments made by those involved seem to lack common sense. This is because they have been “boiled” in the pot of an organization and are under the illusion that this is natural and normal. In your narrow community of laboratories and classrooms, are you sure that you are not turning into a “boiling frog” as well?



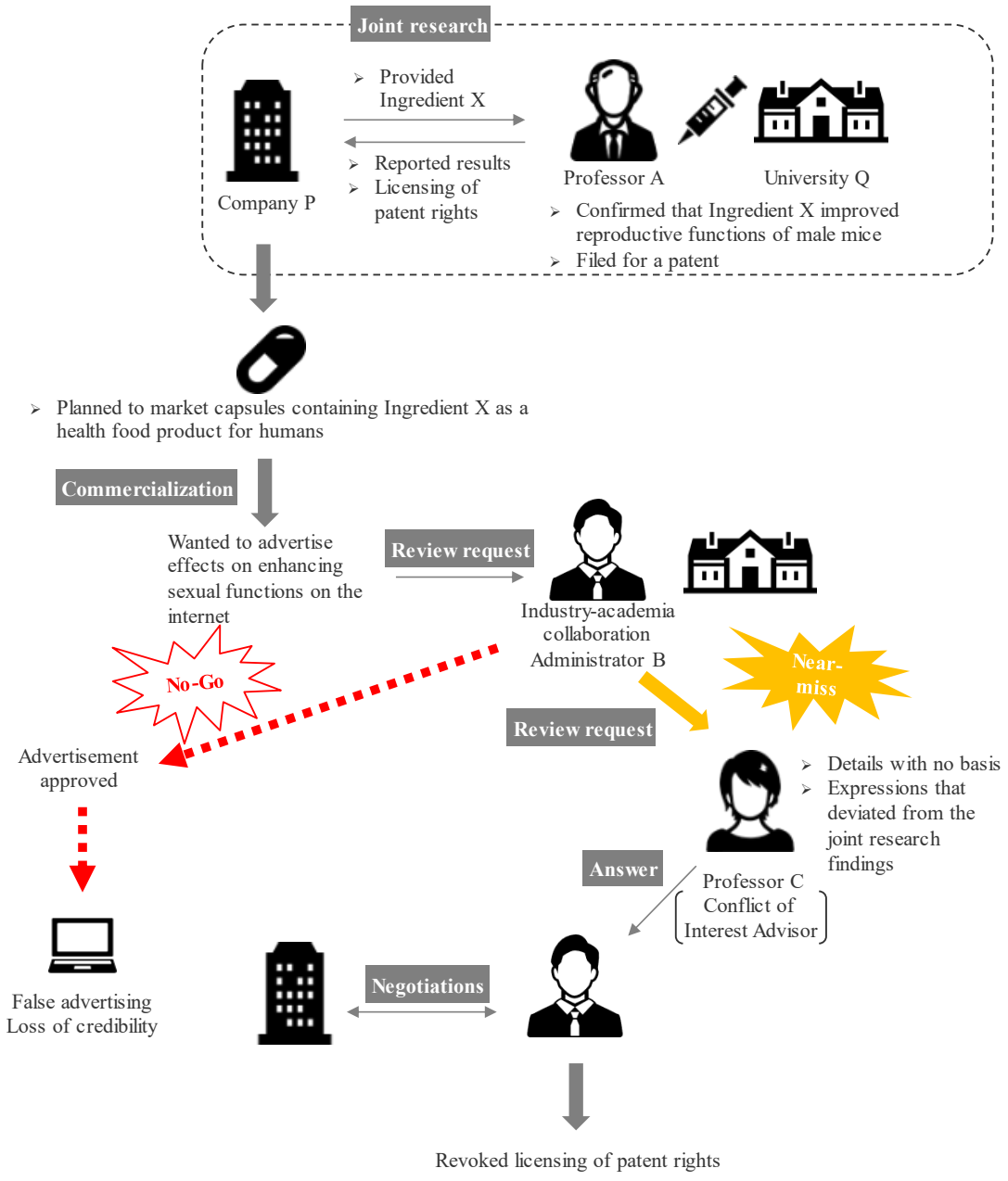
6 Conflict of interest

1. Misleading advertising about the effects of health food product that have only been verified through animal experiments
2. Disclosure of conflict of interest in manuscript
3. Conflict of interest screening of candidates
4. Conflict of interest due to joint research with the parent company*
5. Discrepancy between institutions in checking conflicts of interest in joint research*

Editor’s column 5: Smoking on airplanes

6-1. Misleading advertising about the effects of health food product that have only been verified through animal experiments

Affiliated institution	University, University hospital	Field	Food science



Factors that prevented misconduct

- Administrator B asked Professor C, the Conflict of Interest Advisor, to review the advertisement

1. Case details

- University Q, to which Professor A belongs, was conducting joint research with Company P. University Q filed for a patent after their experiments showed that administering plant-derived ingredient X that was provided by Company P to male mice subjected to certain types of stress improved some of their reproductive functions.
- Company P wanted to market capsules containing Ingredient X as a health food product and advertise their effects on the Internet. Despite the fact that the effects had not been confirmed in humans, the advertisement proclaimed the effects of improving male sexual function, and employed expressions with unclear basis, intentionally exaggerated expressions, and expressions that deviated from the scope of the joint research findings by University Q and company P.
- After Company P requested University Q to review the proposed advertisement, the person responsible for industry-academia collaboration in University Q, Administrator B, consulted with Professor C, a Conflict of Interest Advisor.
  ☜ **Factor that prevented misconduct**
- Professor C then answered that the proposed advertisement has the aforementioned issues.
- Negotiations between the two parties led to University Q revoking the licensing of patent rights to Company P.

2. Backdrop & factors of near-miss incident

- Not only did Company P not understand the need for appropriate regulatory checks on advertisements for health food products, they also failed to recognize that expressions in advertisements that may mislead consumers may be construed as violations of laws and ordinances.
- Company P, who provided the research funding, wanted to make the maximum use of the University Q's name (brand power) in its advertisement.
- Meanwhile, the person responsible for industry-academia collaboration in University Q, was placed in a situation where it was hard to express their opinions since the research was funded by Company P.

3. Factors that prevented misconduct & its backdrop

- Administrator B who was responsible for the industry-academia collaboration was aware of the concept of conflict of interest in research, and asked Professor C, the Conflict of Interest Advisor, to review the proposed advertisement.

4. Possible research misconduct and questionable research practice

- Violations against the Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Pharmaceutical and Medical Device Act), Act against Unjustifiable Premiums and Misleading Representations (Act against UPMR), and Health Promotion Act could have occurred.
- Even if there were no legal violations, University Q's integrity could be opened to questioning and contestation due to the conflict of interest, and the inappropriate advertising expressions could damage the reputation of University Q.

5. Preventive countermeasures

- As many companies request for the use of the name or photos of the university, as well as the publication of comments by faculty members in the findings of joint research, each university needs to establish the rules and regulations for the use of their name in advance.
- There is a need to pay attention to the laws and ordinances because laws like the Pharmaceutical and Medical Device Act and the Act against UPMR may be implicated depending on the product (including health food products and health appliances).

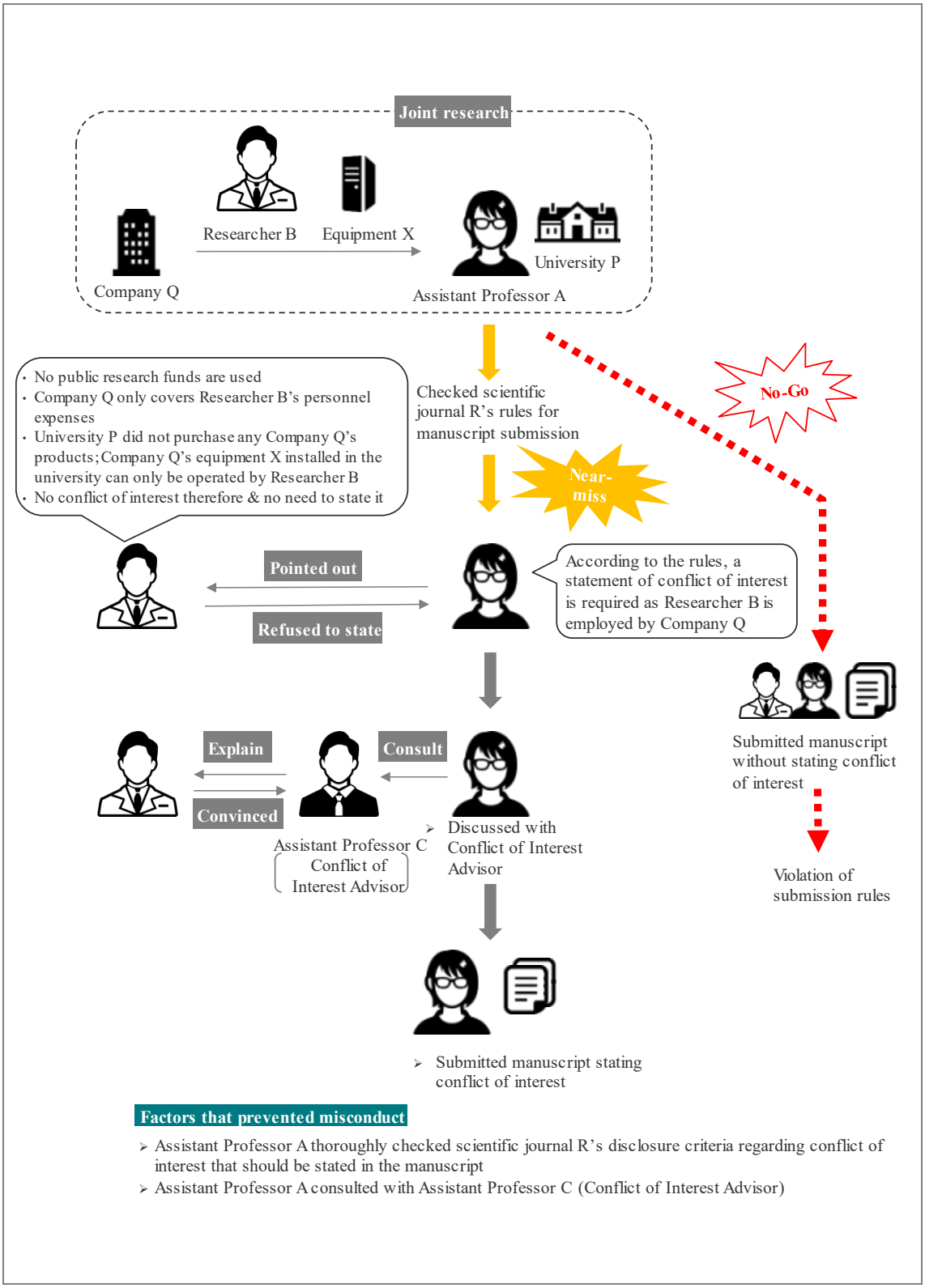
(Commentary)

Although the Pharmaceutical and Medical Device Act does not cover the so-called health food products, they are regarded as unapproved pharmaceuticals or quasi-pharmaceutical products if they are advertised as having any effect on human or animal function, and may violate this Act.

In the event that a product is commercialized as a result of industry-academia collaboration, and an advertisement on the function or efficacy of the product based on scientific evidence is required, researchers and research institutions need to pay extreme care and caution from the perspective of self-protection to ensure that there are no exaggerated expressions or expressions with unclear basis that may lead consumers in the wrong direction.

6-2. Disclosure of conflict of interest in manuscript

Affiliated institution	University, University hospital	Field	Medicine



1. Case details

- Assistant Professor A of University P was conducting joint research with Researcher B of Company Q. They wrote up the manuscript based on their research findings and planned to submit it to the international scientific journal R.
- Assistant Professor A checked scientific journal R's submission rules and came to the conclusion that "Researcher B's employment with Company Q, which is relevant to this manuscript, constitutes a conflict of interest". **Factor that prevented misconduct**
- When Assistant Professor A pointed this out to Researcher B, the latter made the following remark to Assistant Professor A.
  "No public research funds are used in light of Company Q's involvement. University P is also only responsible for the personnel expenses of Assistant Professor A and the expenses related to the experiments, and did not purchase any products of Company Q. Company Q only covers Researcher B's personnel expenses and part of consumables. While the equipment X developed by Company Q is indeed installed at University P for this joint research, it is not considered a loan since equipment X cannot be operated by anyone other than Researcher B. If Company Q had lent Equipment X free of charge, it might be perceived as a special benefit to University P and therefore, I do not want to use the word 'free'. There is no conflict of interest in this case, and I don't think we need to mention it."
- Assistant Professor A thought that Company Q's assertion was based on Researcher B's misunderstanding of joint research and conflict of interest. Assistant Professor A thus consulted with Assistant Professor C, the Conflict of Interest Advisor of University P, and asked Assistant Professor C to explain to Researcher B.
- In the end, they decided to state that "Researcher B is employed by Company Q that developed equipment X" and that "Company Q provided equipment X free of charge to University P for this study" in the manuscript to be submitted to scientific journal R.

2. Backdrop & factors of near-miss incident

- It is common for the university and the company to provide each other with funds, equipment, and researchers when conducting joint research, and conflicts of interest often arise when the company provides the funds or resources. In such cases, the impartiality of the research can be maintained by disclosing the necessary information and appropriately managing any conflicts of interest that may arise.
- Researcher B neither clearly understood the nature of joint research nor knew how to manage conflicts of interest (information disclosure) in joint research. Researcher B was under the mistaken impression that the free loan of equipment X from Company Q to University P constituted a special benefit, which is not allowed in joint research.

3. Factors that prevented misconduct & its backdrop

- Assistant Professor A thoroughly checked scientific journal R's disclosure criteria regarding conflict of interest that should be stated in the manuscript.
- Assistant Professor A consulted with Assistant Professor C (Conflict of Interest Advisor).

4. Possible research misconduct and questionable research practice

- Assistant Professor A and Researcher B could have violated scientific journal R's submission rules.
- Publication of a paper without properly disclosing the conflict of interest.

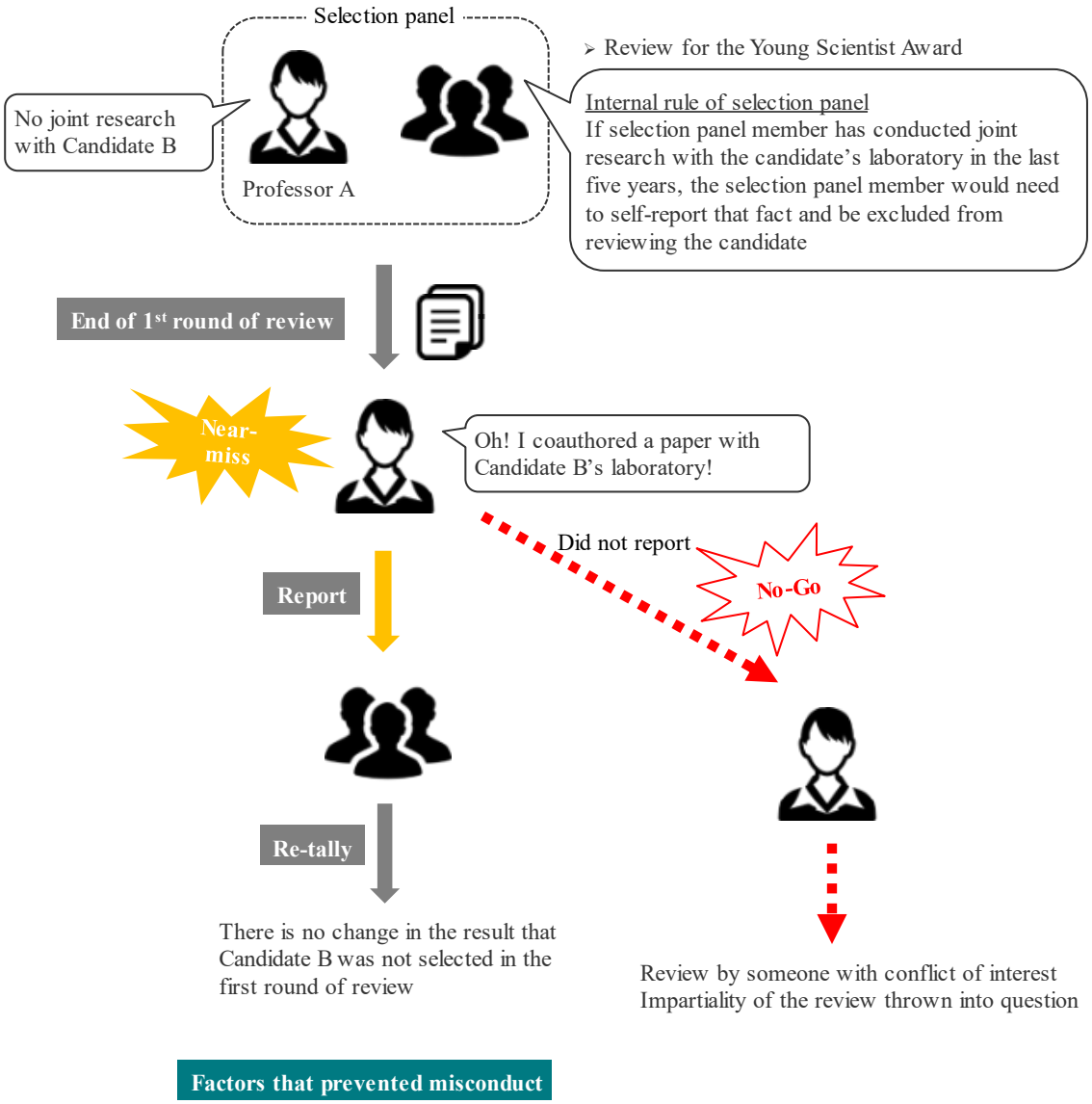
5. Preventive countermeasures

Provide education and training on management of conflict of interest on a regular basis. Since conflicts of interest almost always arise in industry-academia collaborations in particular, both parties involved in the joint research need to have a thorough understanding on the proper management of conflicts of interest that may arise and the information that needs to be disclosed.

When publishing papers based on industry-academia collaborations, the authors must check the journal's disclosure criteria regarding conflict of interest to which they intend to submit the manuscript. Researchers from both the university and the company have to be aware and understand the conflict of interest ahead of the joint study to ensure that they are able to disclose it according to the criteria.

6-3. Conflict of interest screening of candidates

Affiliated institution	University, University hospital	Field	Life sciences



Factors that prevented misconduct

- Professor A remembered that they had coauthored a paper with Candidate B's laboratory
- Professor A promptly informed the members of the selection panel

1. Case details

- Professor A was a member of the selection panel at the branch of the academic society for the Young Scientist Award. The selection panel had an internal rule that if the candidate's laboratory and the selection panel member had conducted joint research in the last five years, the selection panel member would need to self-report that fact and be excluded from reviewing the candidate.
- Professor A participated in the first round of review of Candidate B because they had no memory of conducting joint research with Candidate B.
- Only after the first round of review was over did Professor A remember that they had coauthored a paper with Candidate B's laboratory. Professor A was unable to recognize that because the contents of the coauthored paper were completely different from that of Candidate B's research. Professor A then immediately emailed all the members of the selection panel to explain the situation and redid the tally. ☜ **Factor that prevented misconduct**
- Regardless of whether the tally was redone or not, Candidate B was not selected in the first round of review, so no harm was done.

2. Backdrop & factors of near-miss incident

- Professor A focused on Candidate B's research contents when determining whether or not there were conflicts of interest, and neglected to deeply consider their association with Candidate B's laboratory.

3. Factors that prevented misconduct & its backdrop

- Professor A remembered that they had coauthored a paper with Candidate B's laboratory.
- Professor A immediately explained the situation to all the members of the selection panel and was able to obtain their consent to redo the tally.

4. Possible research misconduct and questionable research practice

- Professor A would have violated the internal rule.
- If Candidate B had won the award, it would have meant that a party with a conflict of interest had participated in the review, which would throw the impartiality of the review into question.

5. Preventive countermeasures

- As strict management of conflict of interest is required of members of the selection panel, it is necessary to confirm the rules on conflict of interest related to the selection process and carefully investigate the conflict-of-interest relationship with the candidates when appointed as a member of the panel.

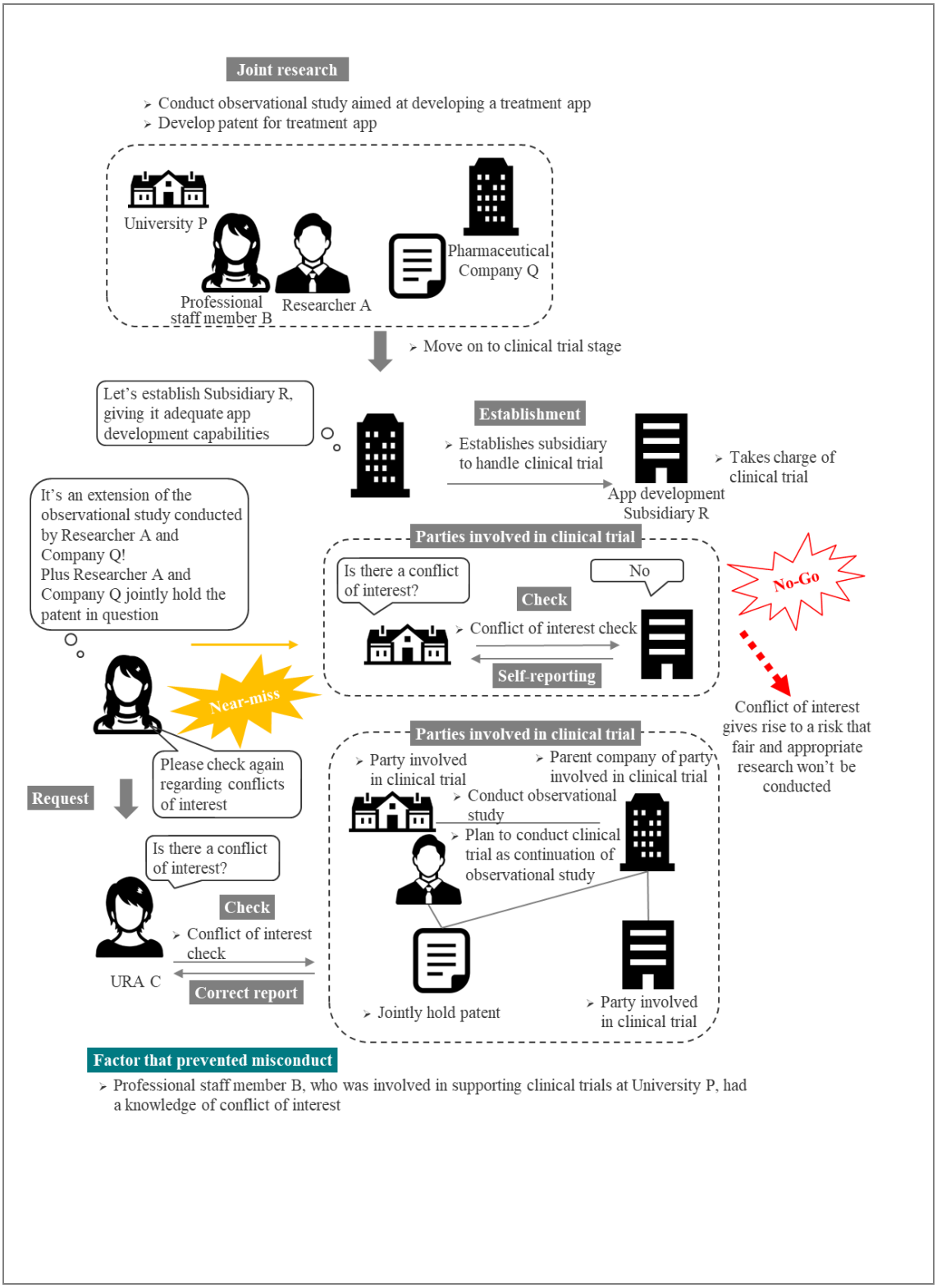
(Commentary)

When researchers think about conflicts of interest, they tend to focus on financial ones where money is involved through industry-academia collaborations. But researchers must also pay attention to any potential conflict of interest when serving as a member of review panel or selection panel for any awards and open call for participation. Problems may also arise in the management of personal or organizational conflict of interest if outsiders are able to objectively recognize that it may affect the impartiality of the judgment yet nothing is done to address it.

When academic societies or conferences select award winners, panel members are required to review and judge candidates from an unbiased and impartial perspective. But even if a panel member did review candidates in good faith, they might still inadvertently violate the internal rules for reviewing or overlook a conflict-of-interest relationship due to oversight. Panel members involved in the task of reviewing need to be fully aware that this can lead to serious problems.

6-4. Conflict of interest due to joint research with the parent company

Affiliated institution	University, University hospital	Field	Clinical medicine, computer science



1. Case details

- Researcher A at University P was conducting a joint observational study with Pharmaceutical Company Q regarding patient behavior and improvements in clinical condition among patients with a particular lifestyle-related disease. As part of the study, a treatment app supporting improvements in clinical condition had been created and a special algorithm developed for app implementation, for which a patent application had already been filed.
- Subsequently, a clinical trial using the treatment app was to be conducted, so Company Q set up Subsidiary R, equipping it with adequate app development capabilities, and decided that Subsidiary R would handle the clinical trial, including the clinical testing of the treatment app, verification of its effects, and the application for approval.
- As the parties involved in the clinical trial were University P and Subsidiary R, University P checked whether Subsidiary R had a conflict of interest, whereupon Subsidiary R self-reported that there were no financial conflicts of interest between them.
- However, professional staff member B, who was involved in supporting clinical trials at University P, realized that the clinical trial was a continuation of the observational study conducted by Researcher A and Company Q, and that the patent for the treatment app to be used in the clinical trial was held jointly by Researcher A and Subsidiary R's parent, Company Q. ☚ **Factor that prevented misconduct**
- Accordingly, University Research Administrator (URA)[1] C, who was in charge of dealing with conflicts of interest at University P, intervened to conduct another check of conflicts of interest before the clinical trial was conducted and had Subsidiary R correctly report the conflict of interest to University P.

2. Backdrop & factors of near-miss incident

- The prior research (observational study) conducted before the clinical trial for the treatment app handled by Subsidiary R and the patent application for the app were carried out by Subsidiary R's parent Company Q and University P, which constituted a conflict of interest. Despite this fact, Subsidiary R failed to report it when making its self-declaration.
- Researcher A, too, was unaware of the risk of a conflict of interest and did not adequately explain to URA C and others at University P the relationship between the observational study and the clinical trial.

3. Factors that prevented misconduct & its backdrop

- Professional staff member B, who was involved in supporting clinical trials at University P, had a knowledge of conflict of interest.

4. Possible research misconduct and questionable research practice

- Even though there was no direct relationship of interest between Researcher A and Subsidiary R, the latter's parent Company Q jointly held the patent with Researcher A, by virtue of having funded it, so having Subsidiary R conduct a clinical trial using that patent is a clear conflict of interest. Failing to report this fact constitutes a violation of the management of conflicts of interest.

