

## ICMJE DISCLOSURE FORM

**Date:** 3/4/2022

**Your Name:** Marijke Hyke Algera

**Manuscript Title:** Modelling Buprenorphine Reduction of Fentanyl-Induced Respiratory Depression

**Manuscript Number (if known):** 156973-INS-CMED-RV-3

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The author's relationships/activities/interests should be defined broadly. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

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I certify that I have answered every question and have not altered the wording of any of the questions on this form.

## ICMJE DISCLOSURE FORM

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**Your Name:** Albert Dahan

**Manuscript Title:** Modelling Buprenorphine Reduction of Fentanyl-Induced Respiratory Depression

**Manuscript Number (if known):** 156973-INS-CMED-RV-3

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**Date:** 3/4/2022

**Your Name:** Robert Dobbins

**Manuscript Title:** Modelling Buprenorphine Reduction of Fentanyl-Induced Respiratory Depression

**Manuscript Number (if known):** 156973-INS-CMED-RV-3

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**Date:** 3/7/2022

**Your Name:** Geert Jan Groeneveld

**Manuscript Title:** Modelling Buprenorphine Reduction of Fentanyl-Induced Respiratory Depression

**Manuscript Number (if known):** 156973-INS-CMED-RV-3

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**Please place an "X" next to the following statement to indicate your agreement:**

I certify that I have answered every question and have not altered the wording of any of the questions on this form.

## ICMJE DISCLOSURE FORM

**Date:** 3/4/2022

**Your Name:** Celine Laffont

**Manuscript Title:** Modelling Buprenorphine Reduction of Fentanyl-Induced Respiratory Depression

**Manuscript Number (if known):** 156973-INS-CMED-RV-3

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

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## ICMJE DISCLOSURE FORM

**Date:** 3/4/2022

**Your Name:** Laurence Moss

**Manuscript Title:** Modelling Buprenorphine Reduction of Fentanyl-Induced Respiratory Depression

**Manuscript Number (if known):** 156973-INS-CMED-RV-3

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		Click the tab key to add additional rows.	
<b>Time frame: past 36 months</b>			
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## ICMJE DISCLOSURE FORM

**Date:** 3/7/2022

**Your Name:** Marieke Niesters

**Manuscript Title:** Modelling Buprenorphine Reduction of Fentanyl-Induced Respiratory Depression

**Manuscript Number (if known):** 156973-INS-CMED-RV-3

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## ICMJE DISCLOSURE FORM

**Date:** 3/4/2022

**Your Name:** Erik Olofsen

**Manuscript Title:** Modelling Buprenorphine Reduction of Fentanyl-Induced Respiratory Depression

**Manuscript Number (if known):** 156973-INS-CMED-RV-3

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the content of your manuscript. "Related" means any relation with for-profit or not-for-profit third parties whose interests may be affected by the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. If you are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The author's relationships/activities/interests should be defined broadly. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

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## ICMJE DISCLOSURE FORM

**Date:** 3/7/2022

**Your Name:** Monique van Velzen

**Manuscript Title:** Modelling Buprenorphine Reduction of Fentanyl-Induced Respiratory Depression

**Manuscript Number (if known):** 156973-INS-CMED-RV-3

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The author's relationships/activities/interests should be defined broadly. For example, if your manuscript pertains to the epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even if that medication is not mentioned in the manuscript.

In item #1 below, report all support for the work reported in this manuscript without time limit. For all other items, the time frame for disclosure is the past 36 months.

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## Checklist for submitting a revised Clinical Medicine manuscript

In addition to addressing the items noted in the decision letter regarding your manuscript, ensure that your revised manuscript adheres to the guidelines below. For full submission details, visit the [JCI website](#).

### Required files

#### Manuscript

- PDF of a clean version of the entire manuscript, including figures, figure legends, and tables
- PDF of a marked-up version of the entire manuscript showing revisions and prefaced by a point-by-point response to reviewer comments
- Word or RTF file of all text of the submission, including Figure legends, Tables, Table legends, and References (without Figures, images, or point-by-point responses)
- Single PDF file of completed ICMJE uniform disclosure forms from all authors
- For clinical trials, PDF of the appropriate reporting checklist (CONSORT, STROBE, etc.)

