

Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. It contains programming that allows appropriate data display. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in six parts.

Identifying information.

The work under consideration for publication.

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Relevant financial activities outside the submitted work.

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4.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

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Section 1. Identifying Infor	mation	·
1. Given Name (First Name) Frank	2. Surname (Last Name) Waldron-Lynch	3. Date 16-July-2018
4. Are you the corresponding author?	Yes No	
5. Manuscript Title DILfrequency: an adaptive trial to ider	ntify optimal interleukin-2 dosing in pa	tients with type 1 diabetes
6. Manuscript Identifying Number (if you 99306-INS-CMED-RV-3_mstext_30473		
Section 2. The Work Under (Consideration for Publication	
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If yes, please fill out the appropriate in Excess rows can be removed by pressi		n one entity press the "ADD" button to add a row.
Name of Institution/Company	Grant? Personal Non-Financial Fees? Support?	Other? Comments
Sir Jules Thorn Trust		
Swiss National Science Foundation (SNSF)		
Wellcome		
IDRF		

Section 3. Relevant financial activities outside the submitted work.

 \checkmark

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the "Add +" box. You should report relationships that were **present during the 36 months prior to publication**,

Are there any relevant conflicts of interest? Yes No

If yes, please fill out the appropriate information below.

NIHR Cambridge Biomedical Research Centre



Name of Entity	Grant? Personal Non-Financial Other? Comments	
Epidarex Capital		
GlaxoSmithKine		
Novo Nordisk		Almanian vorm
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Hoffmann-La Roche		
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Section 4. Intellectual Pr	roperty Patents & Copyrights	
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ection 5. Relationships not covered above

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FWL is currently employed by Novartis AG.

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Section 6. Disclosure Statement

Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

Dr. Waldron-Lynch reports grants from Sir Jules Thorn Trust, grants from Swiss National Science Foundation (SNSF), grants from Wellcome, grants from JDRF, grants from NIHR Cambridge Biomedical Research Centre, during the conduct of the study; personal fees from Epidarex Capital, grants and personal fees from GlaxoSmithKine, personal fees from Novo Nordisk, personal fees from Eli Lilly, grants and personal fees from Hoffmann-La Roche, outside the submitted work; and FWL is currently employed by Novartis AG..

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. Given Name (First Name) Adrian	2. Surname (Last Name) Mander	3. Date 07-September-2018
Are you the corresponding author?	Yes 🖌 No	Corresponding Author's Name Frank Waldron-lynch
i. Manuscript Title Targeting regulatory T cells with Inter abel trial of repeat doses of Aldesleu		diabetes: a response-adaptive, non-randomised, open-
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Dr. Mander has nothing to disclose.

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1, Given Name (First Name) James	2. Surname (Last Name) Howlett	3. Date 10-July-2018	ojani (ka Marijo) (ka posova posova na Marijo) (ka posova posova na Marijo) (ka posova posova posova posova po
4. Are you the corresponding author?	Yes 🖌 No	Corresponding Author's Name Dr Frank Waldron-Lynch	
5. Manuscript Title DILfrequency: an adaptive trial to ide	ntify optimal interleukin-2 d	osing in patients with type 1 diabetes	
6. Manuscript Identifying Number (if you	know it)		
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Mr. Howlett has nothing to disclose.

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If yes, please fill out the appropriate Excess rows can be removed by press Name of Institution/Company r Jules Thorn Charitable Trust Section 3 Relevant financi Place a check in the appropriate box of compensation) with entities as des	information below. If you have sing the "X" button. Grant? Personal No Fees? S I I I Activities outside the ses in the table to indicate wh scribed in the instructions. U	n-Financial Support? Other? Comments
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Dr. Bond reports grants from Sir Jules Thorn Charitable Trust, during the conduct of the study; .

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4. Are you the corresponding author?	Yes 🖌 No	Corresponding Author's Name Frank
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Section 2. The Work Under	Consideration for Publ	ication
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Section 5.

1 **3**. Relationships not covered above

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Section 1. Identifying Infor	mation	
1. Given Name (First Name) James	2. Surname (Last Name) Heywood	3. Date 06-July-2018
4. Are you the corresponding author?	Yes 🖌 No	Corresponding Author's Name Dr. Frank Waldron-Lynch
5. Manuscript Title Targeting regulatory T cells with Inter adaptive, non-randomised, open-labe 6. Manuscript Identifying Number (If you 99306-INS-CMED-TR-2)	el trial of repeat doses of Ald	
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1. Given Name (FIrst Name) Eleonora	2. Surname (Last Name) Seelig	3. Date 04-July-2018
4. Are you the corresponding author?	Yes 🖌 No	Corresponding Author's Name
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1. Given Name (First Name) Ed	2. Surname (Last Name) Rytina	3. Date 05-July-2018
4, Are you the corresponding author?	Yes 🖌 No	Corresponding Author's Name Dr Frank Waldron-Lynch
5. Manuscript Title DILfrequency: an adaptive trial to Ide	ntify optimal interleukin-2 d	osing in patients with type 1 diabetes
6. Manuscript Identifying Number (if you	know it)	
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1, Given Name (First Name) Marcin Lukasz	2. Surname (Last Name) Pekalski	3. Date 09-July-2018
4. Are you the corresponding author?	Yes 🔽 No	Corresponding Author's Name Frank Waldron-Lynch
5. Manuscript Title FargetIng regulatory T cells with Int abel trial of repeat doses of Aldesle		diabetes: a response-adaptive, non-randomised, open-
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Dr. Marcin Pekalski has nothing to disclose.