5. Preventive countermeasures

- When having a company report its conflicts of interest, it is appropriate to oblige the company to report not only on those involved in the clinical trial in question, but also on such matters as the relationship between the parent company and its subsidiaries, and the implementation status of observational studies and the like conducted prior to the clinical trial.
- When having a researcher report their conflicts of interest, it is appropriate to oblige them to report not only on the clinical trial in question, but also on the implementation status of observational studies and the like conducted prior to the clinical trial.

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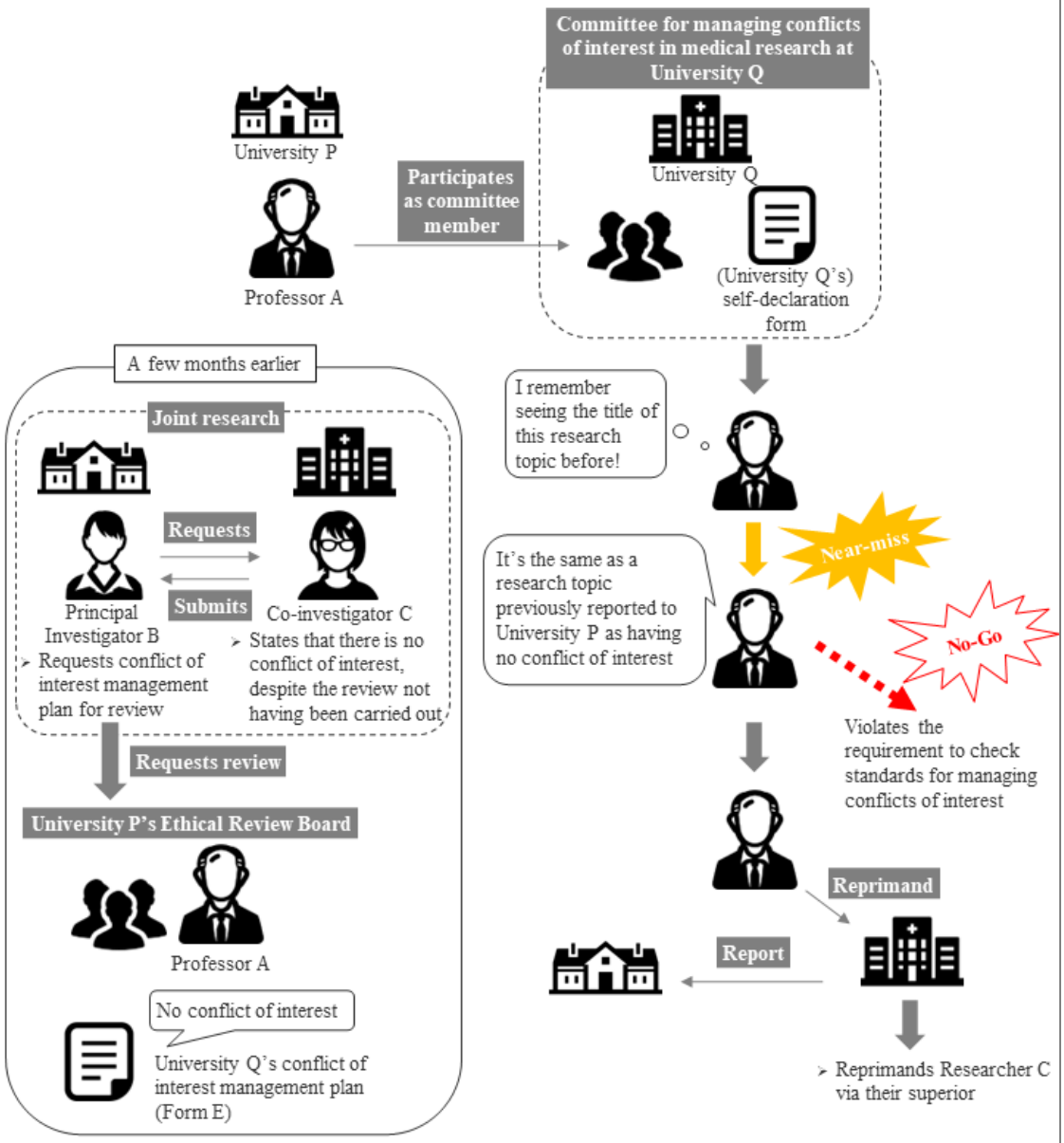
1 University Research Administrator: An individual carrying out such support duties as revitalizing researchers' research activities and enhancing the management of research and development.

6-5. Discrepancy between institutions in checking conflicts of interest in joint research

Affiliated institution	University, University hospital	Field	Clinical medicine



Factor that prevented misconduct

- Because Professor A was a member of both the committee for managing conflicts of interest in medical research at University Q and the Ethical Review Board at University P, they noticed that Co-investigator C at University Q had declared in the conflict of interest management plan that there were no conflicts of interest without waiting for confirmation of this fact

1. Case details

- University P and University Q were conducting joint medical research.
- Professor A at University P was a member of the committee for managing conflicts of interest in medical research at University Q. When checking for conflicts of interest relating to a particular study plan, Professor A recalled having heard the title of the research topic written on the self-declaration form. ☚ **Factor that prevented misconduct**
- When Professor A investigated further, they discovered that the title of the research topic was identical to one given on a conflict of interest management plan previously submitted to the Ethical Review Board at University P, which was the professor's main place of employment. Professor A was also a member of this Ethical Review Board and recalled that, in the previous review at University P, the conflict of interest management plan (Form E)[1] submitted by University Q, which was one of the institutions conducting the joint research, declared that there were no conflicts of interest.
- This meant that the study plan that should already have been reviewed at University Q was actually only now undergoing that review. In other words, whereas the review by University P was supposed to be based on the results of the review by the committee for managing conflicts of interest at University Q, the review by University Q had not actually been completed.
- When Professor A inquired with University Q to check on the study plan, they discovered that the meeting of University Q's committee for managing conflicts of interest had been postponed, resulting in the review being delayed past the time when it should have been completed. It also became apparent that Co-investigator C at University Q did not realize this delay in procedures had occurred and, assuming that the internal review had been completed, had submitted Form E to University P, stating on the form that there were no conflicts of interest.
- Professor A alerted the office at University Q to the situation and informed Co-investigator C at University Q via their superior that they must ensure such a situation never occurs again. University Q also reported to University P that the process had ended up out of sequence on this occasion due to certain circumstances.

2. Backdrop & factors of near-miss incident

- Co-investigator C at University Q and the office staff providing research support failed to fully track the status of the internal review of conflicts of interest at University Q.

3. Factors that prevented misconduct & its backdrop

- Because Professor A was a member of both the committee for managing conflicts of interest in medical research at University Q and the Ethical Review Board at University P, they noticed that Co-investigator C at University Q had declared in the conflict of interest management plan that there were no conflicts of interest without waiting for confirmation of this fact.

4. Possible research misconduct and questionable research practice

- This was a violation of the requirement to check standards for managing conflicts of interest under Article 21 of the Ordinance for Enforcement of the Clinical Trials Act (Ordinance of the Ministry of Health, Labour and Welfare).[2]

5. Preventive countermeasures

- Ensure that Ethical Review Board offices are able to check reports on the current status of conflict of interest management and the results of reviews at each collaborating institution, as needed, and put in place a system enabling the self-declaration forms submitted by each institution to be compared against each other.

(Commentary)

- Members of bodies such as Ethical Review Boards and conflict of interest committees have a duty of confidentiality. What action should a member take if they serve on multiple committees concurrently and notice a deficiency in a study plan?
- In this case, the error stemmed from Co-investigator C's assumption that University Q's internal conflict of interest review had been completed. However, if the researcher had little time to spare, for example, and was under a psychological burden as well, their rush to complete procedures could also have been a trigger for inappropriate conduct in the form of intentionally postponing the review at University Q.

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1 "Managing Conflicts of Interest in Clinical Trials under the Clinical Trials Act" (November 30, 2018 Health Policy Research Notice 1130 No. 17; Notice of the Director of the Research and Development Division, Health Policy Bureau, Ministry of Health, Labour and Welfare) https://www.mhlw.go.jp/content/10800000/000422858.pdf.

2 https://elaws.e-gov.go.jp/document?lawid=430M60000100017

Editor’s column 5: Smoking on airplanes

While smoking on airplanes were allowed in the 1980s, doing so now will raise a storm of vitriol and condemnation, and perpetrators will be charged with a crime. It is now almost a global norm where submitting contents that are almost identical to conference proceedings, giving gift authorship, or handling personal information without going through an ethics review are considered rule violations. What was not explicitly considered as misconduct in the past is now clearly being handled as misconduct or questionable practices.

As researchers, we are always updating research methods, since no one uses the Maxam-Gilbert method of DNA sequencing anymore. Similarly, it is clear that we must strive to understand and practice the latest standards of research ethics. Those who are in a position to lead their respective research fields and veterans whose remarks carry tangible and intangible weight are especially required to adopt an attitude of watching the world’s trends as well as making objective judgments.

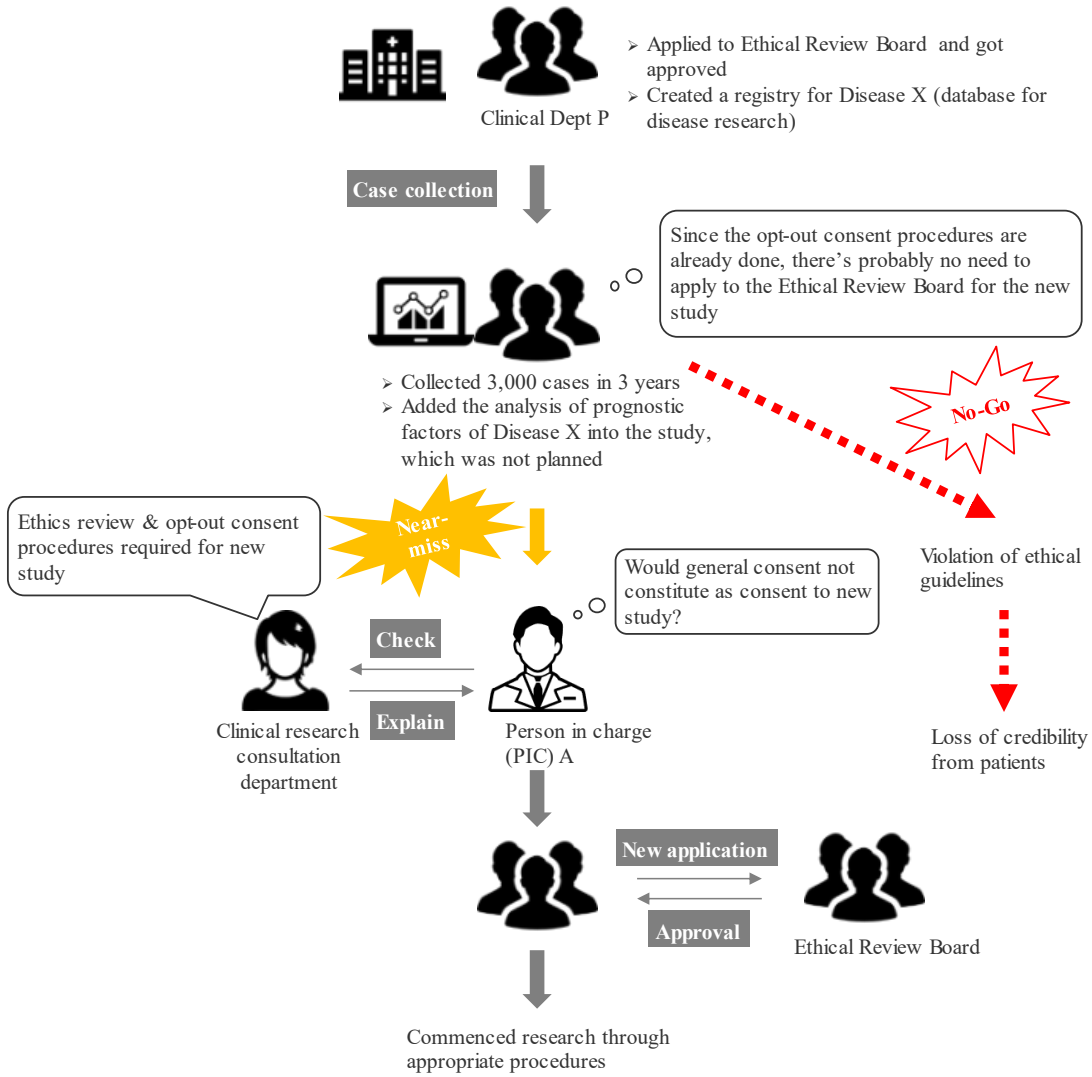
7 Violation of guidelines

1. Prevented violation of ethical guidelines when adding analysis based on registry data
2. Enrollment of more cases than the target sample size
3. Prevented fabrication of radioactive contamination monitoring data in RI facility
4. Failed to submit medical device loan confirmation letter*
5. Deficiency in procedures regarding the handover of specimens and data due to inadequate understanding of the Integrated Guidelines*
6. Use of a document with an outdated format to obtain patient consent*
7. Abuse of an opt-out*

Editor's column 6: Science and law

7-1. Prevented violation of ethical guidelines when adding analysis based on registry data

Affiliated institution	National/local government agency	Field	Medicine



Factors that prevented misconduct

- PIC A from Clinical department P remembered hearing at a workshop in the hospital that obtaining general consent from patients does not constitute consent to individual study plans, and decided to consult the clinical research consultation department out of caution

1. Case details

- Clinical department P created a multicenter disease registry[1] for Disease X.
- Although the Ethical Review Board had approved this study, its scope only involved the collection of medical records from general practice, and no specific analyses other than descriptive statistics were planned.
- Over a period of 3 years, they collected about 3,000 cases. Clinical department P decided to analyze prognostic factors[2] for Disease X in addition to the originally planned study. Since the Ethical Review Board had already approved the use of medical records for the study through opt-out[3] consent procedures, Clinical department P believed that they did not need to reapply to the Ethical Review Board to conduct analysis on the prognostic factors.
- However, the person-in-charge (PIC) A from Clinical department P wanted to perform an analysis that was not described in the study plan. Out of caution, PIC A decided to check with the clinical research consultation department, and was told that a new application for ethics review and opt-out consent procedures would be required. ☜ **Factor that prevented misconduct**
- After the necessary application and paperwork, Clinical department P conducted the study in accordance with the "Ethical Guidelines for Medical and Biological Research Involving Human Subjects (Medical Guidelines)".

2. Backdrop & factors of near-miss incident

- As Clinical department P had obtained the approval from the Ethical Review Board for the creation of this multicenter disease registry and had implemented opt-out consent procedures, they were under the mistaken impression that they could freely use the patient data from said registry for research.

3. Factors that prevented misconduct & its backdrop

- PIC A from Clinical department P remembered hearing at a workshop in the hospital that obtaining general consent from patients does not constitute consent to individual study plans, and decided to consult the clinical research consultation department out of caution.

4. Possible research misconduct and questionable research practice

- If the study was initiated without the opt-out consent procedures stipulated in the Medical Guidelines or without another review by the Ethical Review Board, it could be considered a serious violation of ethical guidelines.

5. Preventive countermeasures

- The Medical Guidelines require those involved in clinical research to undergo training in research ethics. They also need to, in particular, fully understand the necessity of the Ethical Review Board and opt-out consent procedures before engaging in research.
- It is best to have a consultation department for clinical research where researchers can ask questions or discuss without any restraint or hesitation.

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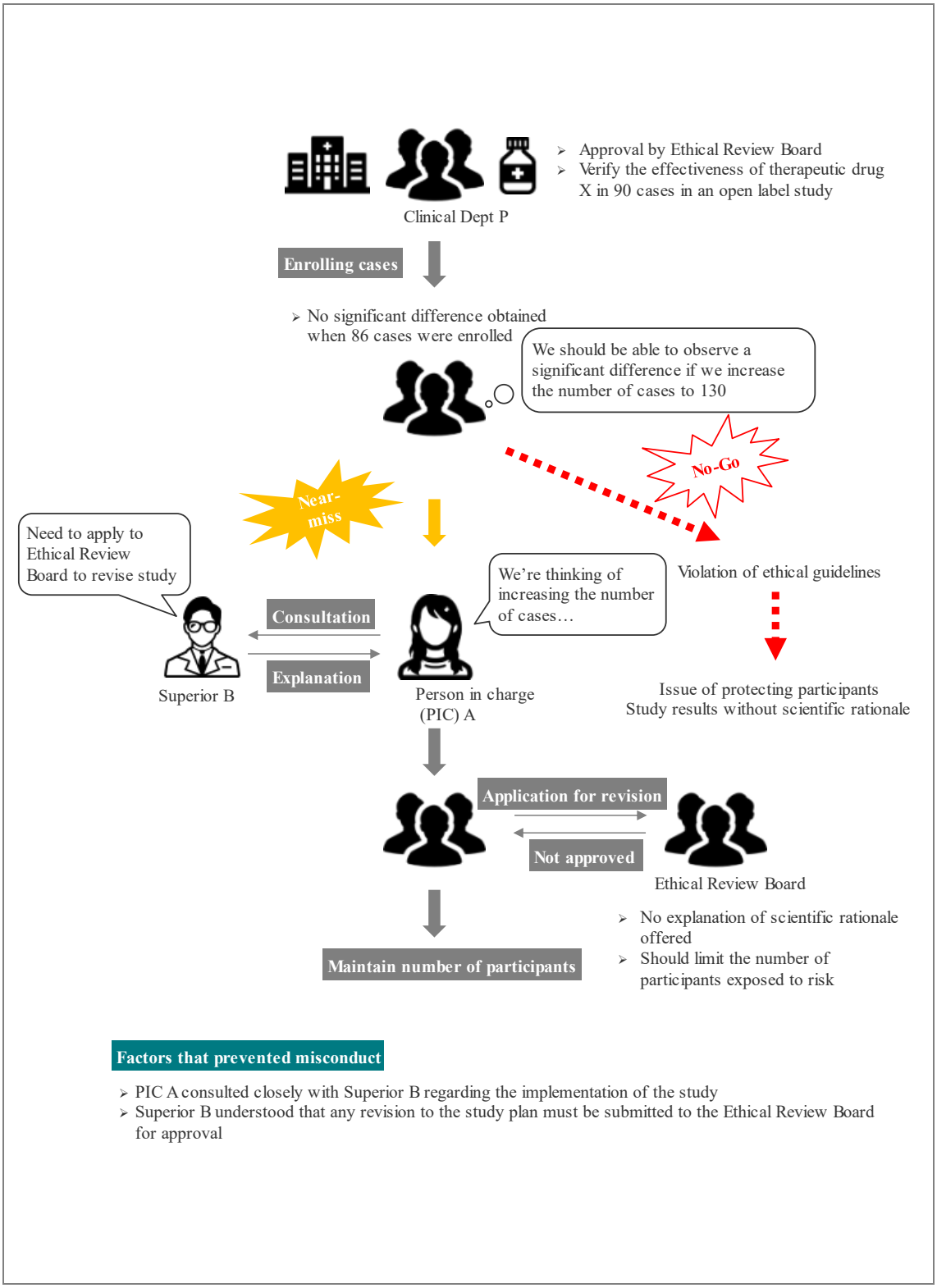
1 A method of statistically analyzing information of patients with a specific disease where multiple institutions collaborate to register their information in a database.
2 Factors that affect outcomes independently of treatment.
3 A method employed in clinical studies that meet certain conditions and use only patient information (such as medical records) where participants, who are informed of the objectives and the details of the study, or otherwise disclosed, are included in the study without direct consent from individual participants while ensuring them opportunities to refuse the study as much as possible.

7-2. Enrollment of more cases than the target sample size

Affiliated institution	University, University hospital	Field	Medicine



Factors that prevented misconduct

- PIC A consulted closely with Superior B regarding the implementation of the study
- Superior B understood that any revision to the study plan must be submitted to the Ethical Review Board for approval

1. Case details

- To examine the effectiveness of therapeutic drug X, Clinical department P conducted an open-label[1] study comparing the outcomes in patients treated with it against those that were not treated with it.
- The study plan approved by the Ethical Review Board listed a target sample size of 90 cases. But by the time 86 cases had been enrolled in the study, the outcomes in the two groups were not as different as expected. This meant that a statistically significant difference was unlikely even if they hit the target sample size.
- Clinical department P thought that increasing the number of cases to 130 would increase the possibility of getting a statistically significant difference, and decided to continue enrolling more cases beyond the target sample size of 90 cases. When person-in-charge (PIC) A asked Superior B if it would be okay to continue the study, PIC A was told that they would need to apply to the Ethical Review Board to revise their study plan, which they did. ☜ **Factor that prevented misconduct**
- The Ethical Review Board found no scientific rationale for the additional enrollment to the target number of cases in their review, and did not approve the request for revision.

2. Backdrop & factors of near-miss incident

- As Clinical department P had already obtained the approval of the Ethical Review Board for the comparative study, they were under the mistaken impression that increasing the number of participants beyond the target sample size so as to achieve good results would not pose any ethical or scientific issues.

3. Factors that prevented misconduct & its backdrop

- PIC A from Clinical department P consulted closely with Superior B regarding the implementation of the study.
- Superior B understood that any revision to the study plan must be submitted to the Ethical Review Board for approval.

4. Possible research misconduct and questionable research practice

- Conducting the study with a sample size bigger than the target number already described in the study plan may expose participants to unnecessary risks. Revising the study plan without getting it reviewed by the Ethical Review Board constitutes a deviation from the ethics of medical and biological research involving human subjects.
- Increasing the number of cases which is not backed by any scientific rationale is highly likely to result in a study with little clinical significance. Moreover, the act of increasing the number of cases by looking at the results of significance tests in the middle of a study could have led to erroneous conclusions due to the problem of statistical multiplicity [2].

5. Preventive countermeasures

- Researchers should share information on the progress of the research with each other, and if necessary, check if there is a need to apply to the Ethical Review Board when reviewing the study plan.
- Prudent judgment is required when increasing the number of cases. The scientific rationale and ethical appropriateness of the revision must be examined by the Ethical Review Board.

(Commentary)

The number of cases required for a study should be established based on scientific evidence; it should not be unnecessarily increased to limit the number of participants exposed to risk and for researchers to make efficient use of research resources.

The revision of eligibility conditions for participants, intervention methods, target sample size, and other parameters of the study plan are considered important revisions from both ethical and scientific perspectives, and such revisions require an application to the Ethical Review Board.

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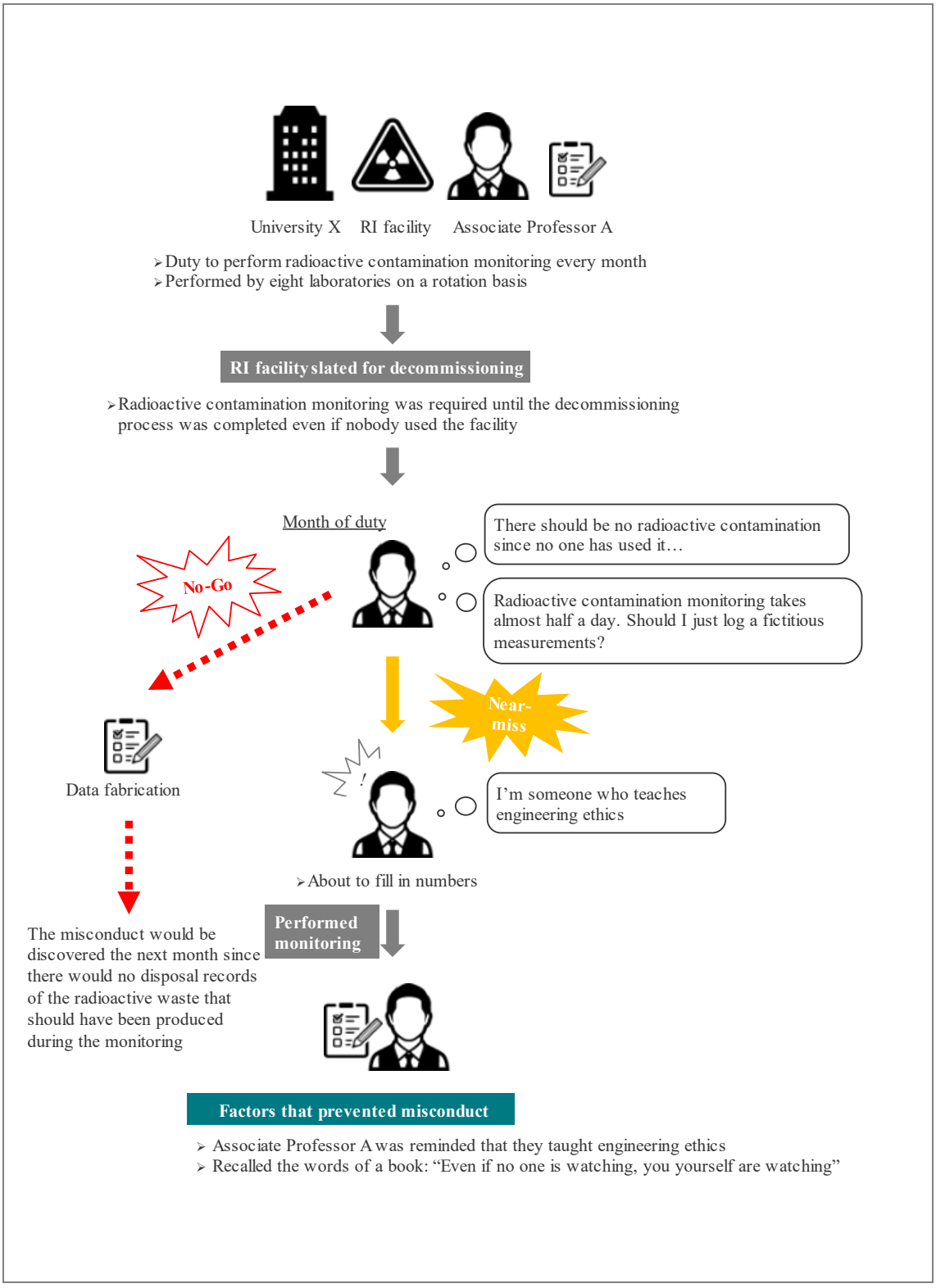
1 A study comparing treatments in which both the medical staff and the patients are aware of the treatment being given. This awareness of which treatment is being given may affect the results, and is less reliable than the blinded approach where both parties are not informed.

2 A problem that performing multiple tests is associated with more likelihood of obtaining a significant result of a certain test. It arises when selecting the most favorable result among several test results obtained.