#### Figures

- Publication-quality figures in TIFF format. See detailed [instructions for figure preparation](#).
- Recommended: Graphical abstract ([details available here](#))

#### Supplemental material

- Single file containing supplemental material, figures, and modest-sized tables, as:
  - (a) (if applicable) a PDF highlighting reviewer-requested changes
  - (b) a clean, publication-quality PDF
- Upload any supplemental videos and/or large Excel files separately

#### Gels

- APDF, PPT, or PPTX file (distinct from any other supplemental material) that shows the entire unedited gel
- Clearly indicate which bands were used for the figures

### Formatting

- Recommended 9,000/maximum 12,000 words (all text inclusive of Title page, Full text, References, Figure legends, and Tables)
- Double-spacing throughout, including references and tables; figure legends may be single spaced if necessary to keep a figure and its legend on the same page
- All pages numbered
- Each section begins on a new page

#### Abbreviations and acronyms

- Standard [JCI abbreviations and acronyms](#) used without definition
- All other abbreviations and acronyms spelled out at first use in the Abstract and again at first use in the main text (with the abbreviated form appearing in parentheses), and used without definition thereafter

#### Gene and protein names and symbols

- Conform to official [NCBI Gene Nomenclature](#)
- Presented according to [JCI Gene nomenclature and style](#)

#### Italicization

- Generally reserved for gene symbols, genotypes, and species names
- Terms such as *in vivo*, *in vitro*, etc., are not italicized

#### Unpublished data, manuscripts in preparation or under review, and personal communications

- Cited parenthetically in the text, not as numbered references; e.g., "(Jane L. Doe, UCLA, Los Angeles, California, USA, unpublished observations)"
- Written permission to cite unpublished observations of someone outside the author's research team (an email is sufficient) is submitted

#### Reference citations

- Appear in parentheses preceded by a space, e.g., "as described previously (1, 2)"; "several research groups (4–10) have found"
- No superscript, bold, italics, etc.

#### Figure and table callouts

- Figures and tables called out in numerical order
- "Figure", "Table", "Supplemental Figure", "Supplemental Table", etc., spelled out
- Callouts in parentheses (no boldface or italics) unless grammatically part of the sentence: "the levels increased (Figure 5A)"; "data shown in Table 2"
- Parts called out as follows: "Figure 1A", "Figure 2, A and B", "Figure 3, B–D"

### Manuscript preparation and required reporting

#### Title page

##### Manuscript title

- Clear, concise, and limited to 15 words, including conjunctions
- Refers to the relevant disease or disease model studied
- No subtitles, colons, periods, or nonstandard abbreviations

##### Authors and affiliations

- Author names provided in full (for example, "Benita J. Sjögren") and in the appropriate order
- No titles, honorifics, degrees, or certifications
- Author affiliations correspond to the period when the work was performed
- For authors whose affiliation has changed since completion of the work, specify the present affiliation and location below the numbered list
- Affiliation footnotes assigned consecutively using superscripted numbers (1, 2, 3, etc.)
- Affiliations include departments, institutions, city, state (if applicable), and country (but not mailing addresses or zip/regional codes)
- Corresponding author's complete name, address, telephone number (including country code if applicable), and email address

##### Consortium/study groups shown as authors (e.g., CARDIoGRAM Consortium)

- Unless the members of the group appear as authors, each individual member and their affiliation are listed in the supplemental material, under the heading Supplemental Acknowledgments

The following sentence appears in Acknowledgments: "See Supplemental Acknowledgments for details on {name of consortium}."