7-3. Prevented fabrication of radioactive contamination monitoring data in RI facility

Affiliated institution	University, University hospital	Field	Life sciences



1. Case details

- The university to which Associate Professor A belongs has a radiation-controlled area (known as an RI facility), where monthly radioactive contamination monitoring was required. The radioactive contamination monitoring was performed by eight laboratories on a rotation basis, where they were supposed to measure and record the radiation levels at 20 locations in the RI facility.
- The RI facility was slated for decommissioning and had not been used at all in the last several months. But the radioactive contamination monitoring was required until the decommissioning process was completed.
- When it was Associate Professor A's turn to perform the radioactive contamination monitoring, they thought that "there should be no radioactive contamination since no one has used the facility for several months", and decided to randomly fill in numbers for the radiation levels in the logbook.
- Just when Associate Professor A was about to fill in the numbers, they remembered their position as a lecturer of engineering ethics. ☜ **Factor that prevented misconduct**
- Associate Professor A changed their mind about fabricating radiation levels data and performed radioactive contamination monitoring as per the rules.

2. Backdrop & factors of near-miss incident

- The radioactive contamination monitoring required wiping areas at 20 locations in the RI facility (such as floors) with filter paper and measuring the radiation level on the wipe by inserting it into a measuring instrument, as well as measuring radioactive aerosols in more than 10 locations with a dosimeter. Associate Professor A deemed it a troublesome task since it would take almost half a day to complete, including cleaning up after the measurement.
- Since the RI facility was slated for decommissioning and had not been used at all in the last several months, Associate Professor A thought there would be no radioactive contamination.

3. Factors that prevented misconduct & its backdrop

- Associate Professor A remembered that they taught engineering ethics and was strongly reminded that he should not fabricate radioactive contamination monitoring data.
- A scene from a book, where a father admonished his son who was about to cheat that "even if no one is watching, you yourself are watching", that Associate Professor A read when they were a student left an indelible impression on them. Associate Professor A had been reminded of that scene several times after reading that book, and he thought that this case was just the same.

4. Possible research misconduct and questionable research practice

- If Associate Professor A had justified to himself that there should be no radioactive contamination since the RI facility had not been used in the last few months, and randomly filled in numbers without performing radioactive contamination monitoring, he would have violated the University's guidelines and his act construed as data fabrication.
- The filter papers used in radioactive contamination monitoring have to be recorded and disposed of as radioactive waste. If Associate Professor A fabricated the data, there would be no record of it in the disposal logbook. At any rate, the misconduct would be discovered at a later time.

5. Preventive countermeasures

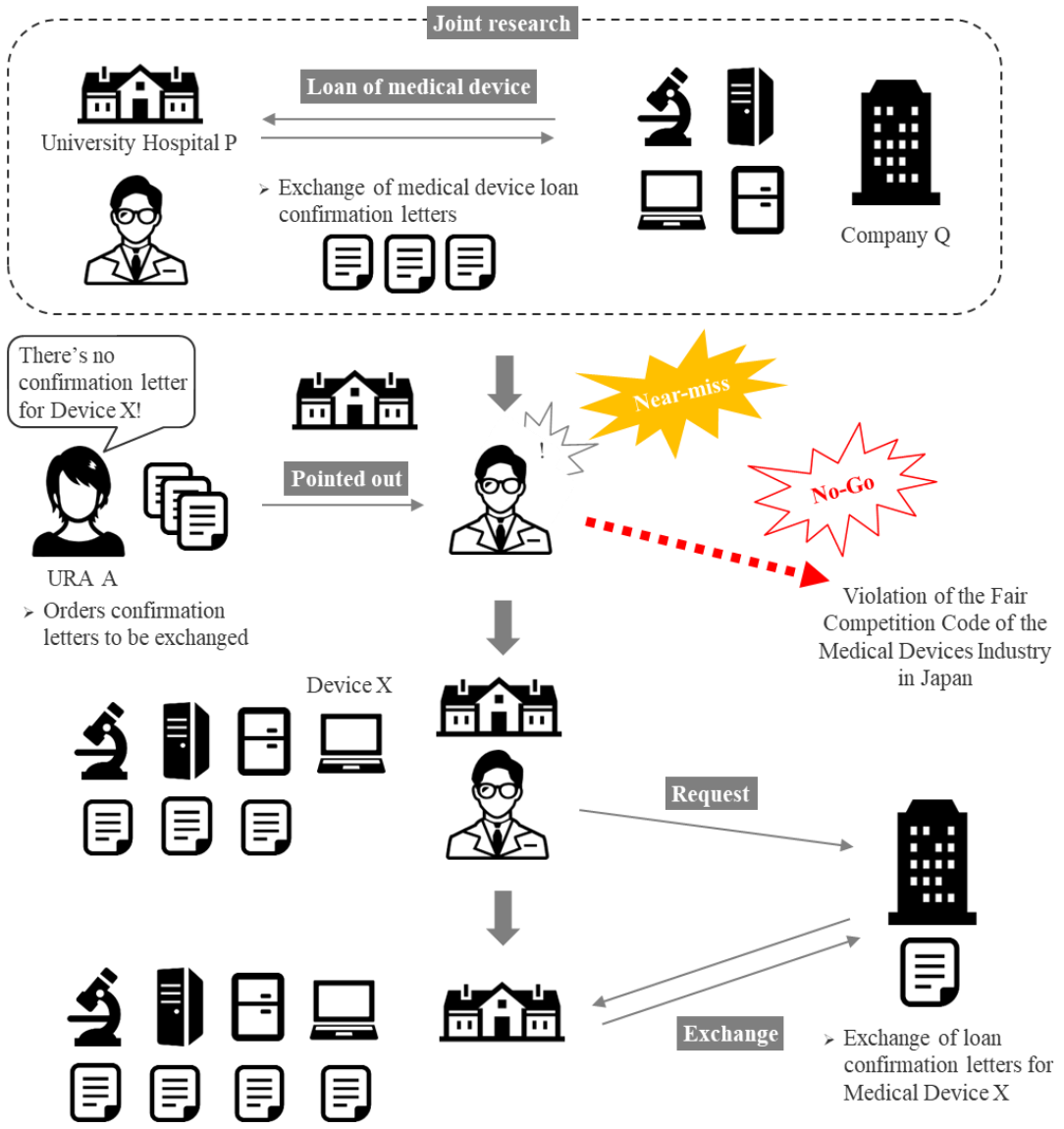
- Users of RI facility are required to undergo education and training to understand and recognize that radioactive contamination monitoring is important not only to protect their health and safety, but also to show nearby residents that the users of the facility are properly following the rules, as well as to remind students and young researchers to be self-disciplined as scientists.

(Commentary)

On the surface, radioactive contamination monitoring of an unused RI facility may appear excessive and inefficient. However, we must not forget that as scientists, we have earned the trust of the public by properly handling harmful and dangerous substances by strictly following the rules. We should also be a role model to the next generation of leaders to not be fixated with short-term gains or losses, or to look for loopholes.

7-4. Failed to submit medical device loan confirmation letter

Affiliated institution	University, University hospital	Field	Medicine



Factor that prevented misconduct

- At University Hospital P, URA A had a wide-ranging knowledge of research procedures and carried out appropriate checks
- University Hospital P had adopted a system under which the URA responsible for dealing with conflicts of interest conducted checks while the IRB was carrying out its review

1. Case details

- University Hospital P was to receive a medical device on loan from Company Q when undertaking joint clinical research with Company Q.
- Under the Fair Competition Code of the Medical Devices Industry in Japan, in the event of the loan of a medical device, University Hospital P and Company Q needed to exchange medical device loan confirmation letters detailing the purpose of the loan, details of the device being loaned, the cost burden, and the duration of the loan.[1]
- When University Hospital P's Institutional Review Board (IRB) checked for conflicts of interest, A, who was the University Research Administrator (URA) handling the matter, realized that no confirmation letter had been submitted for Medical Device X. ☚ **Factor that prevented misconduct**
- URA A notified Company Q of this fact via University Hospital P, and University Hospital P and Company Q exchanged confirmation letters for Medical Device X.

2. Backdrop & factors of near-miss incident

- The front-line coordinators at University Hospital P and Company Q were unaware of the existence and necessity of the confirmation letter.
- Company Q lacked an adequate system for managing and recording the places to which medical devices were lent, including the creation of loan records by having confirmation letters submitted in exchange for the devices.
- University Hospital P lacked an adequate system for managing and recording the companies from which it had received medical devices on loan.

3. Factors that prevented misconduct & its backdrop

- At University Hospital P, URA A had a wide-ranging knowledge of research procedures and carried out appropriate checks.
- University Hospital P had adopted a system under which the URA responsible for dealing with conflicts of interest conducted checks while the IRB was carrying out its review.

4. Possible research misconduct and questionable research practice

- Violation of the Fair Competition Code of the Medical Devices Industry in Japan, which is a set of rules for the medical device industry that has been accredited by the Secretary-General of the Consumer Affairs Agency and the Japan Fair Trade Commission.

5. Preventive countermeasures

- Notify researchers of the rule that medical device loan confirmation letters must be exchanged when receiving medical devices on loan.
- While IRB reviews include checks relating to conflicts of interest described in the study plan (such as the provision of funding or supplies by companies and the like), their role does not usually encompass checks for procedural deficiencies of this kind. Consequently, during ethical reviews, it is effective for the person responsible for dealing with conflicts of interest to also check that there are no violations of codes of this kind.
- Company Q had an adequate understanding of the fair competition code as a company, but there is a risk that a thorough understanding was lacking at the level of individual coordinators. Put in place internal company regulations in the form of a procedure manual for lending out medical devices and a system for checking these, as well as conducting regular in-house training.
- Rather than leaving matters concerning the loan of medical devices to the judgment of front-line staff, Company Q will put in place an integrated recording and management system based on the aforementioned procedure.
- Similarly, University Hospital P will prescribe the procedure for receiving loans of medical devices and put in place an integrated recording and management system based on this procedure, rather than leaving matters concerning the receipt of medical devices to the judgment of front-line staff.

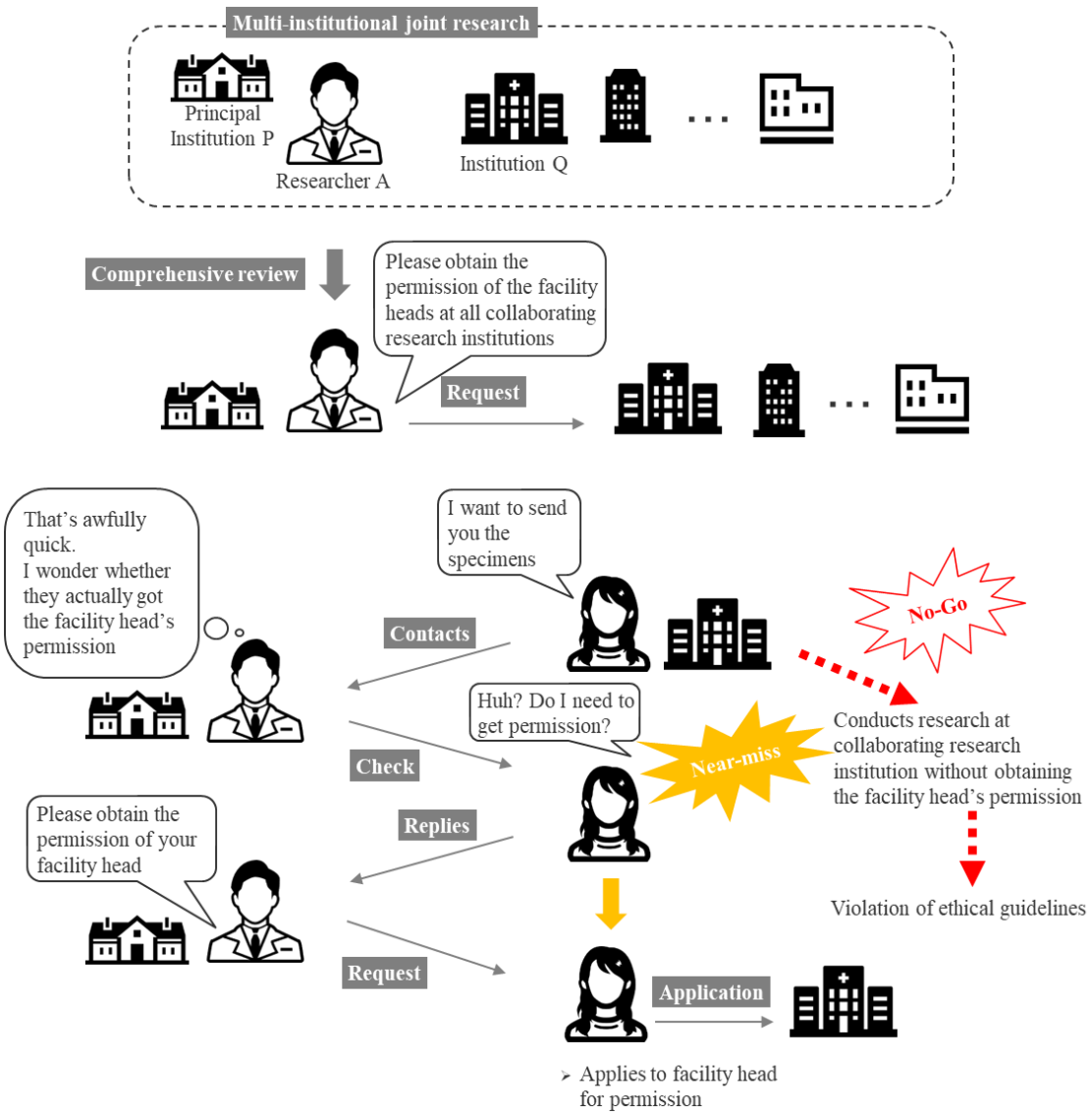
(Commentary)

Formerly, when university hospitals lacked medical devices and the like for dealing with emergencies, companies would lend them at their discretion and management of this practice was often lax, but such loans are now completely prohibited. The code stipulates that free loans must be for no more than 1 month for demonstration purposes, no more than 6 months for the purpose of clinical testing, and no more than 12 months for research at a medical institution.

1 https://www.jftc-mdi.jp/pdf/kashidashi_kijyun_202009.pdf

7-5. Deficiency in procedures regarding the handover of specimens and data due to inadequate understanding of the Integrated Guidelines

Affiliated institution	National/local government agency	Field	Medicine



Factor that prevented misconduct

- Harboring doubts about how early the request for samples had come from Institution Q, Researcher A immediately checked whether the facility head had granted permission.

1. Case details

- Two sets of government guidelines, the Ethical Guidelines for Medical and Health Research Involving Human Subjects (hereinafter, the Guidelines for Medical Research) and the Ethical Guidelines for Human Genome/Gene Analysis Research (hereinafter, the Genome Guidelines), were integrated to create the Ethical Guidelines for Medical and Biological Research Involving Human Subjects[1] (hereinafter, the Integrated Guidelines), which entered into force in June 2021.
- Under the Integrated Guidelines, the principal institution may conduct a comprehensive ethical review, rather than each of the collaborating research institutions involved in the joint study having to conduct their own review. Once approval has been granted on the basis of the comprehensive review, research at each institution can begin, as long as the head of the facility at the institution in question has granted permission.
- In a large-scale multi-institutional joint study of a particular disease, just when institutions had recently switched over to the Integrated Guidelines, Principal Institution P conducted a comprehensive review and the organization's office contacted the collaborating research institutions to request that they obtain the permission of their facility heads.
- Subsequently, Institution Q contacted Principal Institution P, asking to be sent some specimens (existing samples obtained for clinical purposes). As the request to be sent the specimens had been received rather earlier than expected, Researcher A at Principal Institution P decided to err on the side of caution and checked with Institution Q to ensure that there had been no deficiency in the procedure for obtaining permission from the facility head, whereupon they discovered that Institution Q had not obtained the facility head's permission. ☚ **Factor that prevented misconduct**
- Principal Institution P requested that Institution Q obtain permission from the facility head.

2. Backdrop & factors of near-miss incident

- Due to the switchover from the existing Genome Guidelines and Guidelines for Medical Research to the new Integrated Guidelines, some institutions did not fully understand the approach to comprehensive reviews by the principal institution prescribed in the Integrated Guidelines (namely the fact that each collaborating institution needed to obtain permission from the facility head based on the results of the comprehensive review).
- When notifying the participating institutions that approval had been granted as a result of the comprehensive review, Principal Institution P should have informed them that each of them needed to obtain the facility head's permission and have this confirmed by the office before providing information or sending out specimens.

3. Factors that prevented misconduct & its backdrop

- Harboring doubts about how early the request for samples had come from Institution Q, Researcher A immediately checked whether the facility head had granted permission.

4. Possible research misconduct and questionable research practice

- A violation of the Integrated Guidelines, resulting in a risk that research would have been conducted at the collaborating institution without obtaining the facility head's permission.

5. Preventive countermeasures

- Establish more efficient and effective means of communication between participants in joint research. In particular, it is necessary to increase the frequency of communication and ensure thorough information sharing between offices and data centers receiving specimens.
- Establish protocols for the handover of specimens and data, in accordance with the Integrated Guidelines. In particular, ensure full awareness of the fact that specimens and data cannot start being acquired or sent to the principal institution unless the facility head's permission has been obtained.
- Ensure that an understanding of the Integrated Guidelines becomes prevalent among stakeholders at participating institutions, including community hospitals. Hold briefings and training sessions for this purpose.
- If guidelines, etc. have undergone substantial revisions, make a thorough check of the differences between the old and new versions in terms of procedures and the like, and take care to ensure that you do not breach the guidelines, etc.

(Commentary)

In this case, the Integrated Guidelines would have been breached if new specimens had already been collected before obtaining the facility head's permission.

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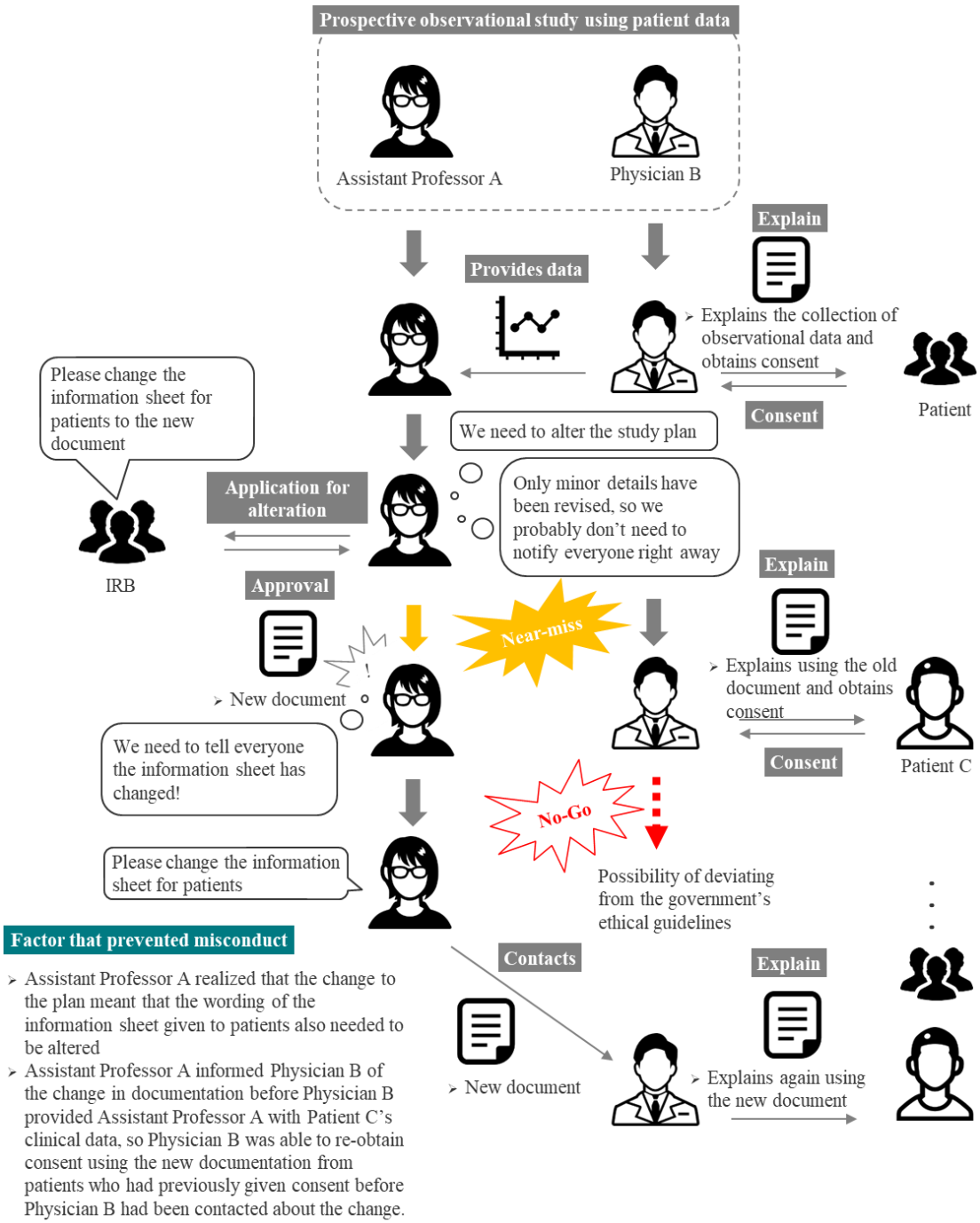
1 Ethical Guidelines for Medical and Biological Research Involving Human Subjects (https://www.mhlw.go.jp/content/000909926.pdf)
Guidance on the Integrated Guidelines (https://www.mhlw.go.jp/content/000946358.pdf)

7-6. Use of a document with an outdated format to obtain patient consent

Affiliated institution	University, University hospital	Field	Clinical study



Factor that prevented misconduct

- Assistant Professor A realized that the change to the plan meant that the wording of the information sheet given to patients also needed to be altered
- Assistant Professor A informed Physician B of the change in documentation before Physician B provided Assistant Professor A with Patient C's clinical data, so Physician B was able to re-obtain consent using the new documentation from patients who had previously given consent before Physician B had been contacted about the change.

1. Case details

- Assistant Professor A was conducting a prospective[1] observational study using patient data.
- The physicians explained the purpose of the study to the patients (or their legal guardians) who came for outpatient consultations and obtained consent to use their clinical data.
- Minor details in the study plan were revised or altered during the course of the study period, so an application to alter the study plan was submitted to the Institutional Review Board (IRB), which granted approval for the changes. Consequently, the information sheet used to explain the purpose of the study to patients was also altered.
- However, Physician B had not been informed of the change in documentation, so used the old document when explaining the study to Patient C, who granted consent.
- Immediately after this, Assistant Professor A contacted Physician B to inform them of the change in documentation, which meant Physician B promptly realized that the explanation given to Patient C was incorrect. ☚ **Factor that prevented misconduct**
- Before receiving the clinical data for the study, Physician B gave Patient C and all the other patients from whom consent had previously been obtained an explanation based on the new document.

2. Backdrop & factors of near-miss incident

- As minor details in the study plan had been revised or altered, those associated with the study thought the impact of the changes would be minor and unimportant. Consequently, the sharing of information about the matter with physicians was regarded as a low priority.

3. Factors that prevented misconduct & its backdrop

- Assistant Professor A realized that the change to the plan meant that the wording of the information sheet given to patients also needed to be altered.
- Assistant Professor A informed Physician B of the change in documentation before Physician B provided Assistant Professor A with Patient C's clinical data, so Physician B was able to re-obtain consent using the new documentation from patients who had previously given consent before Physician B had been contacted about the change.

4. Possible research misconduct and questionable research practice

- There was a possibility that this might fall under "Deficiency in procedures for obtaining informed consent," which is explained in Chapter 6, No. 11, Section 1. (3) 2. of the Guidance on Ethical Guidelines for Medical and Biological Research Involving Human Subjects[2] as something that undermines the ethical validity of research.

5. Preventive countermeasures

- Notify all stakeholders when submitting to the IRB an application to alter the study plan.
- If an information sheet used for obtaining patient consent has been changed, the research office should ensure thorough awareness of and compliance with the practice of collecting the old documents from cabinets, etc. at physicians' outpatient desks and replacing them with the new documents.

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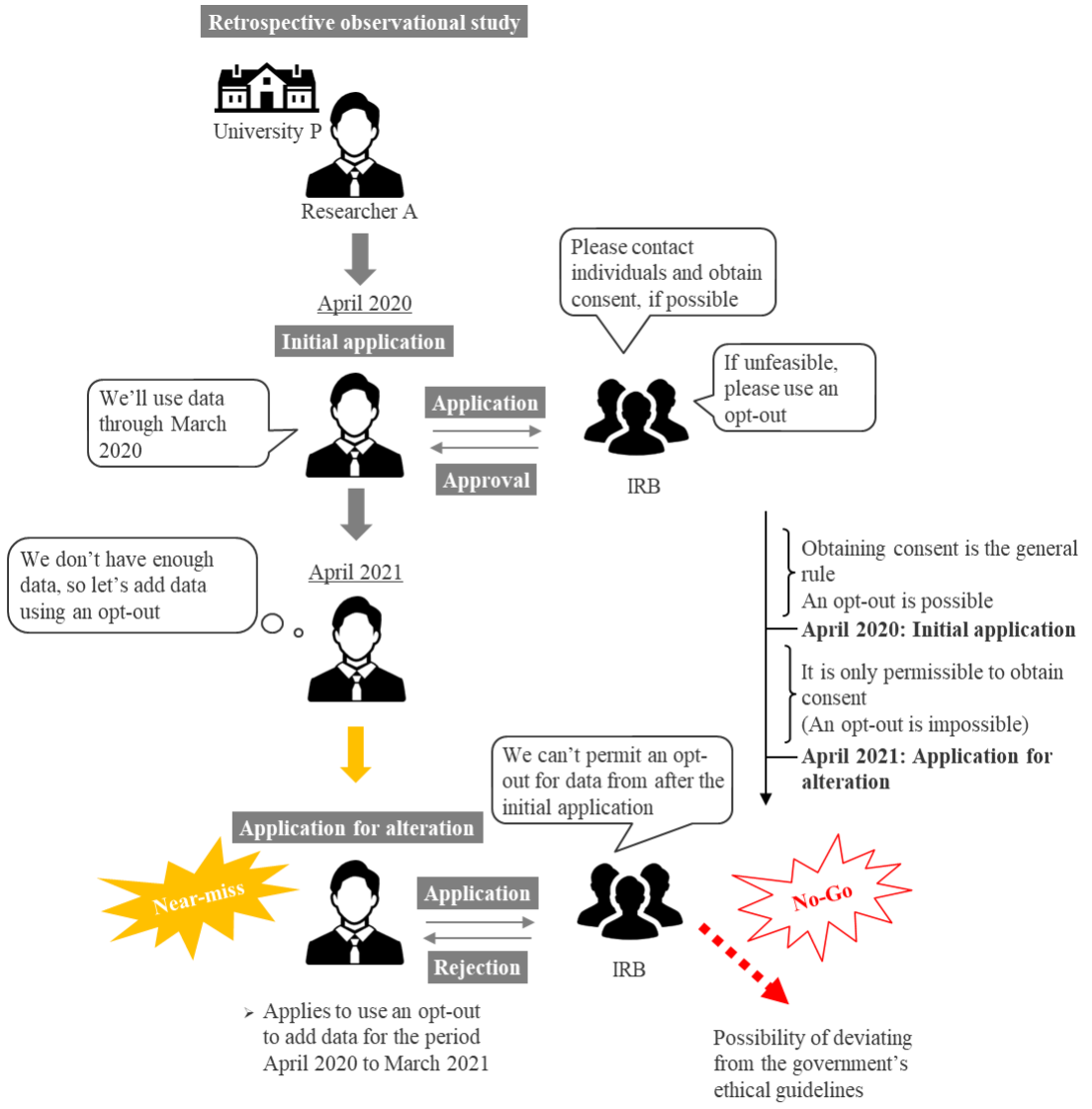
1 A prospective study is a type of epidemiological study in which individuals who were exposed to a suspect factor and individuals who were not are selected from a predefined population and are observed going forward to see whether they develop the disease identified as a problem, with the incidence of the disease in the two groups being compared. It may also be known as a cohort study or a follow-up study. Conversely, a retrospective study focuses on a group that is already suffering from the disease identified as a problem and a group that is not, with researchers gathering information about past exposure to the factor posited as a hypothesis and comparing the two groups. https://www.jaam.jp/dictionary/dictionary/word/0704.html

2 https://www.mhlw.go.jp/content/000946358.pdf

7-7. Abuse of an opt-out

Affiliated institution	University, University hospital	Field	Life sciences



Factor that prevented misconduct

- When the application for alteration of the retrospective study was submitted, the IRB at University P checked the timings of the initial application and the collection of the additional case data obtained, along with the informed consent (IC) procedure

1. Case details

- Researcher A at University P was conducting a retrospective[i] observational study. The study was approved in April 2020 and the study plan involved receiving clinical data obtained between March 2019 and March 2020. It was approved on the basis that data would be received under the opt-out method if it was difficult to obtain consent from research subjects.
- In April 2021, when Researcher A scrutinized the data for the retrospective observational study, they discovered that they had been unable to collect sufficient data for the planned observational study.
- Accordingly, having decided to extend the target period for cases eligible for inclusion in the study to March 2021 and add data via the opt-out method,[ii] Researcher A submitted an application for alteration to the Institutional Review Board (IRB).
- Normally, when receiving clinical data for prospective observational studies, it was the general rule at University P that informed consent (IC) should be obtained verbally or in writing.
- In accordance with this general rule, it was not permitted to change a study plan to receive data under an opt-out, because it is not impossible to obtain consent to receive clinical data collected during a period that is prospective at the time of the initial application. Accordingly, the IRB office did not approve the request for alteration. ☚ **Factor that prevented misconduct**

2. Backdrop & factors of near-miss incident

- Researcher A did not understand that there was a general rule that consent for the provision of data should be obtained verbally or in writing when seeking the provision of clinical data collected during a period that is prospective at the time of the initial application.
- In other retrospective observational studies at University P, there had frequently been applications to the IRB office for alterations aimed at extending the study period, on the grounds of a lack of data (to incorporate cases that were prospective at the time of the initial application). The researcher was not fully aware that casually extending the study period and seeking to obtain data under an opt-out for cases for which consent could be obtained, just because of a lack of data, breached University P's policy on obtaining consent in prospective observational studies.

3. Factors that prevented misconduct & its backdrop

- When the application for alteration of the retrospective study was submitted, the IRB at University P checked the timings of the initial application and the collection of the additional case data obtained, along with the informed consent (IC) procedure.

4. Possible research misconduct and questionable research practice

- Potential to violate Chapter 4, No. 8, Section 1. of the Ethical Guidelines for Medical and Biological Research Involving Human Subjects,[iii] which states, "[A]s a general rule, prior informed consent must be obtained as set out in the study plan for which the head of the research institution has granted permission," and also University P's policy on obtaining consent for prospective observational studies, in accordance with these guidelines.

5. Preventive countermeasures

- Particularly in the case of retrospective studies begun under an opt-out, oblige researchers to state in the study plan that the study will be discontinued if there is insufficient data. At University P, while the study plan template contains wording stating that, in the case of retrospective studies, the study will be abandoned if there is insufficient data, many researchers apparently delete this part of the wording.
- One conceivable response measure would be to end the current study and draw up the final report, and then to apply to conduct a new retrospective study beginning in April 2021. Appropriately establishing the period for the receipt of clinical data would make it possible to obtain data for the period March 2019 to March 2020 and also the subsequent period up to the time of application. For data from April 2020 onward, consent should be obtained from research subjects, as far as possible, with the opt-out procedure being used in cases where this is unfeasible.

(Commentary)

- Regarding opt-outs, the Guidance on the Ethical Guidelines for Medical and Biological Research Involving Human Subjects stipulates the following about describing procedures for obtaining informed consent in the study plan.
  - If using an opt-out for consent, it is necessary to notify research subjects, etc. of the reason for this and also of the fact that the study will be conducted, or to describe such matters as the matters to be placed in a state in which the research subjects, etc. can easily find out about them and the methods to be used for this (e.g. sample notifications or documents to be placed in a state in which the research subjects, etc. can easily find out about them). ...When using an opt-out, sample notifications or documents to be placed in a state in which the research subjects, etc. can easily find out about them must be appended to the study plan and provided to the IRB for review.
- At the time of the initial application, Researcher A planned to conduct a retrospective study and had obtained both IRB approval and the permission of the head of their institution to conduct the study, but ended up needing to use data that was prospective from the perspective of the starting point of the study, so the nature of the study changed. In addition, it was conceivably because of University P's policy that consent should be obtained for prospective observational studies in which obtaining Informed Consent is possible that the IRB refused to approve the application for alteration based on adding cases under an opt-out.
- The guidelines state that researchers, etc. are not necessarily required to obtain informed consent and may employ the opt-out procedure if using existing information (data obtained for the purpose of routine medical care, rather than for research purposes) held at their own research institution for the study (Chapter 4, No. 8, Section 1. (2) b)). University P's policy likely attaches greater importance to the principle of obtaining consent from research subjects, but many other research institutions have also instituted rules and policies over and above the laws, regulations, and guidelines established by the government. When conducting research, it is necessary to thoroughly check and understand the regulations and guidelines at your own institution.
- This case provides an appropriate subject for exchanging views on approaches to informed consent when using data amassed during routine medical care in research.

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i A form of longitudinal study in which data is collected retrospectively for a certain period. This method involves investigating whether subjects have been exposed to a factor that caused a disease or disability (for example, falls in patients who have undergone a total hip replacement), starting from the point at which the study begins and working backwards. https://www.jspt.or.jp/ebpt_glossary/retrospective-study.html

ii As a general rule, entities handling personal information must obtain consent from the individual concerned before supplying their personal information to a third party. In contrast, under the opt-out method, the need to obtain consent individually is removed by disclosing beforehand the items of personal information to be provided to the third party. Under these circumstances, the individual concerned can make a request after the fact, asking for the provision of information to the third party to be halted, and the entity handling personal information is required to ensure that the individual can find out this fact, by such means as notifying the individual directly or posting the information online or at its office.

iii Ethical Guidelines for Medical and Biological Research Involving Human Subjects (March 23, 2021) (https://www.mhlw.go.jp/content/000909926.pdf)

Editor’s column 6: Science and law

Rules and laws can be described as agreements to prevent the occurrence of misconduct or wrongdoing that has been repeatedly committed. On the other hand, as scientists, we value originality and make our living by unravelling what no one knows yet, solving problems that no one can solve yet, and providing the society with new knowledge and conveniences. But like pollution and drug-induced sufferings, new knowledge and conveniences almost always bring forth new problems at the same time. As scientists, we can be the ones who are the first to notice these problems and therefore are able to take the most efficient countermeasures. And this is also why we can be tasked to come up with the new rules necessary to do so.

But it is not enough for scientists to just follow the existing rules. For us to be able to come up with new ones, we need to understand the purpose of the existing rules and interpret them accordingly (looking for loopholes in rules is not what scientists should do) (see Editor’s column 6: “The process of developing ethical awareness”). The establishing of rules also mean that some values will be sacrificed. We scientists need to be aware of the diversity of values so that we can make constructive suggestions from a broad perspective. It can also be said that one of the main purposes of studying general education courses at the university is to learn about this diversity of values.

8 Reliability and reproducibility of research data

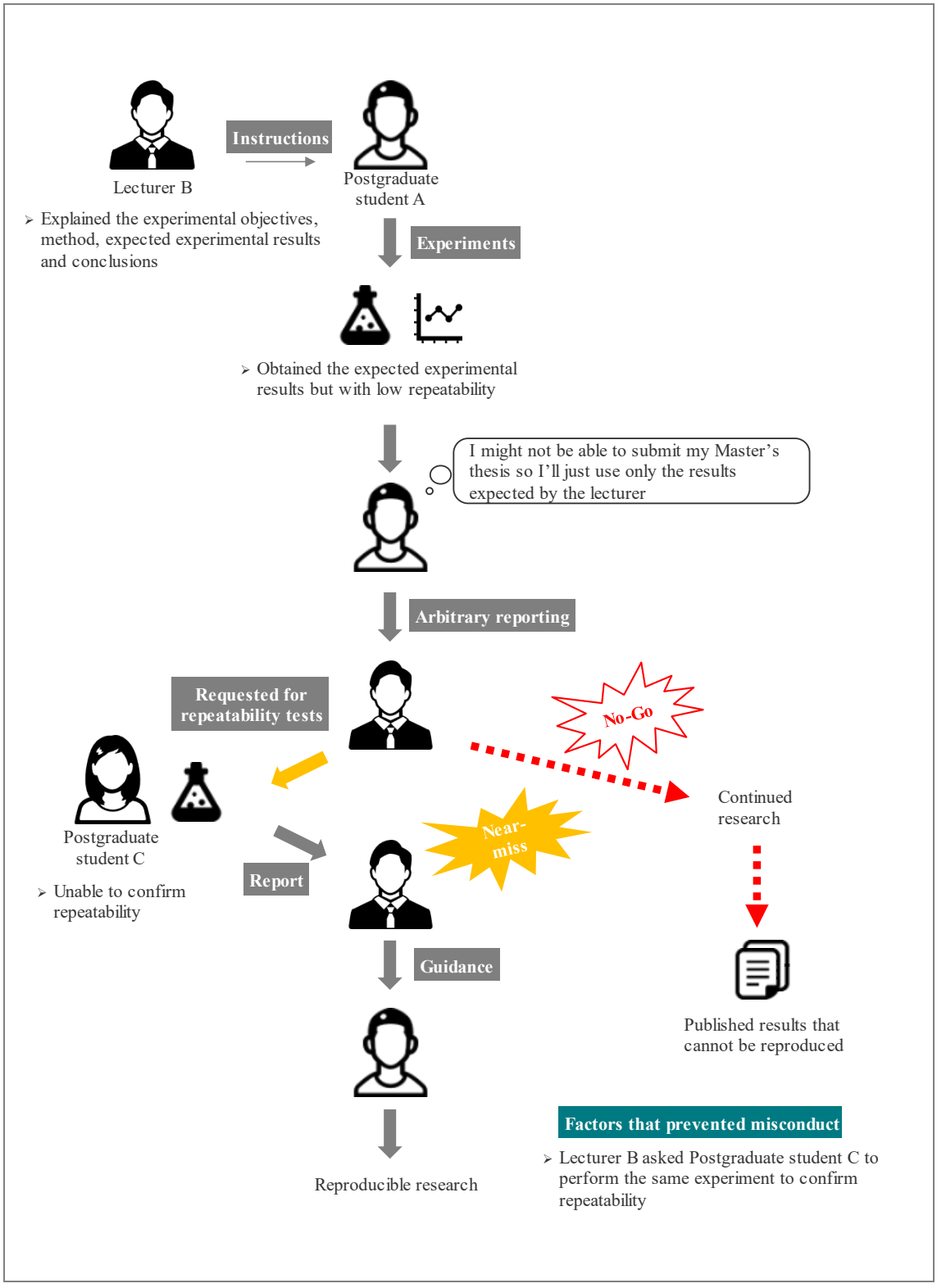
1. Reporting only data as expected by the supervisor
2. Discovery of errors in predecessor's program
3. Case where research was suspended after a problem was pointed out in the research data of a co-researcher
4. Use of investigational drug that was not stored under proper temperature control
5. Protocol violation in a clinical trial
6. Change of clinical study plan after registration with system

Editor's column 7: The process of developing ethical awareness

7. Prevented questionable research practice (HARKing)
8. Prevented questionable research practice (p-hacking)
9. Attempt to report on the outcomes of research differing from the study plan*

8-1. Reporting only data as expected by the supervisor

Affiliated institution	University, University hospital	Field	Basic medical research



1. Case details

- Lecturer B was supervising Postgraduate student A's Master's thesis.
- Lecturer B instructed Postgraduate student A to conduct a certain experiment, and also explained the experimental objectives, method, expected experimental results and the conclusions that could be drawn from them.
- Postgraduate student A conducted the experiment as instructed and did obtain the results that were expected by Lecturer B. But most of the time, the results were not what were expected, meaning that the repeatability of the experimental results was low.
- Postgraduate student A extracted and reported only the results expected by Lecturer B, and made no mention of the unexpected results.
- To confirm the results, Lecturer B instructed another Postgraduate student C to perform the same experiment but the repeatability was low. ☜ **Factor that prevented misconduct**
- When Lecturer B checked with Postgraduate student A, Postgraduate student A revealed that they were aware of the low repeatability. But out of fear that they would be reprimanded if they did not produce the results as expected by Lecturer B, and that they might not be able to submit their Master's thesis, they chose to put the data that would support the hypothesis in the report instead.
- Lecturer B supervised Postgraduate student A again and told them the importance of confirming the repeatability of experimental results and properly considering all results that were obtained.

2. Backdrop & factors of near-miss incident

- Postgraduate student A was not well educated about the importance of repeatability of experimental results.
- Postgraduate student A was under the mistaken impression that they would be reprimanded if they did not produce the experimental results expected by Lecturer B, as well as not being able to submit their Master's thesis and get the degree.
- Postgraduate student A believed online posts such as "there are many fraudulent papers by Japanese researchers" and mistakenly thought that "it is common to commit research misconduct".

3. Factors that prevented misconduct & its backdrop

- Lecturer B asked Postgraduate student C to perform the same experiment to check the repeatability.

4. Possible research misconduct and questionable research practice

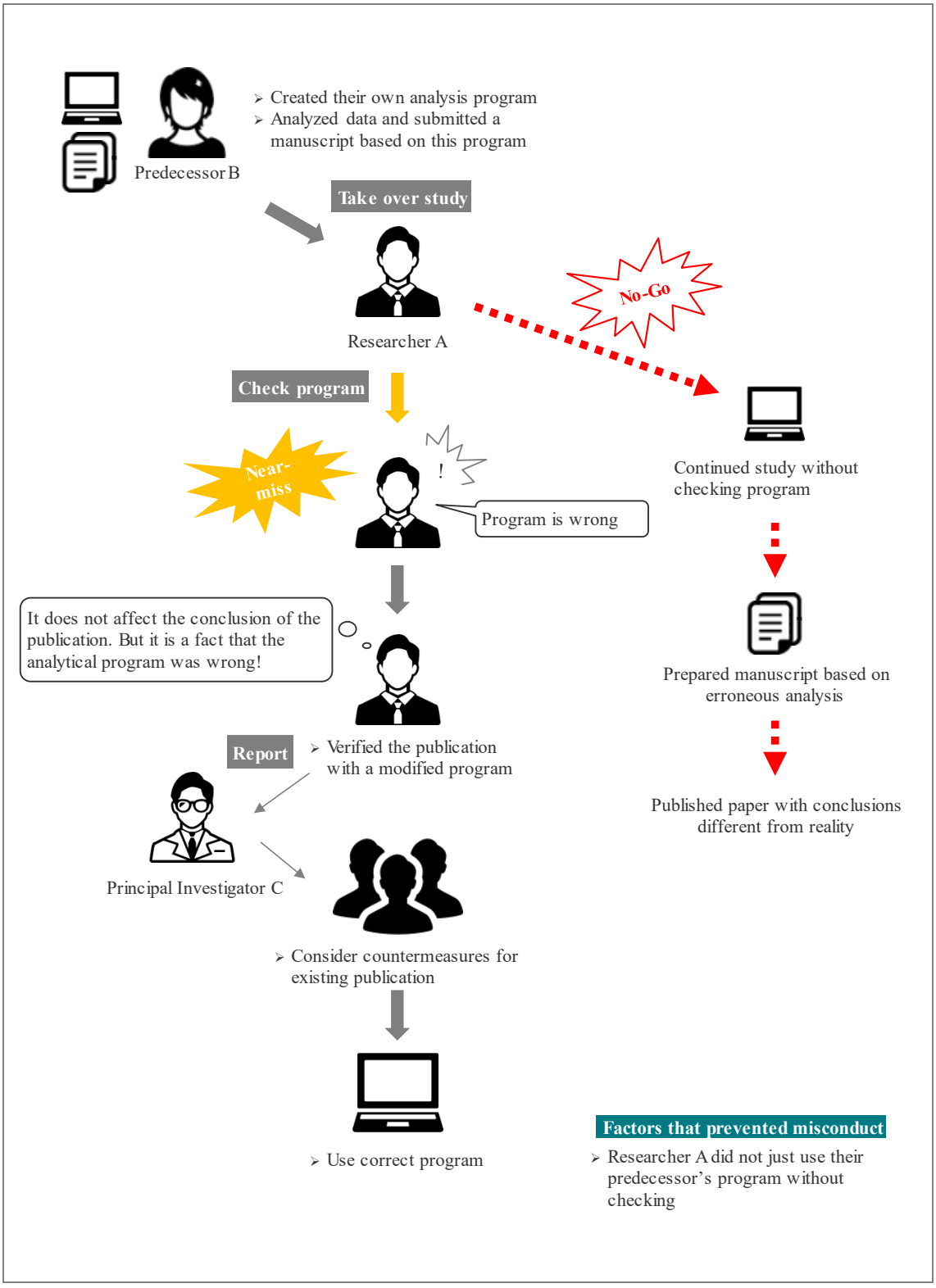
- Their paper that only reported the results that supported their hypothesis could have been published, to which other researchers would not be able to reproduce those experimental results.

5. Preventive countermeasures

- Educate researchers, including students, that reproducibility is one of the most important issues in science.
- Always mention the possibility of unexpected results when providing research guidance.
- Strive to provide an environment that is conducive to free and open communication with the research group to build mutual trust.
- Where possible, get multiple members of the research group to perform the same experiment to confirm the repeatability of the experimental results.
- Educate researchers to understand the risks of unquestioningly believing information from the Internet and other sources, as well as the importance of checking the reliability of data sources and verifying the veracity of information.

8-2. Discovery of errors in predecessor's program

Affiliated institution	University, University hospital	Field	Life sciences



1. Case details

- Researcher A was asked to continue Predecessor B's study during their overseas studies in the United States.
- As Researcher A had to take over the study and use the software that was created by Predecessor B, Predecessor B taught Researcher A how to use the program.
- Through that process, Researcher A carefully examined the program and discovered errors in it. ☜ **Factor that prevented misconduct**
- As a paper had already been published based on the results using the program, Researcher A proceeded to verify the results using the modified program, just to be sure.
- While they did not need to change the conclusion of the publication even with the results obtained from the modified program, Researcher A immediately reported the errors of the program to Principal Investigator C.

2. Backdrop & factors of near-miss incident

- Instead of the genetic code from the International DNA Data Bank (which is usually used by others), the program in question used a proprietary, unique genetic code – a method that would normally be not considered.
- Principal Investigator C left the creation of the program to Predecessor B, and accepted the analysis results without questioning.

3. Factors that prevented misconduct & its backdrop

- Researcher A was able to discover the errors in the program because they thought that they should properly check the software created by Predecessor B before using it.
- Although the errors in the program did not affect the conclusion of the publication, Researcher A immediately reported it to Principal Investigator C.

4. Possible research misconduct and questionable research practice

- A paper with erroneous conclusions could have been published based on results obtained from a study utilizing erroneous analysis.

5. Preventive countermeasures

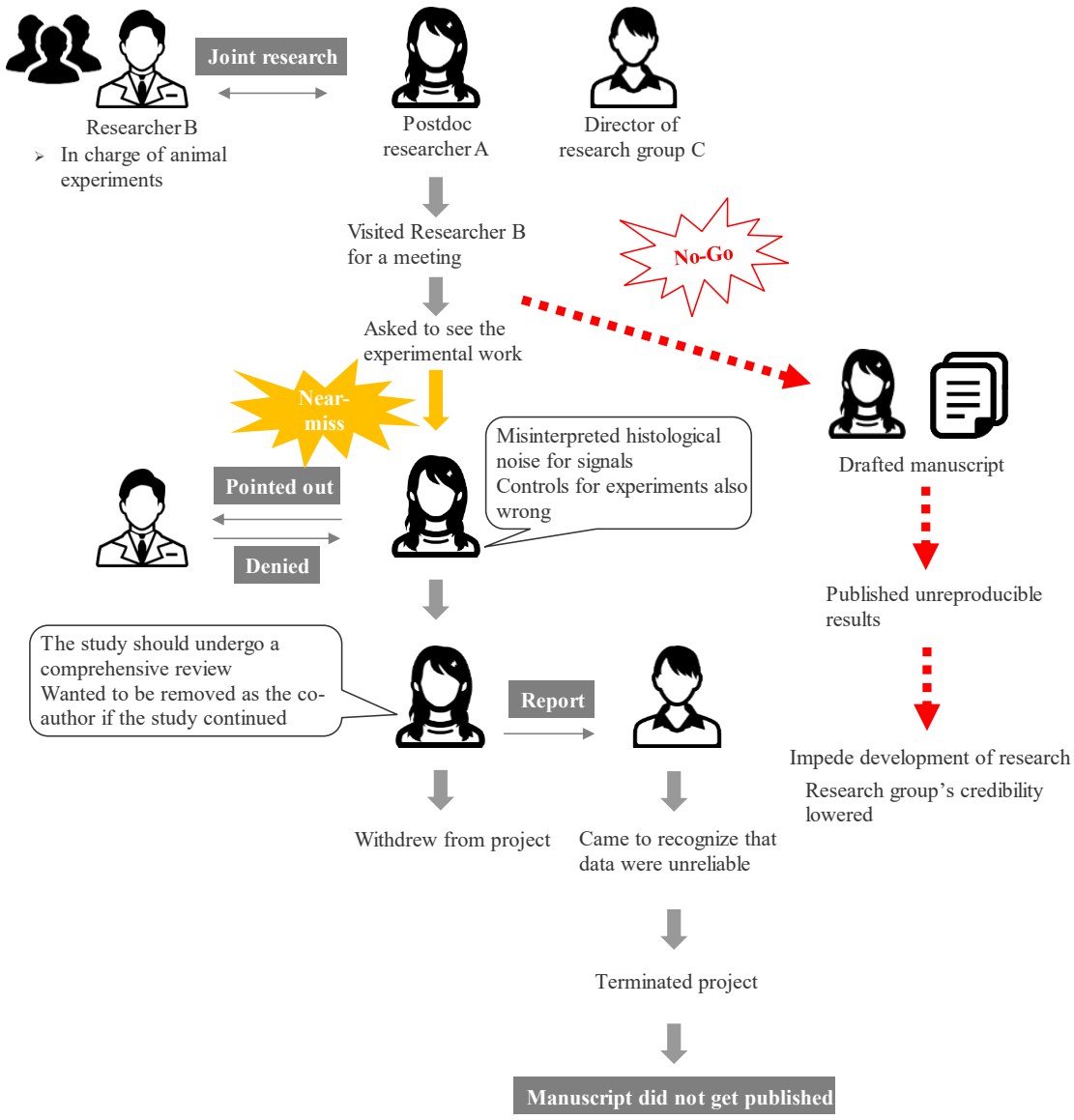
- Use software and programs created and tested by reputable suppliers.
- If you have no choice but to use software or programs that are created by others, you should scrutinize the details of the program and only use it after you have verified that the correct results can be obtained with samples with known, accurate answers.

(Commentary)

If there are errors in one's created program, the researcher must report them to their superior without delay. If there are serious errors in the program that would affect publications, or if a researcher noticed these errors but the program produced favorable results to support the researcher's study, the researcher may hesitate to report them. And this is precisely the kind of situation that must be promptly reported to superiors and dealt with appropriately. Errors are "negligence" that can happen to anyone and should be tolerated, but failure to report them is "deliberate" and unacceptable.

8-3. Case where research was suspended after a problem was pointed out in the research data of a co-researcher

Affiliated institution	University, University hospital	Field	Life sciences (Study involving transplantation of cell lines into experimental animals)



Factors that prevented misconduct

- Researcher A visited their co-researcher's laboratory and noticed that the experimental procedures and interpretation of results were not properly performed

1. Case details

- Researcher A was participating in joint research that involved multiple research groups. Experiments of transplanting cells into animals – the most important part of the study – were entrusted to Researcher B's group that has a dedicated facility.
- When they obtained favorable data and decided the direction of the manuscript to be submitted, Researcher A visited Researcher B's laboratory for a meeting and asked to observe the experimental work. In contrary to what Researcher A had assumed, Researcher B had misinterpreted the completely meaningless noise in the cell images as signals. Researcher A also realized that Researcher B was an extremely inexperienced researcher because they did not conduct the animal experiments with proper controls. Although Researcher A pointed it out on the spot, Researcher B did not acknowledge the mistakes.
- After Researcher A left Researcher B's laboratory, they immediately suggested the Director of research group C to conduct a comprehensive review of the study. As the Director of research group C did not understand Researcher A's concerns in the beginning, Researcher A then strongly insisted that they wanted to be removed as a co-author if they continued the study. ☜ **Factor that prevented misconduct**
- Researcher A withdrew from that study. Shortly thereafter, Director of research group C also came to recognize that Researcher B's data were unreliable and terminated the research project. As a result, they were able to prevent the publication of a paper based on incorrect data in advance.

2. Backdrop & factors of near-miss incident

- In many cases, joint research is conducted based on trusting the other party's Principal Investigator, and there are very few opportunities to confirm the competence of the person actually performing the experimental work or the reliability of the experimental techniques.
- In this joint research, Researcher A trusted their co-researcher to handle everything and did not verify the protocols for the important experimental work and data among the multiple groups.

3. Factors that prevented misconduct & its backdrop

- Researcher A visited their co-researcher's laboratory for a meeting and was able to observe the experimental work for particularly important data.
- Researcher A strongly expressed their concerns to the Director of research group C.