##### Conflict-of-interest statement

- A statement consistent with the Journal's [conflict-of-interest policy](#) is included; if no author has a conflict, state the following: "The authors have declared that no conflict of interest exists."
- If patents are involved, the patent or patent application number(s) are provided, and the names of the associated authors specified

## Abstract

Structured format with the sections Background, Methods, Results, Conclusion, Trial

registration, Funding

Maximum 250 words

No references

All nonstandard abbreviations defined at first use

## Main text (presented in the following order)

### Introduction

### Results

### Discussion

### Methods

Demographic reporting

Reporting on race and ethnicity adheres to [NIH guidelines](#) or other applicable authoritative standards

Descriptors for any demographic identities are clear, unbiased, and up-to-date

Data for any demographic variable are inclusive; if any information is unavailable or incomplete, an explanation is provided

Specify whether the participants or investigators made the classifications; and whether the options were defined by the investigators or participants

Complete manufacturer name (omit location) provided for each proprietary item used

For animal models, precise genotype, strain, number of backcrosses, sex, age, and source are specified

Description of all antibodies used, including the source and catalog/clone number for commercial antibodies or (reference to) a description of the generation of custom antibodies

Source of all cell lines used is indicated

Data sets for gene expression microarrays, SNP arrays, and high-throughput sequencing studies are deposited in a public repository, and accession number(s) provided in Methods the main text (for publication, data must be publicly available)

Statistics

Section appears near the end of Methods (before “Study approval”)

The *P* value used to determine significance is specified; e.g., “A *P* value less than 0.05 was considered significant.”

Analysis appropriately corrects for multiple comparisons (more than 2 groups) and for repeated measures (multiple measurements within subjects)

If samples were excluded, a statement describes inclusion/exclusion criteria

Study approval

Stand-alone paragraph at the end of Methods

Declaration of approval of human and/or animal studies, specifying the name and location of the appropriate institutional review board(s)

For human studies, a statement indicating receipt of written informed consent from participants and/or their parents/guardians

For use of photographs of patients, a separate statement of written informed consent

## Author contributions

Contribution of each author (identified by initials) is specified

Grammatically complete sentences

For manuscripts with 2 or more co-first authors, the method used to assign authorship order among these authors is stated

## Acknowledgments

States sources of support in the form of grants, equipment, or drugs

Grant numbers provided as applicable

Other appropriate acknowledgments, such as of colleagues for advice

## References

Styled according to [Journal reference instructions](#)

## Figure legends

Maximum 300 words

Each begins with stand-alone title, irrespective of the individual parts

Figure parts called out in boldface: **(A)**, **(B–D)**, **(C and E)**

Symbols and abbreviations introduced in figures are defined

In each figure legend where appropriate, the statistical test(s) used is described

Variance around the mean and statistical analysis not provided for figures representing fewer than 3 independent samples

For figure panels representing multiple experiments, exact number of samples (*n*) is reported

For representative experiments, the number of times the experiment was conducted is reported

For histological panels and insets, scale bars are defined or total original magnification is specified in the figure legends

## Figures

Prepared according to [Journal figure instructions](#)

For clinical trials, the appropriate flow diagram appears as a figure

Parts labeled with capital letters: A, B, C, etc., with no designated subparts

Graphs of quantitative data presented as either dot plots, with average and appropriate error bars indicated; or box-and-whisker plots, with values defined in the legend (bounds of the boxes, lines within the boxes, whiskers, and any outlying values); dynamite plunger plots are not permitted

If lanes in a gel or blot image are spliced together into a composite image, the lanes are separated with a thin vertical line (black on gray background; white on black background); a note in the legend states that the lanes were run on the same gel but were noncontiguous

## Tables

Prepared in Word table format (not pasted in from another application)

Self-contained and self-explanatory

Each table fits on a single page and is presented on its own page

Preceded by brief titles

Callouts to footnotes (designated with superscript capital letters) assigned alphabetically row by row

No subparts or subsections (for example, Table 1A and Table 1B)

Column headings in tables apply to all values throughout the column; a new row of column headings may not be introduced within a table

See “Methods” above for demographics reporting

## Supplemental material

A single PDF file includes all supplemental material except videos and spreadsheets. See

“Methods” above for large data sets

Before submission, carefully review all supplemental files; they will not be checked by a copy

editor. The Journal is not responsible for any errors contained in supplemental material.