4. Possible research misconduct and questionable research practice

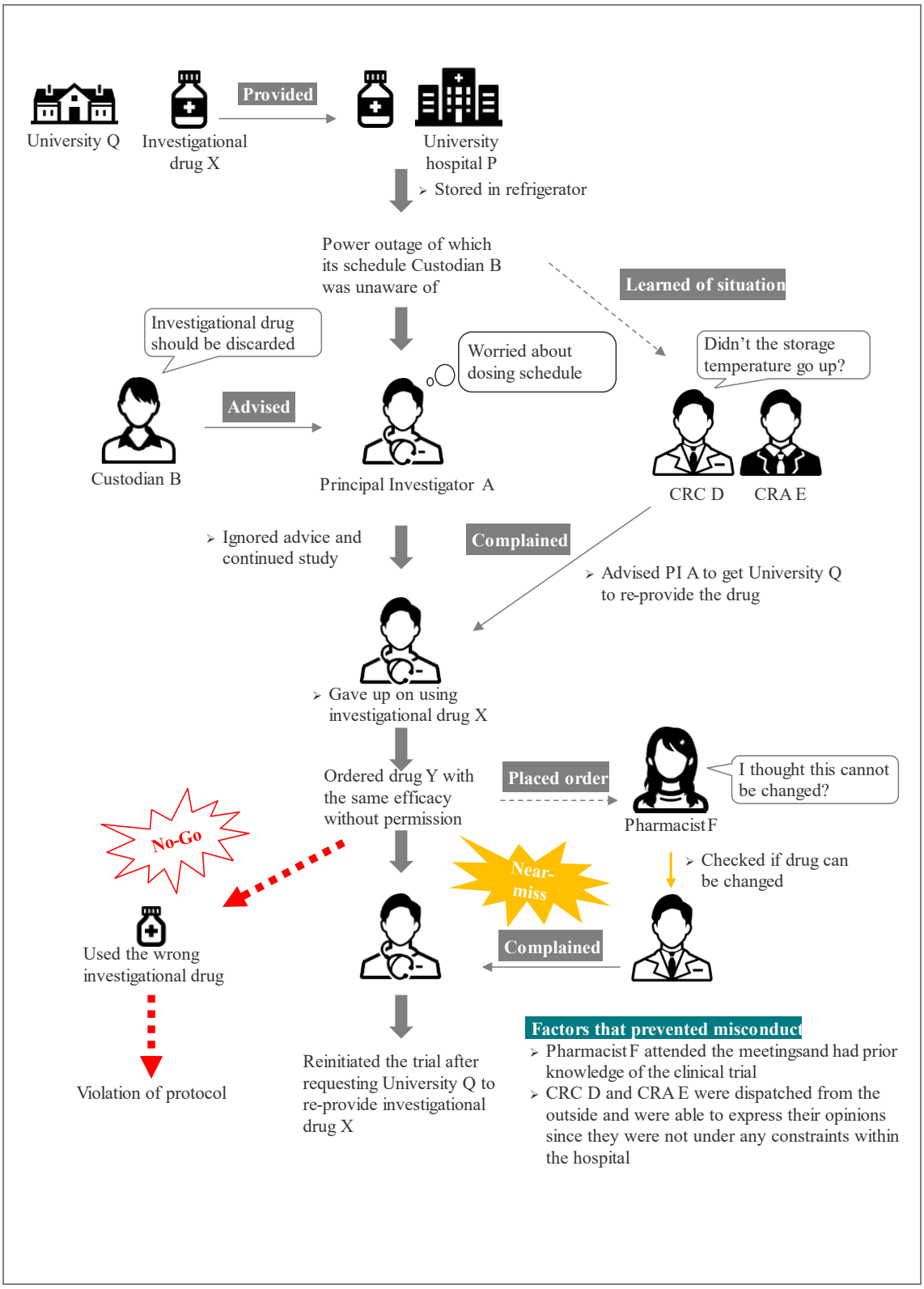
- The extent to which the data were inaccurate is unclear, but if they had trusted the data and used it in the paper, it is highly likely that other researchers would report the paper's results as unreproducible.
- If they had published unreproducible results, not only would that research group lose its credibility and lower its own reputation in their field of research, but also inconvenience the researchers who would reference that paper.

5. Preventive countermeasures

- When conducting joint research, identify the members of the group that will participate in the study, and check their research backgrounds and accomplishments where possible.
- Make arrangements for all parties to verify important data.
- Although it is necessary to trust the other party, the principal investigator must take responsibility to create a system where all parties can verify each other's data, even if the other party is a well-known researcher.
- If the study requires special facilities or equipment, it tends to be left to the group that has that equipment. But when important results are obtained in the joint research, opportunities should be created for everyone to critically examine the accuracy and reproducibility of the data, as well as the detailed conditions and critical experimental procedures.

8-4. Use of investigational drug that was not stored under proper temperature control

Affiliated institution	University, University hospital	Field	Clinical trial



1. Case details

- Principal Investigator A was conducting a clinical trial of investigational drug X provided by University Q at University hospital P. The investigational drug X had to be refrigerated and was managed by Custodian B.
- A power outage, of which its schedule Custodian B was unaware of, happened. The power supply to the refrigerator that contained the investigational drug X was cut off and the temperature rose. Since the refrigerator was not equipped with a temperature data logger, Custodian B advised Principal Investigator A to discard the investigational drug X just to be on the safe side.
- But Principal Investigator A thought that that would interfere with the dosing schedule and attempted to continue using the drug without reporting it to the department managing study safety. When Clinical Research Coordinator (CRC)[1] D and Clinical Research Associate (CRA)[2] E got to know it, they complained to Principal Investigator A and advised him to ask University Q to re-provide investigational drug X.
- Principal Investigator A then gave up on using the investigational drug X managed by Custodian B, but ordered drug Y that had the same efficacy and was stored in the hospital, from the pharmacy instead.
- Pharmacist F, who received the order, checked with CRC D. It then became clear that Principal Investigator A was trying to use drug Y instead of the investigational drug X for the study. ☜ **Factor that prevented misconduct**
- Clinical trial was reinitiated after University Q re-provided investigational drug X.

2. Backdrop & factors of near-miss incident

- Although it started with Custodian B not being aware of the campus's power outage schedule, the investigational drug X had to be refrigerated due to its instability. Principal Investigator A underestimated the importance of temperature control and was extremely worried about the delays in the dosing schedule.
- Principal Investigator A attempted to continue using the investigational drug X without reporting it to the department managing study safety.
- Principal Investigator A also ignored repeated advice from Custodian B, CRC D, and CRA E, and attempted to continue with the trial using drug Y in the hospital.

3. Factors that prevented misconduct & its backdrop

- As CRC D was dispatched from an external site management organization, they could express their opinions without hesitation to Principal Investigator A since they were not part of the hierarchical relationships nor under other constraints within the hospital.
- Since Pharmacist F had attended the clinical trial meetings and understood the details of the trial, they felt the need to confirm with CRC D whether the order for drug Y was appropriate or not.

4. Possible research misconduct and questionable research practice

- If they had used the investigational drug stored under unknown or inconsistent conditions, or drugs that were not described in the protocol, they could have harmed the health of the trial participants and compromised the reliability of the data.

5. Preventive countermeasures

- Diversifying the composition of the members involved in the clinical trial and creating a system that would involve multiple people through their respective roles can increase the chances of discovering errors and inappropriate behavior.
- To avoid excessive pressure on the principal investigator, foster a sense of conducting the study as a team by holding regular meetings and sharing the progress of the study with them.

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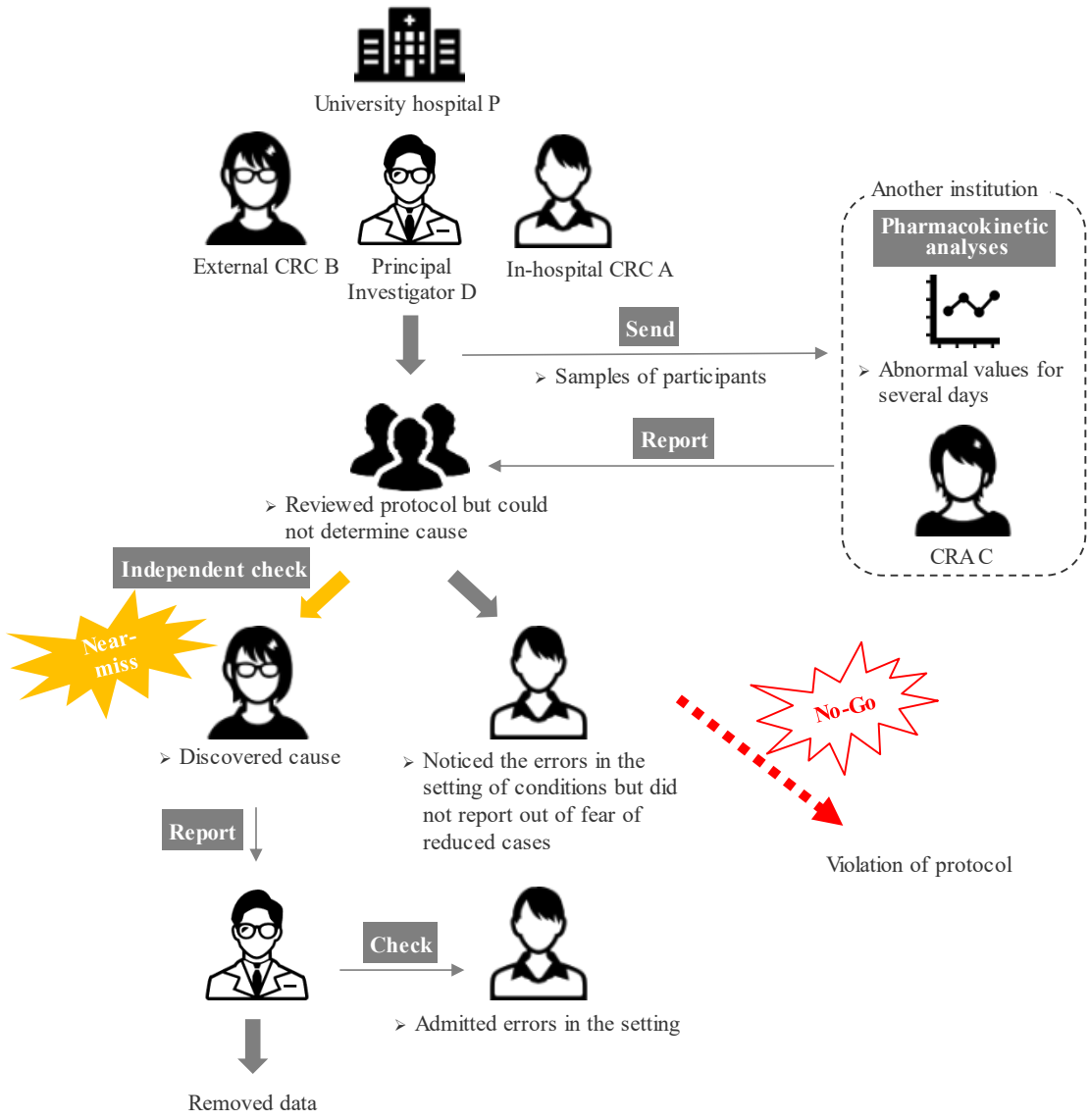
1 Clinical Research Coordinator (CRC) are the intermediary between pharmaceutical companies and trial participants, and provide support for clinical trials by managing schedules, preparing materials, explaining to and caring for participants, as well as communicating and coordinating with them.

2 Clinical Research Associate (CRA) monitor whether the trial is conducted in accordance with the rules.

8-5. Protocol violation in a clinical trial

Affiliated institution	University, University hospital	Field	Clinical trial



Factors that prevented misconduct

- The checks conducted by externally dispatched CRC B on the setting of the conditions worked properly
- CRC B had doubted the competence of CRC A due to CRC A committing errors on a daily basis

1. Case details

- At University hospital P, Principal Investigator D and a team consisting of an in-hospital Clinical Research Coordinator (CRC)[1] A and an external CRC B, were conducting a clinical study of an investigational drug.
- One day, a Clinical Research Associate (CRA)[2] C from the institution responsible for analyzing the pharmacokinetics in the participants, reported that the values had been abnormal for several days. Principal Investigator D and other concerned parties were immediately informed of this anomaly. Although they reviewed the protocol, they could not determine the cause.
- CRC B, who had been dispatched from outside the hospital, had always doubted the competence of in-hospital CRC A. When CRC B independently checked the setting of conditions of the drug dosing, they came to the conclusion that the conditions specified in the protocol might have been mistaken for those for another dosing for those few days, and informed Principal Investigator D of this possibility. ☜ **Factor that prevented misconduct**
- Principal Investigator D checked with in-hospital CRC A about the events that happened and found that the abnormal values were indeed due to errors in the setting of conditions, as per CRC B's conjecture, and that this had already been shared within the in-hospital CRC team. In other words, the in-hospital CRC team recorded the raw data on the case report form (CRF) without reporting the errors even though they knew that the conditions were incorrect.
- The data in question was excluded from the analysis in the study.

2. Backdrop & factors of near-miss incident

- In-hospital CRC A failed to report probably because they were concerned about insufficient data due to violation of protocol.

3. Factors that prevented misconduct & its backdrop

- The check by external CRC B led to the discovery of the errors in the setting of conditions. The checks conducted by the externally dispatched CRC worked in this study.
- External CRC B suspected that in-hospital CRC A was incompetent due to a number of errors made on a daily basis.

4. Possible research misconduct and questionable research practice

- The use of data obtained under conditions different from those specified in the protocol would construe as a protocol violation, which would also throw the reliability of the research data into question.

5. Preventive countermeasures

- Diversifying the composition of the members involved in the clinical trial and creating a system that would involve multiple people through their respective roles can increase the chances of discovering errors and inappropriate behavior.
- To avoid excessive pressure on the parties that committed the errors, create an open-minded environment that would allow them to easily raise questions or point out doubts.

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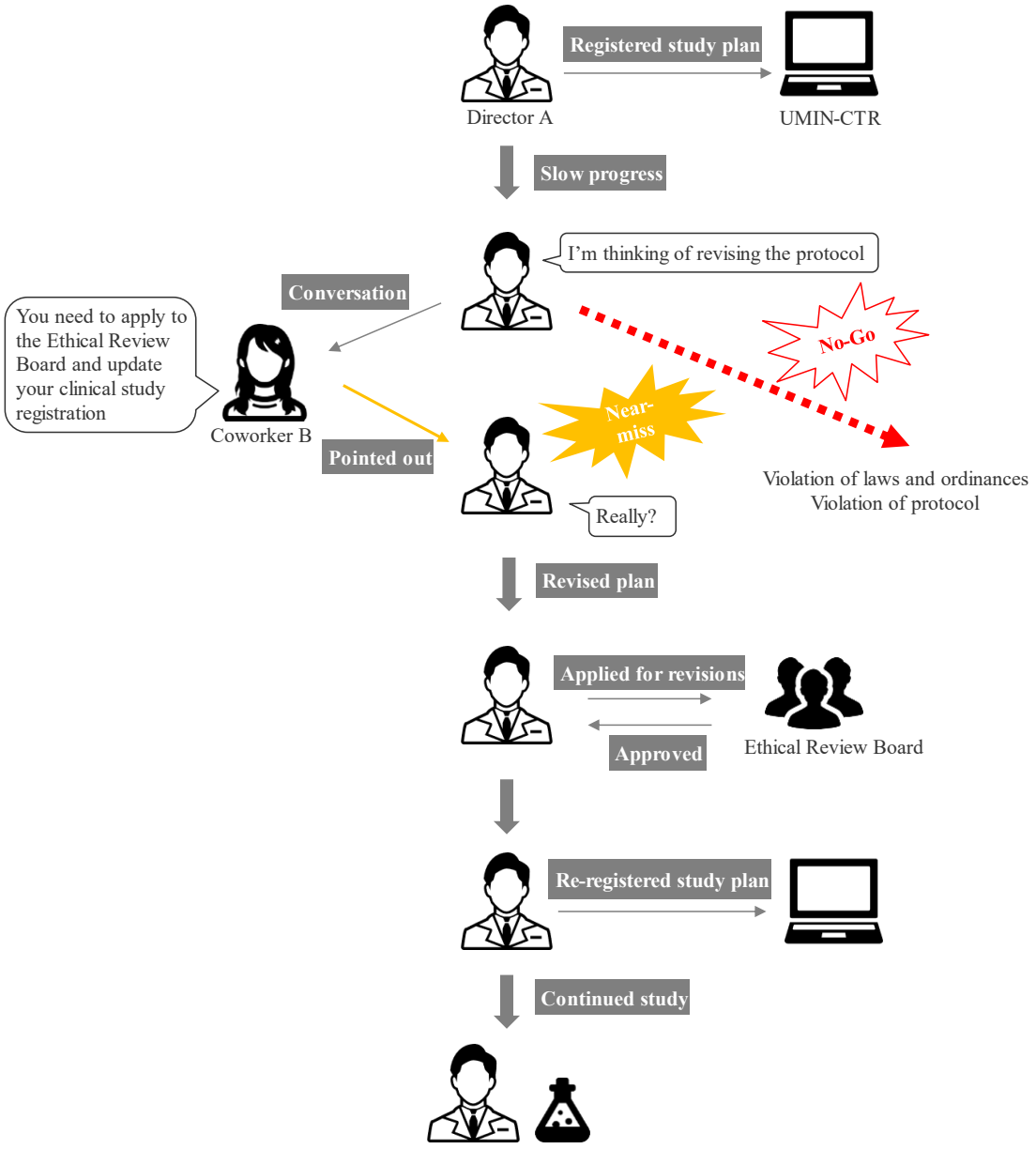
1 Clinical Research Coordinator (CRC) are the intermediary between pharmaceutical companies and trial participants, and provide support for clinical trials by managing schedules, preparing materials, explaining to and caring for participants, as well as communicating and coordinating with them. There are cases where CRCs are employed by hospitals, such as A, and those who are dispatched by companies, such as B.

2 Clinical Research Associate (CRA) monitor whether the trial is conducted in accordance with the rules.

8-6. Change of clinical study plan after registration with system

Affiliated institution	National/local government agency	Field	Clinical medicine



Factors that prevented misconduct

- Director A talked to Coworker B, to which the potential misconduct was pointed out
- Coworker B understood the rules concerning the registration of study plan

1. Case details

- Director A started conducting a clinical study after registering it in the UMIN clinical trial registration system (UMIN-CTR: University hospital Medical Information Network – Clinical Trial Registry)[1].
- As the study did not proceed as originally planned, Director A decided to revise the study plan and continue with the study.
- When Director A conveyed to Coworker B of the same laboratory their intention, Coworker B pointed out that Director A "must update the study plan registered in the UMIN-CTR after the Ethical Review Board approved the revisions to the study plan". ☜ **Factor that prevented misconduct**
- Director A applied to the Ethical Review Board to revise the study plan. After the revisions were approved, they edited the study plan registered in the UMIN-CTR and continued the study based on the updated study plan.

2. Backdrop & factors of near-miss incident

- Director A did not know that any revisions made to the study plan must be reflected in the study plan registered in the UMIN-CTR as well.

3. Factors that prevented misconduct & its backdrop

- Through the conversation with colleague B, Director A was able to recognize the potential misconduct and avoid violating the rule.
- When making changes or revisions to the clinical study plan, there was no framework in place that would allow laboratory members to check each other for potential violations, if any, and this included procedures. If Director A had proceeded with the revisions without telling or checking with anyone, Director A could have proceeded with the study without applying to the Ethical Review Board for the revisions or reflecting them in the study plan in the UMIN-CTR.

4. Possible research misconduct and questionable research practice

- Director A could have violated the laws and ordinances or deviated from the guidelines for clinical study if they had revised the study plan without getting it approved by the Ethical Review Board.
- Director A could have violated the rules that when making changes or revisions to a study plan registered in a clinical trial registry such as the UMIN-CTR, one must promptly reflect the revisions in the study plan after the revisions are made.
- Conducting a clinical study that is different from the study plan registered in the system may impede the fair publication of research results and lead to publication bias or breach of ethical obligations concerning the publication.

5. Preventive countermeasures

- Create a checklist of the necessary actions to take when conducting a clinical study, such as applying to the Ethical Review Board when making changes or revisions to the study plan and reflecting the revisions in the study plan registered in the clinical trial registry, to prevent oversight.
- When considering making changes or revisions to the clinical study plan, establish a relationship where everyone can make suggestions to each other by, for example, putting in place a framework where one can consult with others or get the revisions checked by a superior.
- Regularly conduct training on the necessity of ethics reviews and clinical trial registries, and the relevant procedures required.

[1] https://www.umin.ac.jp/ctr/index.htm

(Commentary)

The necessity of registering clinical studies can be explained with three points: scientific rationale (to prevent publication bias), ethical obligations, and the facilitation of enrolling participants for the clinical trial.

Registering a clinical trial allows the researcher or scientist to check on its progress from registration (start) to publication of results (goal). The data also provides evidence for the existence of "publication bias", in which positive results are more likely to be published.

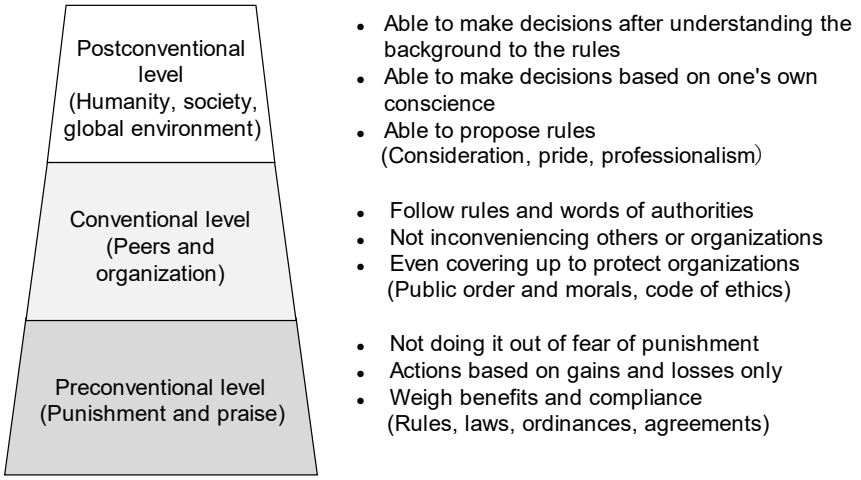
The Declaration of Helsinki, which provides ethical guidelines for those involved in medical research, includes a paragraph stating that "negative and inconclusive as well as positive results should be published or otherwise made publicly available". The fair publication of research results, including negative ones, is required in light of ethical considerations for the clinical trial participants who want their results to be utilized for the benefit of the society.

This registration system was introduced in the hope that prompt publication of information of clinical trials would facilitate the enrolling of participants, which would in turn lead to the rapid acquisition of research results. It is thus considered an important means of facilitating the development of treatments.

Editor's column 7: The process of developing ethical awareness

Psychologist Kohlberg splits the development process of a person's ethical awareness into three levels[1,2]. The three levels are: (i) preconventional level where one judges right and wrong based on whether they are praised or punished, and choosing actions based on gains or losses; (ii) conventional level where one regards acts that are approved by others as good; and (iii) postconventional level where one regards acts that are in line with one's conscience as good. The mindset of not doing certain things because we will be punished, or prioritizing gains over rules, puts us at a level of ethical awareness not beyond that of an infant, which is the preconventional level. Rules and laws actually correspond to this level. As one grows older, one becomes more considerate of others and organizations, obeys rules and follows majority decisions, and develops a conventional level of ethical awareness of public order and morals. But as scientists, this is still not enough. Scientists must be able to predict problems that come with the creation of knowledge and convenience, and propose new rules to prevent their occurrence. And in order to do that, scientists are required to have a postconventional level of ethical awareness that allows them to understand the background to the existing rules and the words of authorities so as to make decisions based on one's own conscience.

Once you recognize that research misconduct is nothing more than the preconventional level of gains or losses, you will also come to the realization that most of the excuses introduced in the "Fraud Triangle" that attempt to justify research misconduct do not hold water.

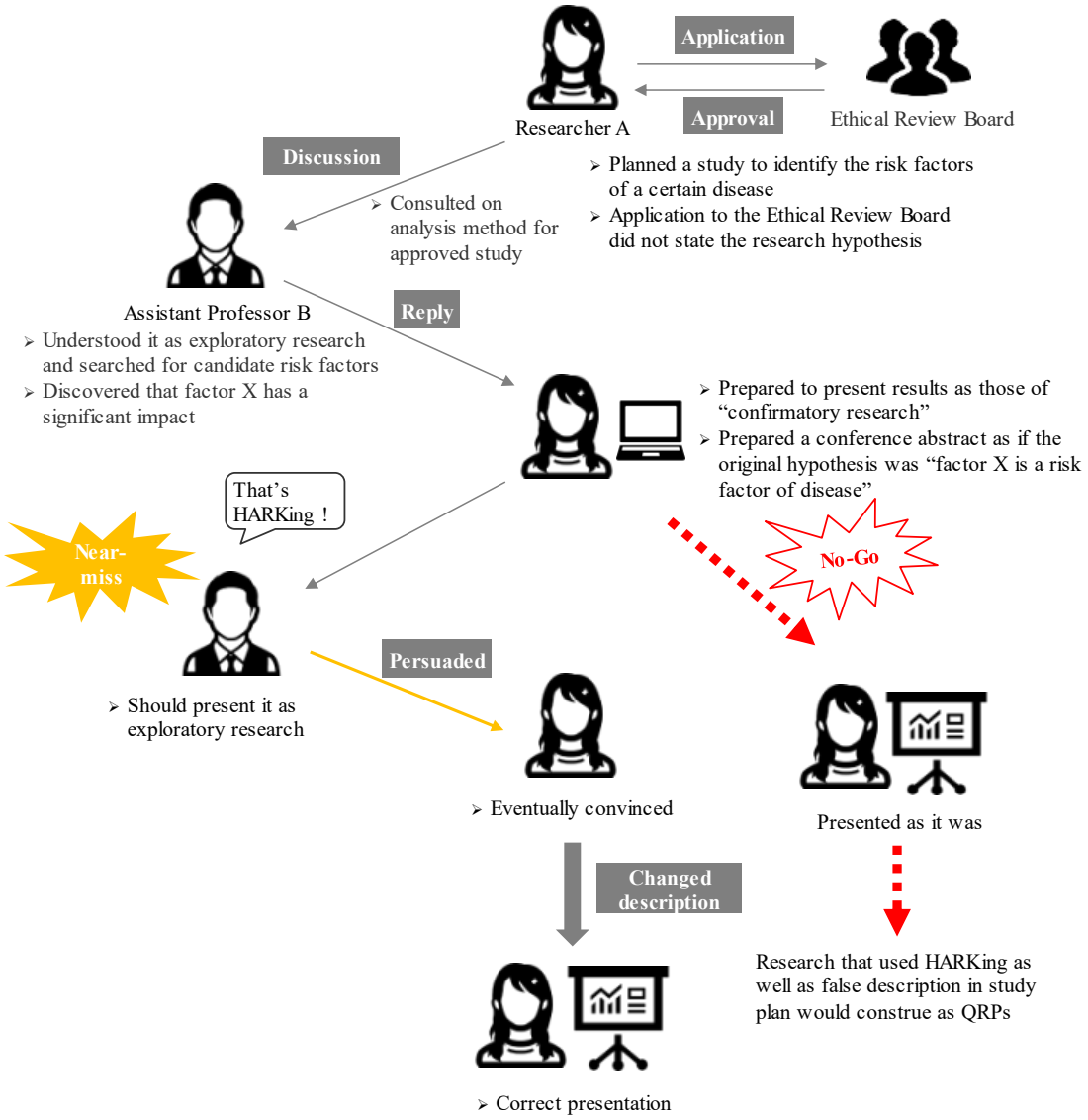


1 Lawrence Kohlberg (translated by Nobumichi Iwasa), "Moral Stages & Moral Education", pp. 171-173, Reitaku University Press (1987)

2 Yoshio Katakura, "Safety and Ethics in Engineering", Japanese Society for Engineering Education 63 (5), pp. 13-17 (2015)

8-7. Prevented questionable research practice (HARKing)

Affiliated institution	University, University hospital	Field	Clinical study



Factors that prevented misconduct

- Assistant Professor B had understanding of HARKing
- Researcher A was convinced by Assistant Professor B

1. Case details

- Assistant Professor B was often consulted on study designs and biostatistics in clinical studies.
- Researcher A consulted with Assistant Professor B about the analysis method for a clinical study on the identification of risk factors of a disease, which had already been approved by the Ethical Review Board.
- As the study plan did not indicate any specific candidate risk factors, Assistant Professor B understood the study as an "exploratory research[1]" to identify risk factors, and proceeded to analyze multiple elements as candidate risk factors.
- Results of the statistical analysis revealed a certain factor X to be statistically significant as a candidate risk factor. When Assistant Professor B told Researcher A about this, Researcher A prepared a conference abstract as if the original hypothesis right from the beginning was that "factor X is a risk factor of said disease" and attempted to present it as the results of "confirmatory research[2]".
- Assistant Professor B considered it as "exploratory research" rather than "confirmatory research" because there was no such research hypothesis in the original study plan. Assistant Professor B explained that what Researcher A did was a "questionable research practice (QRP)"[3,4] known as HARKing (Hypothesizing After the Results are Known), and should be avoided in terms of research reproducibility. ☜ **Factor that prevented misconduct**
- Researcher A was not convinced in the beginning, but finally understood and changed the description of the study to an appropriate one.

2. Backdrop & factors of near-miss incident

- HARKing is not a well-known questionable research practice (QRP).
- Since it takes some time from applying to the Ethical Review Board to getting it approved, rushing out a hasty application may cause the researcher to not adequately consider the hypothesis. In addition, if the ethics reviewers are overly concerned about the delay in research activities, they may end up approving confirmatory research in which hypotheses have not been thoroughly considered.
- If a researcher is convinced that confirmatory research has a stronger impact on papers and conferences than exploratory research, they may be motivated to publish exploratory research as confirmatory research instead.

3. Factors that prevented misconduct & its backdrop

- Assistant Professor B was aware that HARKing was a questionable research practice.
- Researcher A proceeded with the clinical study while consulting with Assistant Professor B, who was knowledgeable.

4. Possible research misconduct and questionable research practice

- Researcher A could have used HARKing and published the paper, and HARKing would not have been found out.
- An increase in the number of HARKed research publications might reduce the reproducibility of research results as well as the credibility of science.

5. Preventive countermeasures

- Get more people involved in the study design and presentations so that it is easier to notice possible research misconduct.
- Researchers have to be fully aware that HARKing may cause problems for others to reproduce the research results.
- Reviewers should scrutinize papers with HARKing in mind if it is suspected.

(Commentary)

Making the right decision will vary depending on the situation. It is crucial to seek a wide range of opinions rather than leaving the decision-making to a limited number of people.

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1 Research where some systematic associations or new hypothesis are inductively found in the data obtained without specifying a hypothesis in advance.

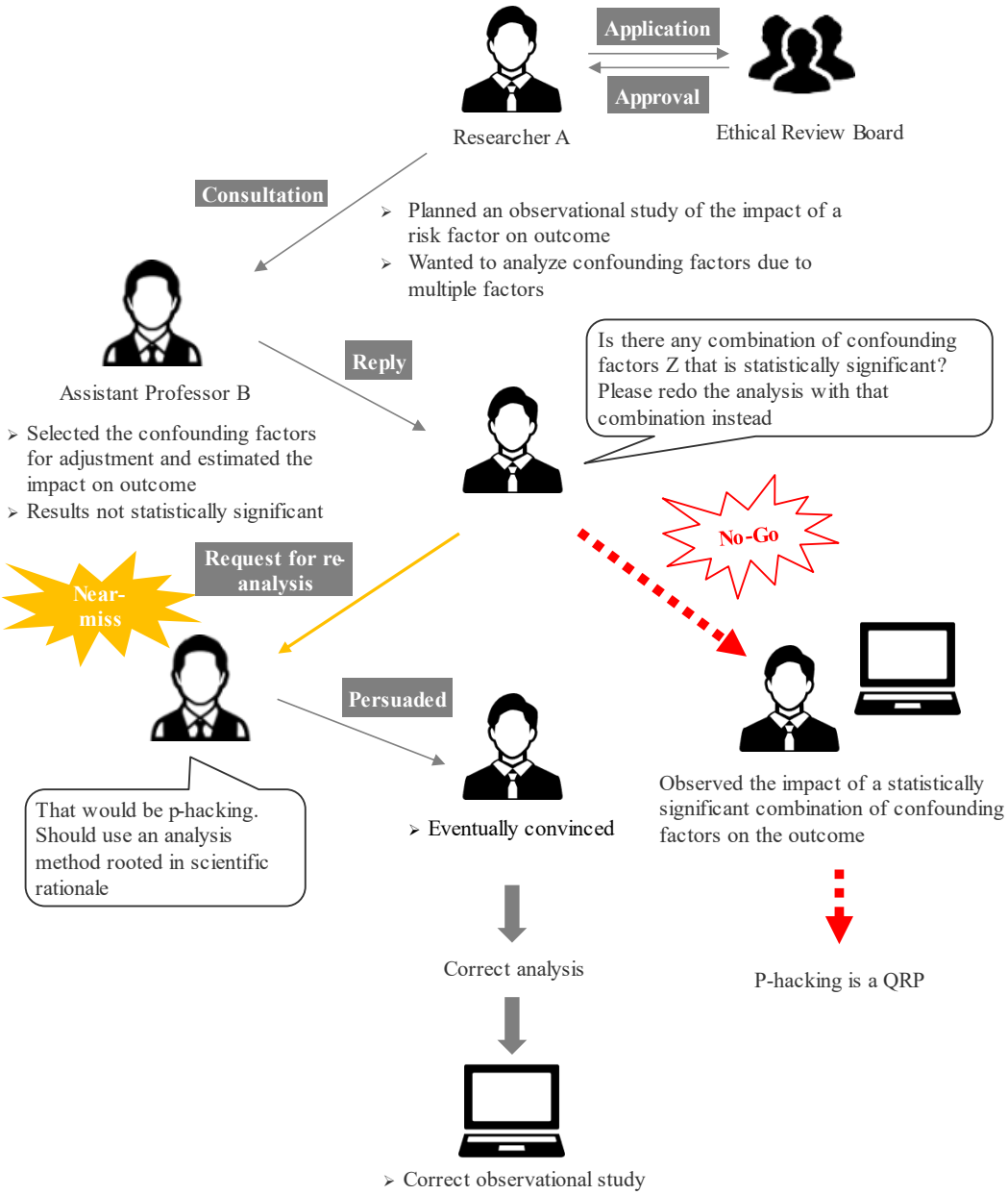
2 Research where a hypothesis is established in advance and the data is used to test whether or not it is correct.

3 Japan Society for the Promotion of Science Editing Committee, "For the Sound Development of Science", "For the Sound Development of Science – The Attitude of a Conscientious Scientist –", pp. 38-39
Online edition (English): https://www.jsps.go.jp/j-kousei/data/rinri_e.pdf

4 National Academy of Science *et al*., "Responsible Science: Ensuring the Integrity of the Research Process", Vol. 1, p. 28, National Academy Press, 1992

8-8. Prevented questionable research practice (p-hacking)

Affiliated institution	University, University hospital	Field	Clinical study



Factors that prevented misconduct

- Assistant Professor Bhad understanding of p-hacking
- Researcher A was convinced by Assistant Professor B

1. Case details

- Assistant Professor B was often consulted on study designs and biostatistics in clinical studies.
- Researcher A consulted with Assistant Professor B on how to adjust for confounding factors[1] for a clinical study that had already been approved by the Ethical Review Board. It was an observational study (confirmatory research) on the impact of risk factor X on outcome Y, where multiple factors Z (Z_1, Z_2, Z_3, …Z_n) were assumed to be confounding factors.
- Assistant Professor B selected the confounding factors for adjustment based on several basis such as scientific literature and causal diagram (DAG: Directed Acyclic Graph), and estimated the impact of X on Y. The results revealed that X was not a statistically significant risk factor even though it impacted Y.
- When Assistant Professor B informed Researcher A of this result, Researcher A in turn requested Assistant Professor B: "Is there any combination of confounding factors Z that is statistically significant? Please redo the analysis with that combination instead."
- Selecting variables on the basis of what appears to be statistically significant ($p<0.05$) is a statistically incorrect approach. Assistant Professor B also explained to Researcher A that searching for results with $p<0.05$ and selectively reporting only those results was a "questionable research practice (QRP)"[2, 3] known as p-hacking.[4] ☜ **Factor that prevented misconduct**
- Researcher A was not convinced in the beginning, but was finally persuaded by Assistant Professor B and eventually used an analysis method that was rooted in scientific rationale.

2. Backdrop & factors of near-miss incident

- It is not well-known that p-hacking is considered a questionable research practice.
- The assumption that medical academic societies and journals place an emphasis on whether the results are statistically significant ($p<0.05$) or not in turn promotes the mistaken idea that one is required to analyze the data to obtain statistically significant results ($p<0.05$).
- The fact that p-hacking is usually difficult to uncover may be a possible motive for the researcher.

3. Factors that prevented misconduct & its backdrop

- Assistant Professor B had understanding of p-hacking and that it was a questionable research practice.
- Researcher A proceeded with the clinical study while consulting with Assistant Professor B, who was knowledgeable.

4. Possible research misconduct and questionable research practice

- Researcher A could have used p-hacking and published the paper, and p-hacking would not have been found out.
- An increase in the number of p-hacked research publications might reduce the reproducibility of research results as well as the credibility of science.

5. Preventive countermeasures

- The drafting of study designs and review of the presentation contents should be subjected to checks with various viewpoints, such as those in leadership positions and those with statistical knowledge, so that it is easier to notice questionable research practice, if any.
- Provide training on acts and research practices that would affect the reproducibility and reliability of research, and to get researchers to be fully aware of practices such as p-hacking.
- Reviewers and journal editors should evaluate papers without any biased view about $p<0.05$.

(Commentary)

Making the right decision will vary depending on the situation. It is crucial to seek a wide range of opinions rather than leaving the decision-making to a limited number of people.

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1 Factor C has an actual causal relationship to data A and B; yet data A and B do not have a causal relationship but have a spurious correlation.

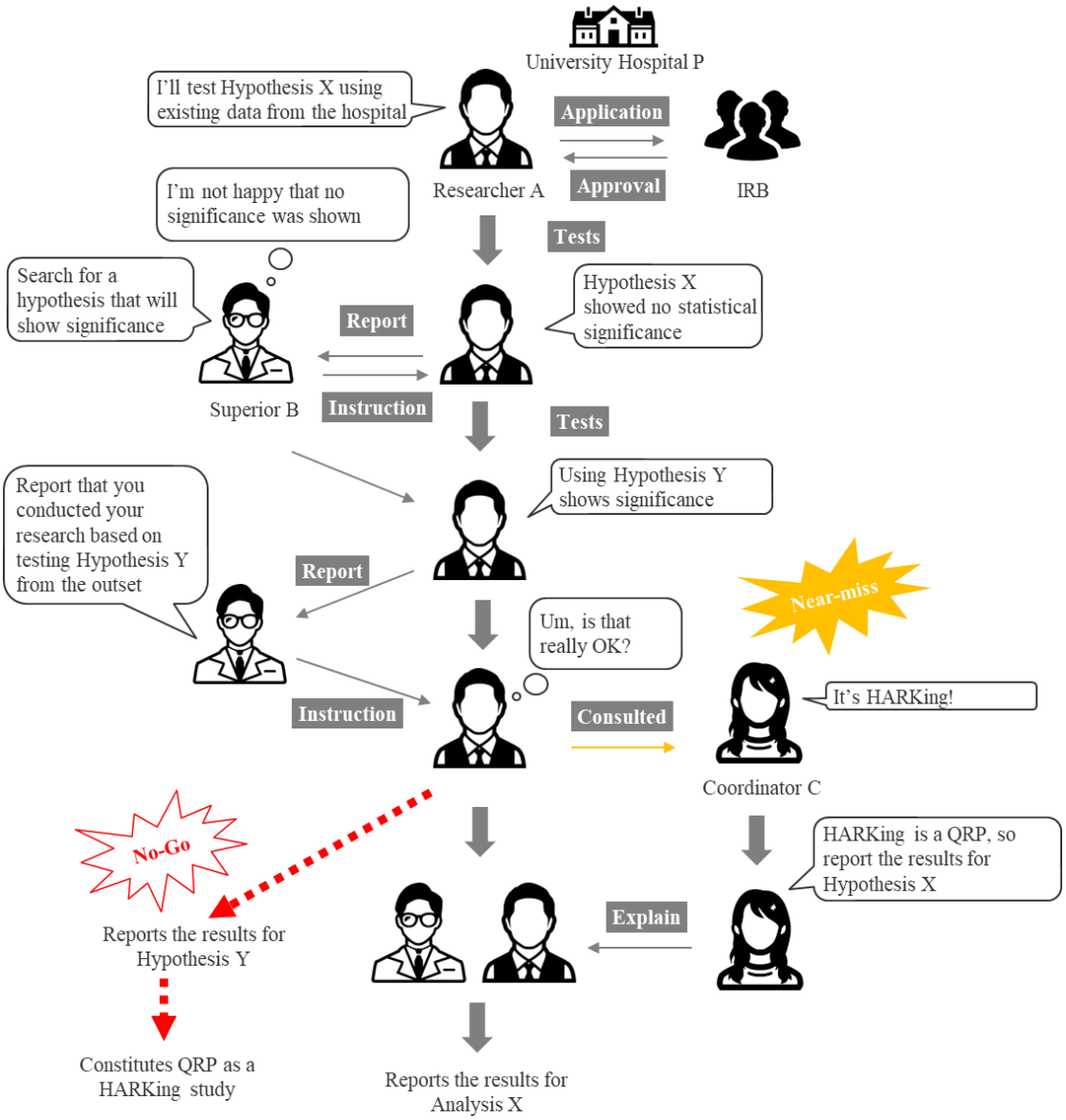
2 Japan Society for the Promotion of Science Editing Committee, "For the Sound Development of Science", "For the Sound Development of Science – The Attitude of a Conscientious Scientist –", pp. 38-39
Online edition (English): https://www.jsps.go.jp/j-kousei/data/rinri_e.pdf

3 National Academy of Science et al., "Responsible Science: Ensuring the Integrity of the Research Process", Vol. 1, p. 28, National Academy Press, 1992

4 Practice of manipulating data analysis methods and performing repeated analyses so as to obtain statistically significant results

8-9. Attempt to report on the outcomes of research differing from the study plan

Affiliated institution	University, University hospital	Field	Clinical study



Factor that prevented misconduct

- Researcher A sought advice from Research Support Coordinator C (in charge of analysis) about the fact that Superior B had instructed them to compile their results on the basis of Hypothesis Y
- Coordinator C had a wealth of knowledge concerning research integrity and, realizing that HARKing was a questionable research practice (QRP), explained this fact to Researcher A and Superior B

1. Case details

- Researcher A at University Hospital Q submitted to the Institutional Review Board (IRB) a plan to conduct a confirmatory study that would involve collecting existing data from the hospital and using it to test Hypothesis X. The IRB approved the plan.
- While the results of the study did not show any statistical significance for Hypothesis X, Researcher A prepared a report on these results, as a finding that no significance was shown is in itself a useful scientific finding.
- However, Researcher A's boss, Superior B, did not approve of results that did not show statistical significance and instructed Researcher A to search for a hypothesis that would demonstrate significance. As a result, Researcher A found Hypothesis Y, which did demonstrate significance, so Superior B instructed Researcher A to prepare a report on the results of the study that made it seem as though Researcher A had conducted the study on the basis of Hypothesis Y from the outset.
- Harboring doubts about Superior B's instruction, Researcher A sought advice from Research Support Coordinator C (in charge of analysis). Research Support Coordinator C explained to all concerned, including Superior B, that this course of action was undesirable, as it constituted HARKing (Hypothesizing After the Results are Known),[1] which is a questionable research practice.[2] ☚ **Factor that prevented misconduct**
- As a results, Researcher A compiled their report on the study on the basis of the original Hypothesis X, rather than Hypothesis Y.

2. Backdrop & factors of near-miss incident

- Superior B would not accept that results showing no significance for Hypothesis X constituted a scientifically useful finding.
- Superior B instructed Researcher A to prepare a report on the results of the study that made it seem as though Researcher A had conducted the study on the basis of Hypothesis Y from the outset.
- There was a lack of adequate awareness that HARKing is a questionable research practice (QRP). In addition, the researcher did not understand the difference between a confirmatory study and an exploratory study.

3. Factors that prevented misconduct & its backdrop

- Researcher A sought advice from Research Support Coordinator C (in charge of analysis) about the fact that Superior B had instructed them to compile their results on the basis of Hypothesis Y.
- Coordinator C had a wealth of knowledge concerning research integrity and, realizing that HARKing was a questionable research practice (QRP), explained this fact to Researcher A and Superior B.

4. Possible research misconduct and questionable research practice

- Publication of research based on HARKing and failure to disclose the fact that HARKing had occurred.
- If the publication of research based on HARKing increases, the reproducibility of research outcomes will decline, which has the potential to reduce the credibility of science.

5. Preventive countermeasures

- Ensure researchers are fully aware of the potential for HARKing to cause problems in the reproducibility of research.

1 N. L. Kerr, “HARKing: hypothesizing after the results are known”, pp.196-217, 2(3), Personality and Social Psychology Review, 1998 (https://pubmed.ncbi.nlm.nih.gov/15647155/)

HARKing is a practice in which, for example, when the results of experiments conducted on the basis of a hypothesis formulated at the time the study began do not support the hypothesis, the researcher devises a hypothesis that is supported by the results obtained and reports on the study as though this hypothesis had been the hypothesis from the outset.

In confirmatory studies in particular, the design of the study – including the experiments, investigations, and statistical techniques used for data analysis – is determined in accordance with the hypothesis devised on the basis of findings prior to the study’s start, and the study involved confirming whether or not the hypothesis is correct within the initially foreseen scope. Altering the initial hypothesis to suit the results obtained means reporting something that is untrue and could be described as an act that distorts the truth of the research activities themselves. The act of changing the hypothesis forming the basic premise of a study to suit one’s own convenience, just because the results do not support the original hypothesis, skews the perceptions of the researcher themselves and promotes bias. Moreover, it also leads to unconscious acts such as overlooking diverse viewpoints gained from the results of the study, and this fact could potentially end up having a major impact on the reproducibility of the study itself.

However, attitudes to HARKing vary and some take the stance that judgments on whether or not it is inappropriate should be based on consideration of the experimental evidence in the results of the study and whether these affect the credibility of the findings derived from them. Debate around this issue is still ongoing at present, so you need to understand that this is not yet necessarily an established norm.

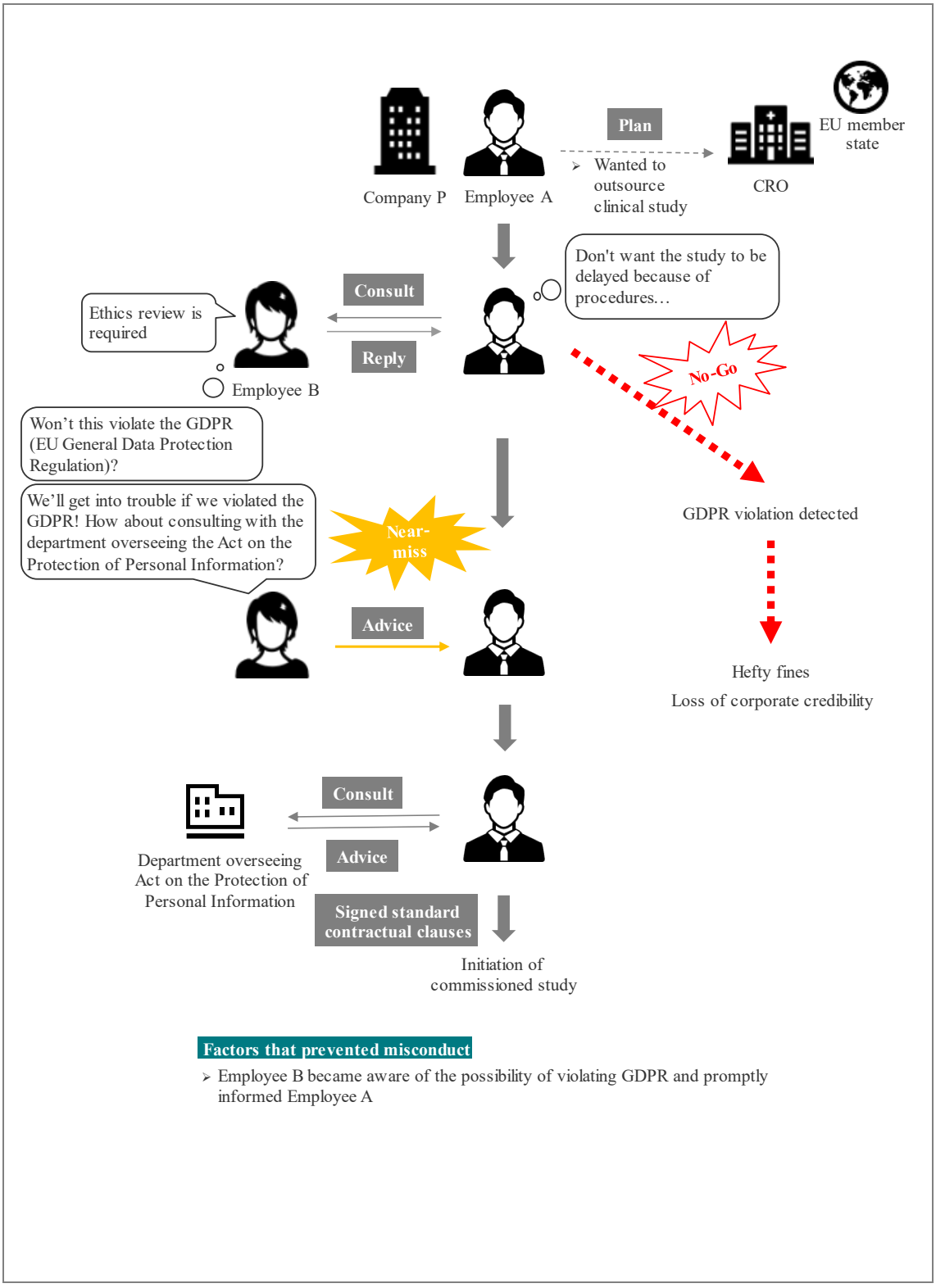
2 Japan Society for the Promotion of Science Editing Committee, “For the Sound Development of Science”, “For the Sound Development of Science – The Attitude of a Conscientious Scientist –”, pp. 51-52, Maruzen Publishing, 2015

9 International joint research

1. Prevented violations of laws and ordinances regarding acquisition of overseas medical information
2. Prevented the sending of samples to overseas universities via incomplete procedures

9-1. Prevented violations of laws and ordinances regarding acquisition of overseas medical information

Affiliated institution	Corporate	Field	Clinical study



Factors that prevented misconduct

- Employee B became aware of the possibility of violating GDPR and promptly informed Employee A

1. Case details

- Employee A of Company P wanted to outsource a clinical study to a contract research organization (CRO)[1] in an EU member state.
- Employee A asked Employee B about the "necessary procedures for outsourcing studies". Employee B checked the protocol of the clinical study and found that Company P planned to get the CRO to conduct the study as well as obtain the measurement results and background information (anonymized health information so that individuals could not be identified) of the study participants.
- When Employee B explained that the "company needs to conduct an ethics review of the study", Employee A replied that they were "in a hurry and don't want the screening process to take too long", and seemed to find the procedure a hassle.
- At that time, the GDPR[2] (EU General Data Protection Regulation) just came into force, and Employee B thought that obtaining anonymized health information from a CRO in an EU member state might violate the GDPR.
- Despite the fact that Employee A might have to go through more procedures, Employee B told Employee A that if they were found to have violated the GDPR, they would be in serious trouble (including hefty fines), and advised Employee A to consult with the department in charge of Act on the Protection of Personal Information. **Factor that prevented misconduct**
- When Employee B talked to Employee A at a later date, they found that it was necessary to sign standard contractual clauses and Company P had already determined the relevant procedures because compliance with the GDPR was required for various internal company operations.
- Employee A followed the predetermined procedures and the CRO initiated the clinical study without any delay.

2. Backdrop & factors of near-miss incident

- Employee A did not understand that when outsourcing a clinical study to an overseas institution, it was necessary to comply not only with the laws and ordinances and guidelines for clinical studies, but also with the laws and ordinances regarding the protection of personal information.
- Employee A was in a hurry to initiate the study and thought that it was a hassle to follow the various time-consuming procedures.

3. Factors that prevented misconduct & its backdrop

- This case happened right after the GDPR came into force, and its strict regulations and hefty fines made headlines in the news. Employee B therefore remembered that the transfer of personal data from the European Economic Area (EEA) to outside the region was prohibited in principle.
- Even if Employee B had not given any suggestions, the Ethical Review Board would have most likely pointed out the need to comply with the GDPR. But Employee B decided that "it was better to inform Employee A as soon as possible", which led to them taking early actions.

4. Possible research misconduct and questionable research practice

- Violation of the GDPR.
- If they could not take the relevant actions with regards to the GDPR early enough, the clinical study would have been delayed, which would in turn delay the application of research results in the society.

5. Preventive countermeasures

- Provide researchers with education and training on the protection of personal information as personal data (one's health information, such as the name of the injury or illness, details of medications, and results of examination and measurement) is often used in clinical studies and medical research.
- Those engaged in research should understand the necessity and significance of research-related procedures.
- Build an open-minded relationship between employees and researchers where all communication is encouraged.
- Since the Ethical Review Board is made up of members who can review from various angles and perspectives (such as a medicine and medical care professional, a professional in ethics and law), development of or any changes or revisions made to a clinical study plan must be reviewed by the Ethical Review Board.

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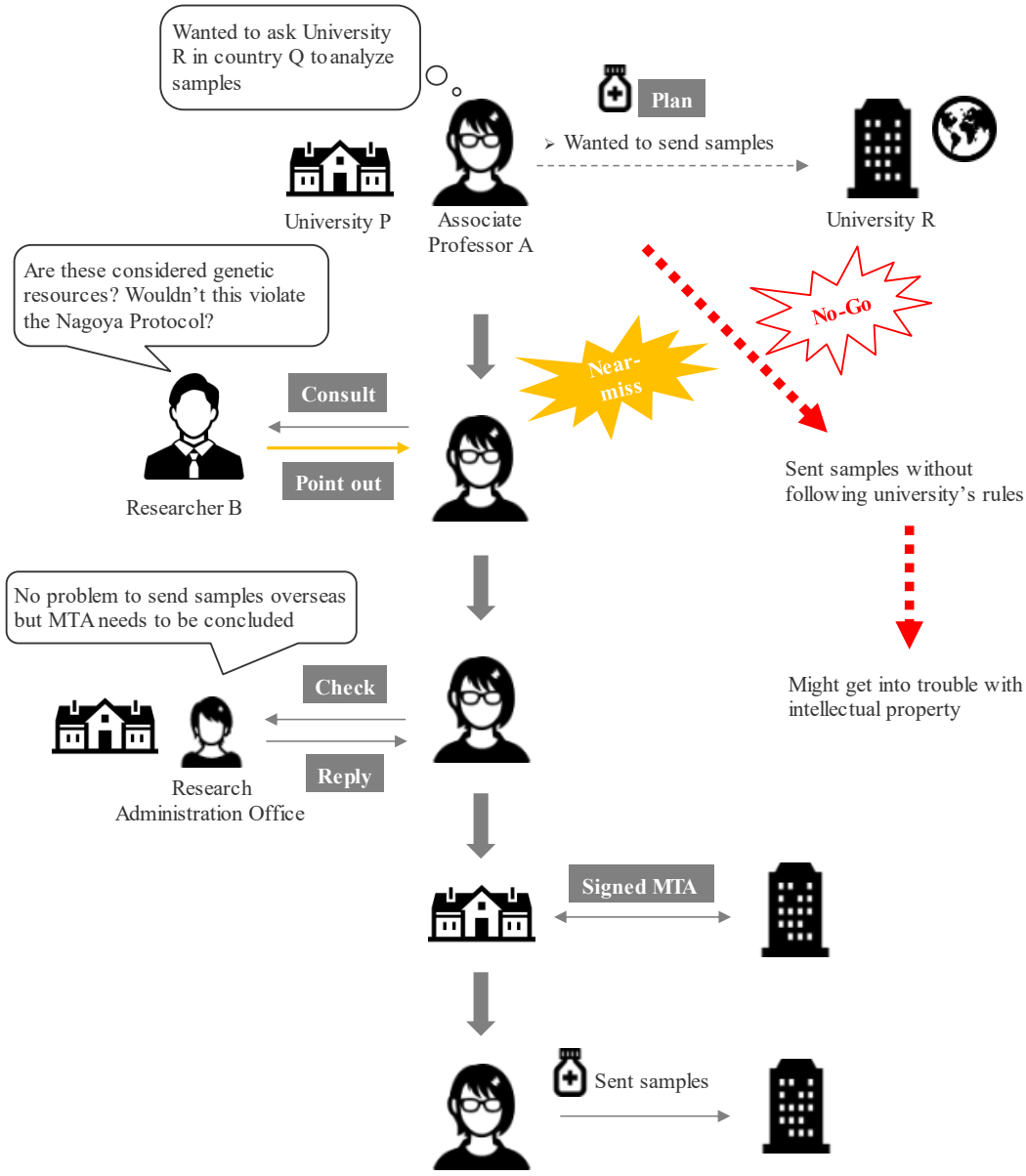
1 Contract Research Organizations (CROs) offer a variety of services and provide support for clinical trials and postmarketing surveillance on behalf of their clients so as to increase the efficiency of drug development and create new drugs more quickly.

2 Abbreviation for General Data Protection Regulation. The GDPR was adopted on May 24, 2016 and became enforceable beginning May 25, 2018. It is a regulation that aims to ensure the fundamental human right to the protection of personal data in the EU and prohibits, in principle, the transfer of personal data acquired within the European Economic Area (EEA), including the EU, outside the EEA.

9-2. Prevented the sending of samples to overseas universities via incomplete procedures

Affiliated institution	University, University hospital	Field	Life sciences



Factors that prevented misconduct

- Researcher B thought that Associate Professor A's samples might be considered genetic resources and told Associate Professor A the need to follow procedures
- Associate Professor A consulted with University P's Research Administration Office on how to go about sending samples and learned that according to the university's rules, an MTA had to be concluded between University P and the recipient University R first

1. Case details

- Associate Professor A of University P was about to send samples to University R in country Q for analysis.
- When Associate Professor A consulted with Researcher B while preparing to send the samples, Researcher B pointed out that "those samples may contain genetic resources[1]. Wouldn't you violate the Nagoya Protocol (Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity)[2] if you sent the samples just like that?". ☜ **Factor that prevented misconduct**
- When Associate Professor A made an inquiry to the Research Administration Office of University P, they replied that "sending these samples from Japan to other countries will not pose an issue", but Associate Professor A would have to get "a Material Transfer Agreement (MTA) concluded between University P and the recipient University R according to the university's rules"[3].
- Associate Professor A proceeded to ask the Research Administration Office to conclude an MTA between University P and the overseas University R.
- After the MTA was signed, Associate Professor A sent the samples to University R.

2. Backdrop & factors of near-miss incident

- Although Associate Professor A was aware of the Convention on Biological Diversity and the Nagoya Protocol, they had a skewed impression that materials such as plants and bacteria would be deemed as genetic resources, and assumed that their samples would not be considered genetic resources.

3. Factors that prevented misconduct & its backdrop

- Researcher B thought that Associate Professor A's samples might be considered genetic resources, and pointed it out to Associate Professor A.
- Associate Professor A consulted with University P's Research Administration Office on how to go about sending samples.

4. Possible research misconduct and questionable research practice

- Associate Professor A could have sent samples overseas without following the university's rules or getting an MTA concluded.
- Sending samples overseas without having determined ahead of time how to handle intellectual property of samples and what to do with them after the analysis is over may lead to problems later on.

5. Preventive countermeasures

- When sending samples to other institutions in Japan or other countries, be sure to consult with the departments in charge of the affiliated institutions in advance regarding the necessary procedures.

(Commentary)[4]

At present, there are no special laws regarding Access to Genetic Resources and Benefit Sharing (ABS) in Japan. However, there are laws and ordinances that are partially or indirectly related to the provision of Japanese genetic resources to foreign countries, and one should take note of them, namely in the fields of agriculture, forestry and fisheries; intellectual property rights; civil and commercial matters related to various rights; as well as those that are related to the designation of various zones; import and export regulations; and criminal offenses involving illegal activities.

It is also crucial to establish mutually agreed terms (MAT) with the other party and ensure the fair and equitable distribution of benefits as a provider of genetic resources.

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1 Genetic material of plant, animal, microbial origin, or other origin containing functional units of heredity, which have an actual or potential value

2 On August 20, 2017, Japan became a party to the Nagoya Protocol and established the ABS Guidelines (Access to genetic resources and Benefit Sharing, Guidelines on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from Their Utilization), domestic-level ABS measures that entered into force at the same time. The three basic ABS rules based on the Convention on Biological Diversity are:

- Obtaining prior informed consent (PIC) of the country in which the genetic resource is located before accessing the resource.
- Establishment of mutually agreed terms (MAT) with the contracting party providing the genetic resources.
- Acquisition of genetic resources and sharing of benefits arising from their utilization in accordance with the MAT.

ABS Guidelines: http://abs.env.go.jp/pdf/pamphlet_en.pdf

3 The Nagoya Protocol calls for clarification and transparency of ABS regulations in the event that PIC is required by the contracting party providing the genetic resources. The PIC of the Government of Japan is not required for the provision of access to genetic resources existing in Japan. When transferring genetic resources, an MTA may be concluded between the providing party and the utilizing party of the genetic resources. The MTA is a type of Mutually Agreed Terms (MAT) where various terms and conditions associated with the transfer of materials are established. They include the type and amount of materials to be transferred, the purpose of utilization, discussions when intellectual property is generated, and the handling of materials after the contractual period is over. https://www.mabs.jp/eng/index.html

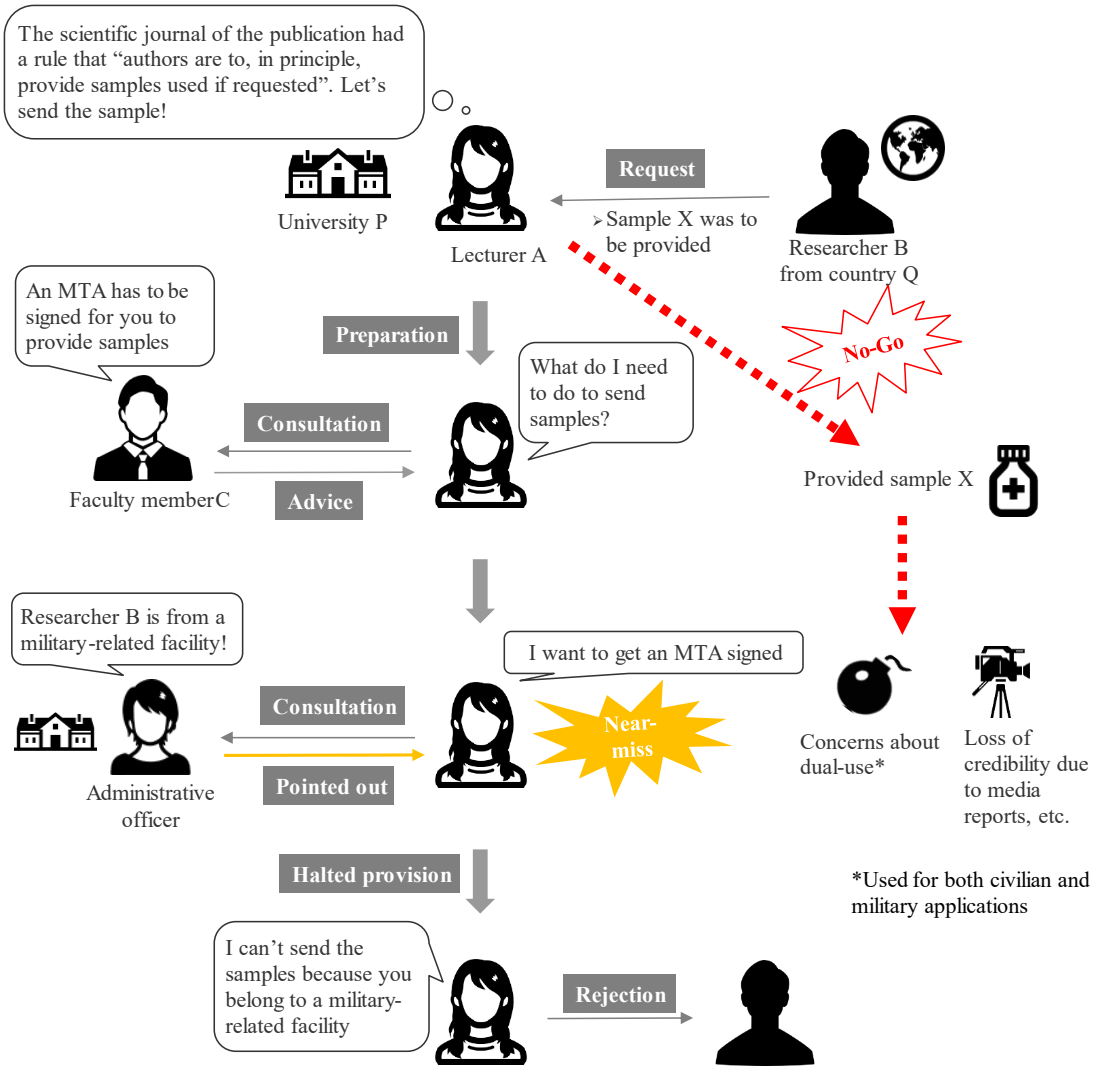
4 https://www.mabs.jp/eng/index.html

10 Security export control

1. Prevented the sending of research samples to overseas military-related facilities
2. Export control prescreening procedures for accepting international students

10-1. Prevented the sending of research samples to overseas military-related facilities

Affiliated institution	University, University hospital	Field	Basic medical research



Factors that prevented misconduct

- When Lecturer A consulted with Faculty member C about how to send sample X, Faculty member C pointed out that there was an internal rule about concluding an MTA with the receiving institution to provide the samples
- When Lecturer Aconsulted with the university's administrative officer about concluding the MTA, they found out that Researcher B belonged to a military-related facility of another country

1. Case details

- Lecturer A from University P received an email from Researcher B from country Q requesting for "Please send us some research sample X that was used in Lecturer A's publication".
- The scientific journal that published Lecturer A's paper had a rule that "authors are to, in principle, provide samples used in the publication if requested". Lecturer A then started preparing to send sample X to Researcher B.
- When Lecturer A consulted with Faculty member C from the same laboratory about how to send the sample, the latter pointed out that "University P and the recipient's affiliated institution are required to sign an MTA (material transfer agreement) before providing samples".
- Lecturer A then consulted with University P's administrative officer about concluding an MTA. The latter then found out after investigation that Researcher B actually belonged to a military-related facility of country Q. ☜ **Factor that prevented misconduct**
- If Lecturer A had unwittingly sent sample X to Researcher B, the latter might use the sample for military purposes since he was conducting experiments at a military-related facility then. Lecturer A halted the preparations to send sample X and informed Researcher B of their inability to help out with the request.

2. Backdrop & factors of near-miss incident

- Lecturer A strongly felt that they had to abide with the scientific journal's rule where "authors are to, in principle, provide samples used in the publication if requested".
- Lecturer A did not understand that an MTA must be concluded between University P and the recipient's affiliated institution in order to provide samples.
- Lecturer A was not fully aware of the requester's (Researcher B) affiliation or purpose of use when they were about to provide sample X.

3. Factors that prevented misconduct & its backdrop

- When Lecturer A consulted with Faculty member C about how to send sample X, Faculty member C pointed out that there was an internal rule about concluding an MTA with the receiving institution.
- When Lecturer A consulted with the university's administrative officer about concluding the MTA, they then found out that Researcher B belonged to a military-related facility of country Q.

4. Possible research misconduct and questionable research practice

- The research material provided could have been unintentionally used for military research by other countries.
- If the media were to put out an article on the inappropriate export of research materials by University P, University P might lose its public credibility.

5. Preventive countermeasures

- When asked to provide research samples, thoroughly investigate the requester's affiliation and the details of their research.
- When sending research samples, make sure that an MTA that stipulates ownership and usage is concluded first.
- Raise awareness of rules of university regarding the provision of research samples, including its significance and necessity, and prevent oversights and lapses by regularly providing training, as well as build relationships that allow people within the university to point out each other's mistakes.

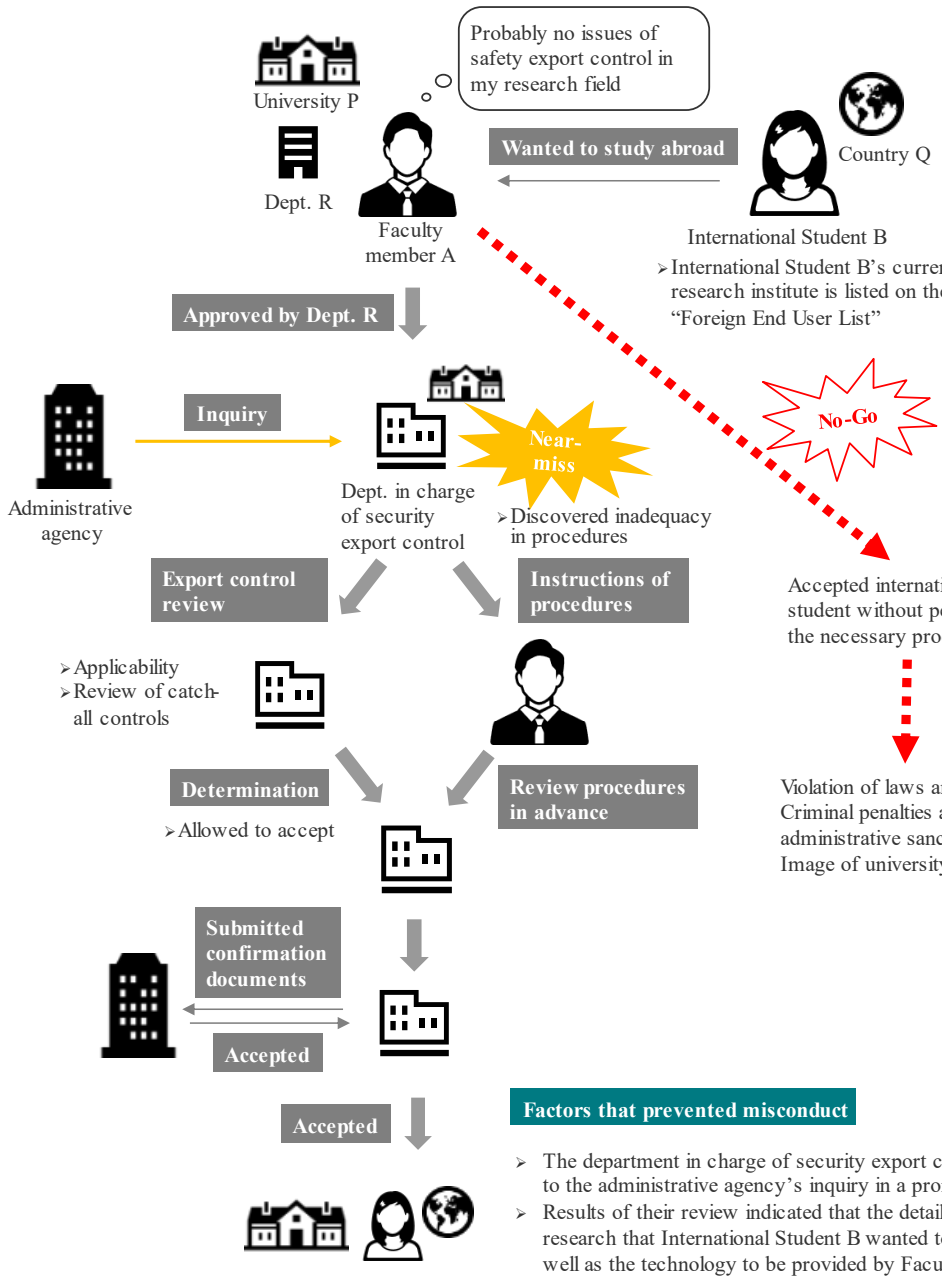
(Commentary)

For more information on export control, please refer to the website of the General Incorporated Foundation, Center for Information on Security Trade Control.

https://www.cistec.or.jp/english/index.html

10-2. Export control prescreening procedures for accepting international students

Affiliated institution	University, University hospital	Field	Life sciences



Factors that prevented misconduct

- The department in charge of security export control responded to the administrative agency's inquiry in a prompt manner
- Results of their review indicated that the details of the research that International Student B wanted to conduct, as well as the technology to be provided by Faculty member A, did not fall under the category of sensitive technologies (such as nuclear weapons and missiles)

1. Case details

- Faculty member A of University P had decided to accept a government-sponsored International Student B (university recommendation) from country Q, and was moving ahead with the procedures with the manager of Department R.
- The administrative agency then made a direct inquiry with the department in charge of security export control at University P, and discovered that the procedures for export control performed by Faculty member A and Department R were inadequate. ☜ **Factor that prevented misconduct**
- The research institute that International Student B was affiliated with at that time was listed in the "Foreign End User List [1]". To accept International Student B, it was necessary to comply with the Standards for Exporters to meet as stipulated in the Foreign Exchange and Foreign Trade Act ("FEFTA") as well as perform the preliminary procedures for export control review in accordance with the university's regulations. But Faculty member A and the manager of Department R did not follow those procedures.
- The department in charge of security export control at University P immediately verified the facts with Department R and instructed Faculty member A to follow the prescribed procedures.
- The department in charge of security export control proceeded to promptly conduct an export control review (applicability[2], review of catch-all controls[3]) and found that International Student B's research theme did not fall under the category of sensitive technologies (such as nuclear weapons and missiles). The same department determined that University P was allowed to accept International Student B, and proceeded to submit confirmation documents to the administrative agency, which were accepted.

2. Backdrop & factors of near-miss incident

- Faculty member A and Department R lacked awareness of security export controls. As International Student B belonged to an institution listed in FEFTA's "Foreign End User List", their acceptance was a matter that should be carefully reviewed in advance according to the prescribed procedures.
- Faculty member A assumed that his research field had nothing to do with security export control, and was under the mistaken impression that there were no precedents where procedures had to be performed in advance when accepting researchers from other countries.
- Despite the fact that Faculty member A did not check if any procedures were required to be performed in advance as stipulated by FEFTA or university's regulations regarding the acceptance of International Student B, Faculty member A checked the "FEFTA Confirmed" box on the recommendation form for International Student B.
- At University P, the person in charge of "export control" was different from the person in charge of "student support" and coordination of the recommendation forms. The person in charge of "student support" therefore proceeded with the procedures to accept International Student B based on the checked "FEFTA Confirmed" box on the recommendation form.

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1 Information provided by the Ministry of Economy, Trade and Industry on organizations (e.g., companies, universities, research institutes) located in other countries where concerns about the development of weapons of mass destruction cannot be allayed for reference purposes. As of January 20, 2023, 670 institutions from 15 countries are listed.
https://www.meti.go.jp/policy/anpo/20221104-3.pdf

2 To determine whether or not the goods to be exported or the technologies (including programs) to be provided fall under the category of List Control Goods.
https://www.meti.go.jp/policy/anpo/englishpage.html

3 A system where permission from the Minister of Economy, Trade and Industry is required for the export or provision of goods that do not fall under the category of List Control Goods (export of goods or provision of technology for which prior permission must be obtained), under certain conditions.
https://www.meti.go.jp/policy/anpo/englishpage.html

3. Factors that prevented misconduct & its backdrop

- The department in charge of security export control received an inquiry from the administrative agency, to which they proceeded to verify the facts with Department R and instructed Faculty member A to follow the prescribed procedures.
- The department in charge of security export control promptly conducted an export control review (applicability, review of catch-all controls). After they reviewed the details of the research that International Student B wanted to conduct, as well as the technology to be provided by and the affiliation institution of Faculty member A, and came to the conclusion that there were no concerns regarding export control.

4. Possible research misconduct and questionable research practice

- Unauthorized provision of controlled technologies through international students may result in criminal penalties and administrative sanctions under FEFTA.
- If it had been deemed unacceptable to accept International Student B due to concerns regarding export control, which all started with Faculty member A's lack of awareness and procedural blunders, the image of not only Faculty member A, but also the University as a whole, might have been tarnished.

5. Preventive countermeasures

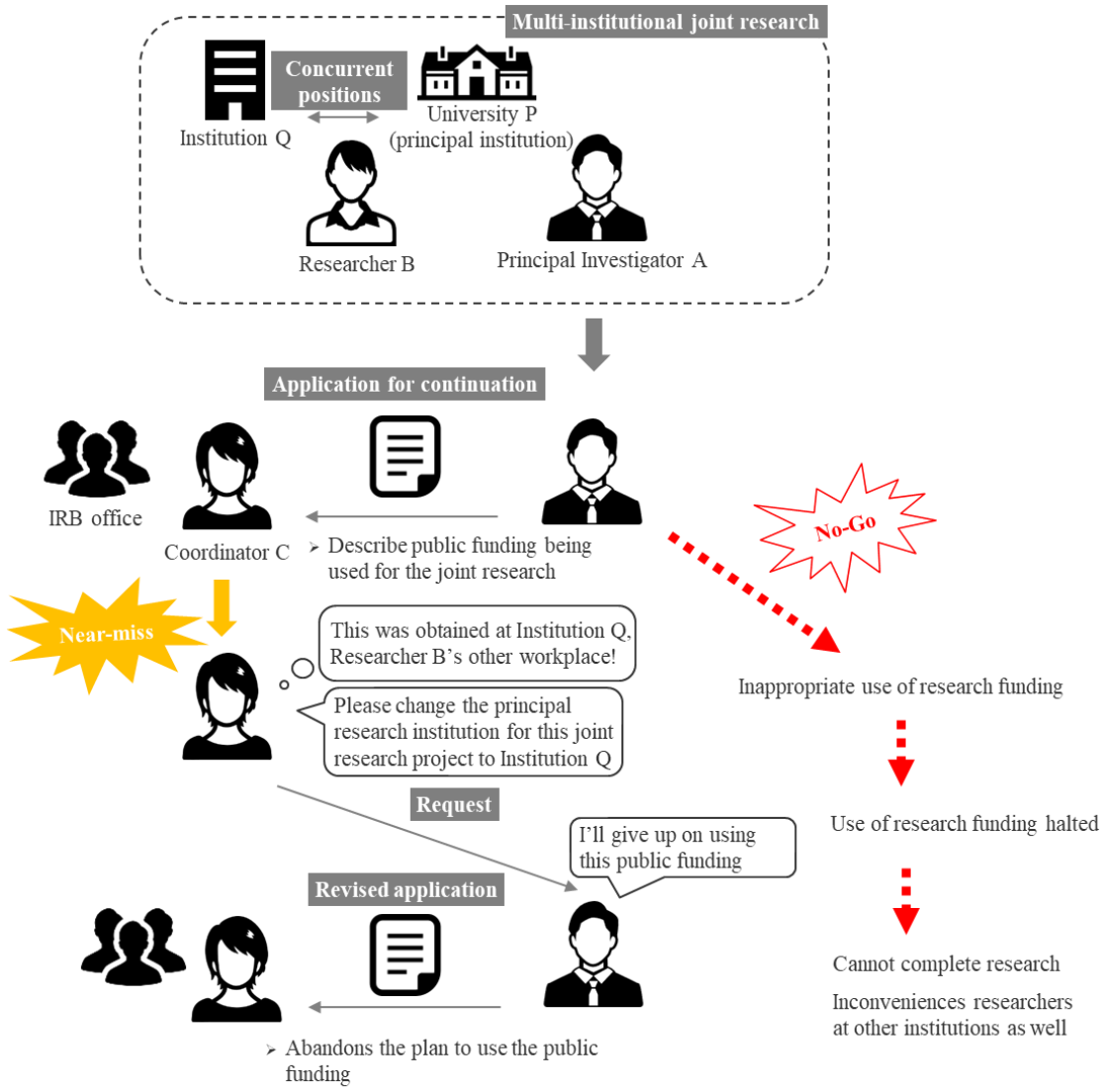
- Thoroughly inform all faculty and staff at research institutions, including universities, of the need to follow export control procedures when it comes to accepting international students.
- Also, provide regular education and training for faculty and staff in each department and division to raise their awareness of export control, and repeatedly remind them of the necessary procedures.
- The department in charge of security export control should confirm that all the departments have completed the export control application by the time the decision to accept international students who have passed the entrance examination is made.

11. Improper use of research funds

1. Discrepancy between the affiliation of the recipient of research funding and the principal research institution*

11-1. Discrepancy between the affiliation of the recipient of research funding and the principal research institution

Affiliated institution	University, University hospital	Field	Life sciences



Factor that prevented misconduct

- Coordinator C from the IRB office conducted careful checks when the application for continuation was received
- In the past, there had been a case in which research funding received by a researcher who was not a principal investigator had been listed on an IRB application form as having been received by the principal investigator; the IRB had pointed this out and asked the principal investigator to amend the application. Based on this experience, University P required details of research funding to be provided when submitting applications to the IRB

1. Case details

- Professor A at University P was serving as principal investigator for a multi-institutional joint research project in which University P was the principal institution. Researcher B, who held posts at both University P and Institution Q, was listed in this joint research project as being affiliated to Institution Q.
- As the study period for the joint research project was longer than five years, Professor A submitted an application for continuation to the Institutional Review Board (IRB) at University P, as the principal institution.
- University P required a detailed description of any public funding to be used for joint research to be provided in any application to the IRB. When Coordinator C from the IRB office checked the experiment protocol in the submitted application for continuation, they noticed that Researcher B was listed as the principal investigator in respect of the public funding. They sought detailed information from the department in charge at University P and discovered that the research funding had been obtained based on Researcher B being treated as affiliated to Institution Q, at which they held a concurrent post, rather than as a member of University P. ☚ **Factor that prevented misconduct**
- As it was not possible to use research funding obtained by Researcher B as a member of Institution Q for a multi-institutional joint research project in which University P was the principal institution, Coordinator C informed Professor A that they should reapply, changing the principal institution to Institution Q in order to use the public funding in question.
- Professor A ultimately decided not to use the public funding for this research project and, after amending the application form, resubmitted it to the IRB.

2. Backdrop & factors of near-miss incident

- Professor A was not sufficiently aware of the rule that the affiliation of the recipient of public funding to be used for research must match the study's principal institution.
- They were also under the misapprehension that public funding received by Researcher B as the principal investigator, who was treated as being affiliated to Institution Q, could be used unconditionally and without Researcher B contacting University P for a joint research project in which Professor A was the principal investigator and which was originally a separate project.

3. Factors that prevented misconduct & its backdrop

- Coordinator C from the IRB office conducted careful checks when the application for continuation was received.
- In the past, there had been a case in which research funding received by a researcher who was not a principal investigator had been listed on an IRB application form as having been received by the principal investigator; the IRB had pointed this out and asked the principal investigator to amend the application. Based on this experience, University P required details of research funding to be provided when submitting applications to the IRB.

4. Possible research misconduct and questionable research practice

- There is a possibility that the study would not have been able to be completed if the research team had been ordered to cease using the funding on the grounds of inappropriate use of public funds.
- As it was a multi-institutional joint research project, this would have inconvenienced researchers at other institutions as well.

5. Preventive countermeasures

- Universities must not only provide researchers with support for obtaining research funding, but also ensure full awareness of the following:
- There are cases in which mixing multiple packages of research funding is not permissible, even if there is only partial overlap or similarity in study plans;
- Even where the research funding has been obtained by the principal investigator, there are cases in which restrictions are placed on the scope of budget implementation, where transferring between institutions or taking on additional posts means that the principal investigator is affiliated to multiple institutions.

(Commentary)

Checks by the IRB functioned effectively in this case. It suggests the importance of leveraging this knowledge for future reference in regard to matters needing to be checked by the IRB, such as conflicts of interest or the use of public funding. For example, matters pointed out in past reviews and experiences of near-miss incidents could be used as the basis for preparing checklists or incorporated into guidance for applicants.

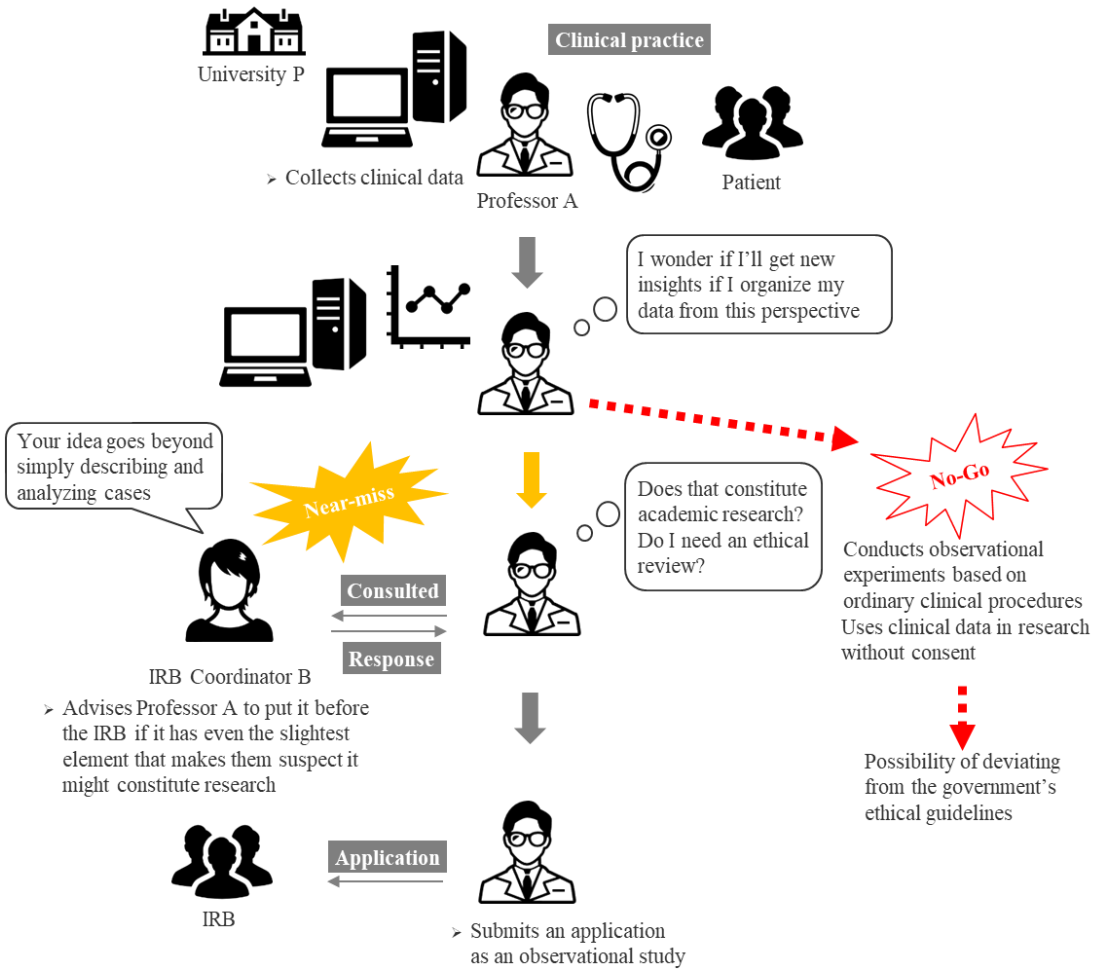
12. Other

1. Difficulty in distinguishing between an observational study and clinical practice*
2. Handling of personal information and intellectual property rights by a company serving as a joint research partner*
3. Approach to addressing situations where researchers are themselves subjects*

Editor’s column 8: Voluntary participation and subjects’ well-being*

12-1. Difficulty in distinguishing between an observational study and clinical practice

Affiliated institution	University, University hospital	Field	Medicine



Factor that prevented misconduct

- Researchers tend to be reluctant to engage in procedures such as ethical reviews or to seek advice from staff in charge of ethical matters, but Professor A was able to obtain advice from IRB Coordinator B after explaining their situation and concerns to them

1. Case details

- Professor A at University Hospital P routinely engaged in clinical practice and collected clinical data on patients.
- In the course of their clinical practice, Professor A realized there was a possibility that analyzing the clinical data amassed to date from a particular perspective could provide new discoveries and lead to progress in the field of medical science.
- Accordingly, Professor A made plans to conduct an observational study based on their ordinary clinical practice and was about to begin actually analyzing some of the clinical data.
- However, it occurred to Professor A that this course of action constituted scientific research and might therefore need to be put before the Institutional Review Board (IRB), so they decided to seek advice from IRB Coordinator B. ☜ **Factor that prevented misconduct**
- IRB Coordinator B stated that, while the ethical guidelines certainly did state that case reports and the like did not constitute research, Professor A's idea went beyond simply describing and analyzing cases, and encouraged Professor A to put the study before the IRB if it had even the slightest element that might constitute research.
- Professor A accepted this and submitted their plan to the IRB as an observational study.

2. Backdrop & factors of near-miss incident

- While it is easy to distinguish between medical care and research in the case of interventional studies, it is more difficult in the case of observational studies, which often involve collecting and analyzing data from research subjects in the form of patients suffering from a particular illness or injury, and tracking their outcomes. There is a risk that researchers who are physicians can do this without realizing, with few opportunities for discovery by third parties.
- In addition, due in part to the fact that the ethical guidelines state that case reports do not constitute research, there are times when it is difficult for individual researchers to identify the dividing line between clinical practice and research.

3. Factors that prevented misconduct & its backdrop

- Researchers tend to be reluctant to engage in procedures such as ethical reviews or to seek advice from staff in charge of ethical matters, but Professor A was able to obtain advice from IRB Coordinator B after explaining their situation and concerns to them.

4. Possible research misconduct and questionable research practice

- Using clinical data in research could constitute a serious case of noncompliance with the guidelines, etc. if the researcher conducts the study without going through such procedures as gaining IRB approval and obtaining consent from research subjects.

5. Preventive countermeasures

- An agreement was reached at the level of University Hospital P's IRB office, to the effect that university hospital researchers will be warned in advance about distinguishing clinical practice and research.

(Commentary)

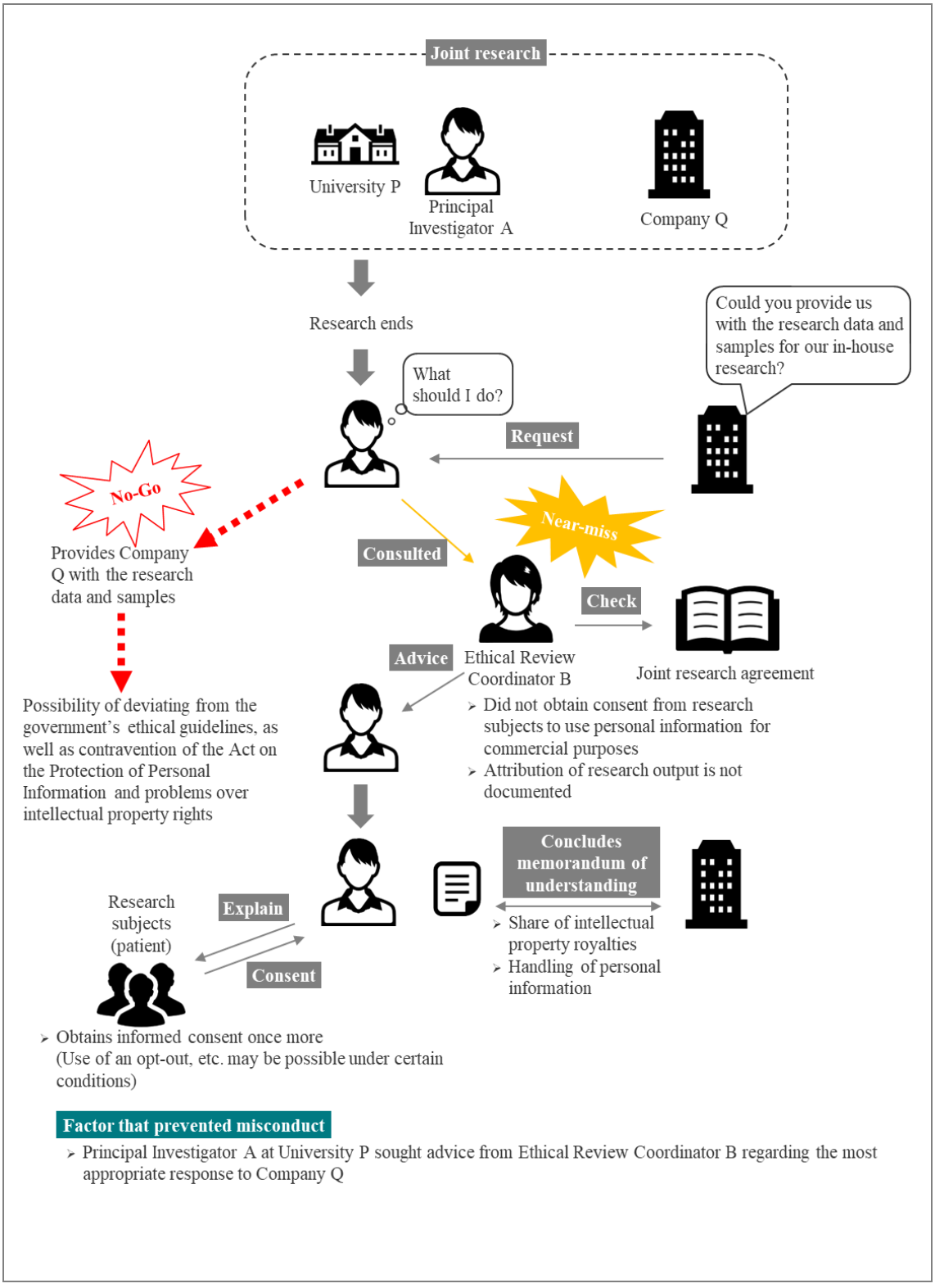
Researchers tend to be reluctant to engage in procedures such as ethical reviews or to seek advice from staff in charge of ethical matters. It is easier for researchers to seek advice if they maintain the attitude that IRB coordinators are there to provide support in protecting researchers' careers.

It can be difficult for individual researchers to identify the dividing line between clinical practice and research. If researchers have the slightest hesitation, such as in cases where their plan includes analytical activities spanning multiple cases, they should seek advice from those associated with IRBs and the like, rather than relying on their own judgment. Furthermore, it is desirable for researchers to build day-to-day relationships that enable them to readily seek advice from those associated with IRBs when situations like these arise.

In addition, if a researcher is thinking about publishing anything other than a case report as a paper or conference presentation, they should regard it as an observational study.

12-2. Handling of personal information and intellectual property rights by a company serving as a joint research partner

Affiliated institution	University, University hospital	Field	Medicine



Factor that prevented misconduct

- Principal Investigator A at University P sought advice from Ethical Review Coordinator B regarding the most appropriate response to Company Q

1. Case details

- University P and Company Q were conducting joint clinical pharmaceutical research with funding provided by Company Q.
- After the joint research had been completed, Company Q contacted University P to find out whether the university would be willing to provide it with the research data and samples from the study.
- Principal Investigator A at University P sought advice from Ethical Review Coordinator B regarding the most appropriate response to Company Q. ☜ **Factor that prevented misconduct**
- Ethical Review Coordinator B checked and found that, when obtaining informed consent for their joint research project, University P and Company Q had obtained research subjects' consent to acquire their personal information for the purpose of academic research, but had not clearly obtained consent for its use for commercial purposes. In addition, the joint research agreement between University P and Company Q stated only that matters concerning the attribution of research output would be specified separately, so it was necessary to document again how intellectual property rights were to be handled.
- Accordingly, University P and Company Q concluded an additional memorandum of understanding that set out their shares of royalties for intellectual property rights, with a view to approval by the Pharmaceuticals and Medical Devices Agency (PMDA).[1] After receiving Institutional Review Board (IRB) approval based on this, informed consent was obtained once more from all research subjects (an opt-out could also have been used under certain conditions) and consent was also obtained for the use of subjects' personal information for commercial purposes and for the provision of research data and samples to Company Q.
- University P then handed over the research data and samples to Company Q.

2. Backdrop & factors of near-miss incident

- At the time University P and Company Q concluded their joint research agreement, the two parties needed to reach a clear agreement on the handling of research data and samples after completing the research and the attribution of the output.
- If the handling of research data, samples, and output is not properly stipulated beforehand, there is a possibility that problems could arise after the study ends. It also means that the explanation provided when obtaining consent from research subjects is inadequate, which has the potential to prevent the information required from being provided correctly.

3. Factors that prevented misconduct & its backdrop

- Principal Investigator A at University P sought advice from Ethical Review Coordinator B regarding the most appropriate response to Company Q.

4. Possible research misconduct and questionable research practice

- Under the Ethical Guidelines for Medical and Biological Research Involving Human Subjects, this constitutes a case that undermines the proper conduct of research and risks being deemed noncompliant with the guidelines.
- There is also a risk that it conflicts with the Act on the Protection of Personal Information.
- In addition, there is a risk that problems concerning intellectual property rights could arise between University P and Company Q.

5. Preventive countermeasures

- Seek prior advice from the academic-industrial collaboration coordinator, IRB coordinator or similar individual.
- When seeking an ethical review for joint research, describe the attribution of intellectual property rights and ownership of samples and information in the study plan, and have it reviewed to ensure that it does not contain any discrepancies with the content of the informed consent form.

(Commentary)

The Guidance on the Ethical Guidelines for Medical and Biological Research Involving Human Subjects[2] explains that, when obtaining informed consent, it is desirable for the individual research institution to exercise its discretion in adding certain matters to the explanation as needed, including not only the matters that the guidelines state should be explained to research subjects, but also other matters deemed necessary, such as the attribution of intellectual property rights and ownership of samples and information, depending on the content of the study.

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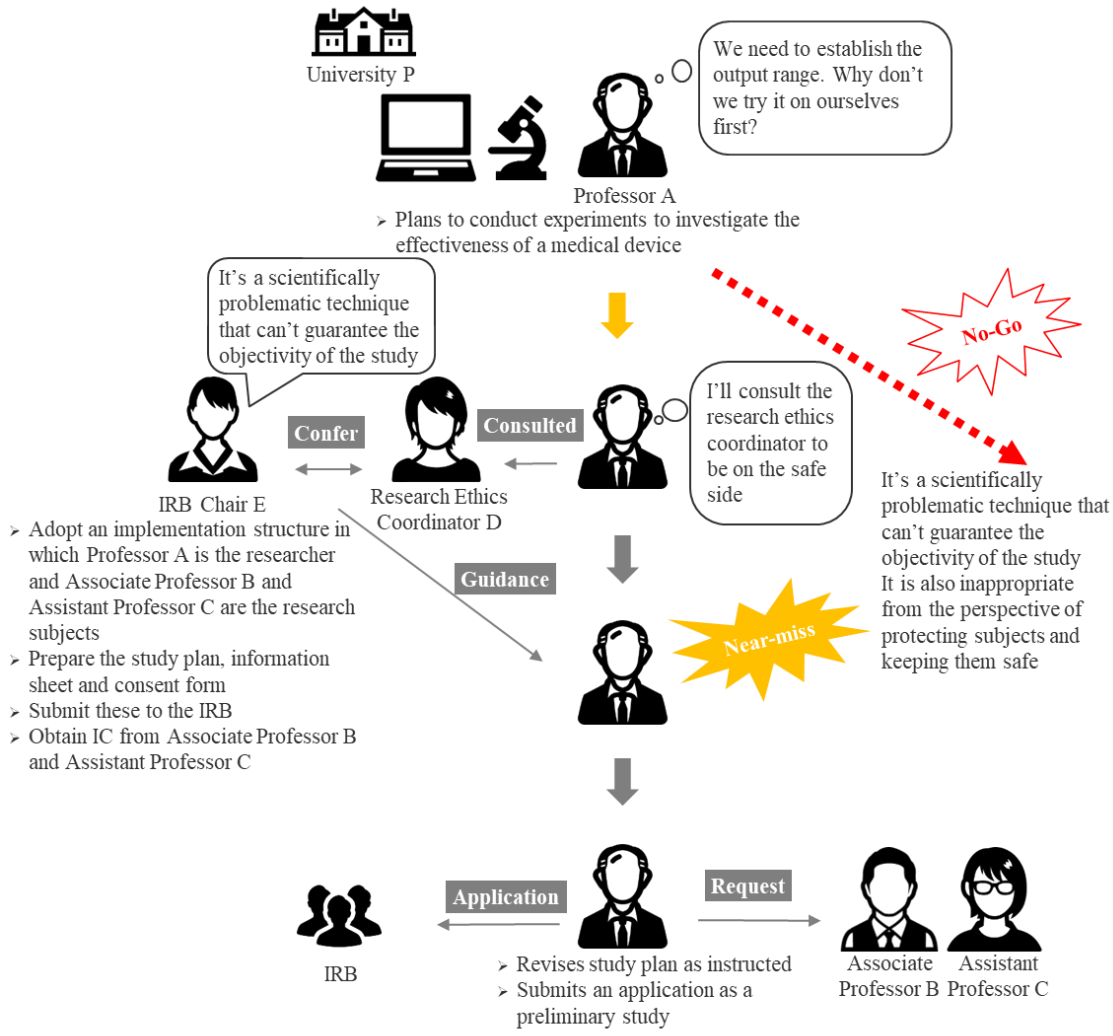
1 The PMDA's approval and review services involve reviewing the quality, effectiveness, and safety of individual pharmaceuticals, medical devices, and regenerative medicine products used in clinical settings, and over-the-counter drugs, behind-the-counter drugs, and quasi-drugs used in everyday life. https://www.pmda.go.jp/review-services/drug-reviews/0001.html

2 https://www.mhlw.go.jp/content/000946358.pdf

12-3. Approach to addressing situations where researchers are themselves subjects

Affiliated institution	University, University hospital	Field	Medical engineering



Factor that prevented misconduct

- Professor A felt vaguely uneasy about their course of action, so sought advice from Research Ethics Coordinator D
- Research Ethics Coordinator D and IRB Chair E conferred and identified the correct policy

1. Case details

- Professor A at University P was planning a study aimed at verifying the effectiveness and safety of a medical device.
- Professor A thought it was necessary to establish the output range to be used during the actual study by identifying the output at which the impact on the human body would be minor, while still being effective as medical intervention.
- Accordingly, Professor A decided to conduct preliminary deliberations ahead of the study by testing the medical device on themselves and other members of the research team.
- Professor A did not think it was necessary to draw up a study plan and submit it for ethical review, as the research team were only conducting preliminary tests of the device on themselves, but decided to seek advice from Research Ethics Coordinator D, as they felt slightly uneasy about their approach to the study. ☚ **Factor that prevented misconduct**
- Research Ethics Coordinator D reported the situation to Institutional Review Board (IRB) Chair E and, following the discussion, determined that the objectivity of the study could not be guaranteed unless the researcher and the research subject were kept separate. They also thought that the technique was scientifically problematic and inappropriate from the perspective of protecting subjects and keeping them safe.
- Accordingly, they decided that Professor A should employ an implementation structure in which Professor A was the researcher and Associate Professor B and Assistant Professor C were the research subjects. They also decided on the policy that Professor A should draw up a study plan, along with an explanation sheet and consent form, and should obtain informed consent from Associate Professor B and Assistant Professor C. Furthermore, they told Professor A that even though these were preliminary deliberations, they were still positioned as research, so Professor A should refer the plan for an ethical review.
- Professor A revised the study design in accordance with this advice and submitted it to the IRB as a preliminary study.

2. Backdrop & factors of near-miss incident

- As it merely involved preliminary tests of the device on themselves, Professor A did not think it constituted research to which the Ethical Guidelines for Medical and Biological Research Involving Human Subjects[1] were applicable.
- Still less did Professor A think that obtaining informed consent from themselves would be necessary.

3. Factors that prevented misconduct & its backdrop

- Professor A felt vaguely uneasy about their course of action, so sought advice from Research Ethics Coordinator D.
- Research Ethics Coordinator D and IRB Chair E conferred and identified the correct policy.

4. Possible research misconduct and questionable research practice

- It would seem to have been a scientifically problematic technique that could not guarantee the objectivity of the study.
- It was also inappropriate from the perspective of protecting subjects and keeping them safe.

5. Preventive countermeasures

- Ensure that institutional ethics training makes participants fully aware of the fact that, in medical engineering research and development focused on medical devices, allowing researchers to serve also as research subjects is problematic, and that such actions may be regarded as part of a study, even if they take place prior to the study proper.

(Commentary)

With regard to consent based on free will, the guidance on the government's ethical guidelines states, "When seeking informed consent for participation in research, particular care must be taken regarding the question of whether the research subject, etc. is in a dependent relationship to the researcher, etc. or whether there is a risk that their consent has been granted under duress." There are concerns about whether Associate Professor B and Assistant Professor C consented to participate in the study as research subjects of their own free will, given that they are under Professor A's influence. In terms of ensuring participation based on free will, it would seem preferable to recruit research subjects from within the university, etc. You should also be aware that some universities prohibit students who are taking the researcher's lectures or who belong to the researcher's laboratory from serving as research subjects.

[1] Ethical Guidelines for Medical and Biological Research Involving Human Subjects (March 23, 2021) (https://www.mhlw.go.jp/content/000909926.pdf)

Editor's column 8: Voluntary participation and subjects' well-being

It is said that individuals will tolerate up to three orders of magnitude greater risk for voluntary activities than for involuntary activities.[1] For example, whereas people who smoke do so voluntarily, those around them do not inhale the smoke voluntarily, which gives rise to a major disparity in how people feel about the risks of smoking and there is a sense that neither side can understand the other.

In recent years, scientific research into well-being has been conducted. It has been reported that self-awareness of well-being can be measured and that it consists of five elements: positive emotion (happiness arising from spending time enjoyably), engagement (happiness enabling the individual to become so absorbed that they lose track of time), relationship (happiness arising from being able to maintain friendly relationships), meaning and purpose (happiness arising from contributing to something one recognizes as having value), and achievement (happiness arising from achieving something). Meaning and purpose is regarded as the most important of these five elements.

In the case of medical treatment, informed consent attaches importance to providing people with a convincing prior explanation of the risks arising from that treatment, but in the case of research, it is also important for potential subjects to understand the significance of the study and to cooperate voluntarily. This is because cooperating on the basis of voluntary behavior helps to reduce the sense of risk felt by subjects, and also because cooperating in research promotes subjects' well-being.

1 Starr C. (1969) Social benefit versus technological risk, Science, 165, 1232-1238.

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We are grateful to all who have provided the cases listed in this document.

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Many of the icons used in the flow charts for each case are from Icon-rainbow (https://icon-rainbow.com/).

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