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4.

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1. Given Name (First Name) Mark	2. Surname (Last Name) Evans	newsken (felset) i visiel i newske felser (freeksjoel i nekstool i newsken i news	3. Date 06-July-2018
4. Are you the corresponding author?	Yes 🖌 No	Corresponding Author Seelig	"s Name
5. Manuscript Title Fargeting regulatory T cells with Inter abel trial of repeat doses of Aldesleuk		1 diabetes: a response-	adaptive, non-randomised, open-
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Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the "Add +" box. You should report relationships that were **present during the 36 months prior to publication**.

Are there any relevant conflicts of Interest? Yes

🖌 No

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work?

V No



Section 5.

on D. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

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Dr. Evans reports grants from SIr Jules Thorne Trust, grants from UK NIHR , during the conduct of the study; .

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1. Given Name (First Name) Jane	2. Surname (Last Name) Kennet	3. Date 05-July-2018
4. Are you the corresponding author?	Yes 🖌 No	Corresponding Author's Name Dr Frank Waldron-Lynch
5. Manuscript Title DILfrequency: an adaptive trial to ide	ntify optimal Interleukin-2 d	osing in patients with type 1 diabetes
6. Manuscript IdentifyIng Number (if you	know it)	
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1. Given Name (First Name) John	2. Surname (Last Name) Todd	3. Date 06-July-2018
4. Are you the corresponding author?	Yes 🖌 No	Corresponding Author's Name F Waldron-Lynch
5. Manuscript Title Targeting regulatory T cells with Inter label trial of repeat doses of Aldesleul		diabetes: a response-adaptive, non-randomised, open-
6. Manuscript Identifying Number (if you		
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5.1



1. Given Name (First Name) Linda	2. Surname (Last Name) Wicker	3. Date 05-July-2018
4. Are you the corresponding author?	Yes 🗸 No	Corresponding Author's Name Frank Waldron-Lynch
5. Manuscript Title Targeting regulatory T cells with Inter label trial of repeat doses of Aldesleul		diabetes: a response-adaptive, non-randomised, open-
6. Manuscript Identifying Number (if you	BRANCH BRANCH CONTRACTOR OF COMPANY AND A CONTRACT OF CONT	
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Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work?	\checkmark	Yes	No No	
If yes, please fill out the appropriate information below. If you have more than one entity press	the	* "ADD"	button to add	d a row.
Excess rows can be removed by pressing the "X" button.				



Patent?	Pending	Issued?	Licensed [?]	Royalties	Licensee?	Comments
Interleukin-2 fusion proteins and uses thereof US20140044675A1						Assigned to Roche Glycart no financial interest
Interleukin-2 fusion proteins and uses thereof US20150218260A1						Assigned to Roche Glycart no financial interest

Section 5. Relationships not covered above

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Section 6. Disclosure Statement

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Dr. Wicker reports grants and non-financial support from Roche Pharmaceutical , outside the submitted work; In addition, Dr. Wicker has a patent Interleukin-2 fusion proteins and uses thereof US20140044675A1 pending, and a patent Interleukin-2 fusion proteins and uses thereof US20150218260A1 pending.

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Instructions

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. It contains programming that allows appropriate data display. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in six parts.

Identifying information.

The work under consideration for publication.

This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking "No" means that you did the work without receiving any financial support from any third party — that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check "Yes".

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This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work. For example, if your article is about testing an epidermal growth factor receptor (EGFR) antagonist in lung cancer, you should report all associations with entities pursuing diagnostic or therapeutic strategies in cancer in general, not just in the area of EGFR or lung cancer.

Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.

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Non-Financial Support: Examples Include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc.

Other: Anything not covered under the previous three boxes Pending: The patent has been filed but not issued Issued: The patent has been issued by the agency Licensed: The patent has been licensed to an entity, whether earning royalties or not Royalties: Funds are coming in to you or your institution due to your patent



1. Given Name (First Name) Lucy	2. Surname (Last Name) Truman	3. Date 07-June-2018
4. Are you the corresponding author?	Yes 🖌 No	Corresponding Author's Name Eleonora Seelig
5. Manuscript Title Targeting regulatory T cells with Inte label trial of repeat doses of Aldesleu	• •	dlabetes: a response-adaptive, non-randomised, open-
6. Manuscript Identifying Number (if you (our reference 99306-INS-CMED-TR-2	know it)	
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Dr. Truman has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

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CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	ltem No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	No (adaptive trial design)
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and	2a	Scientific background and explanation of rationale	3
objectives	2b	Specific objectives or hypotheses	3
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	9
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	5
Participants	4a	Eligibility criteria for participants	9
	4b	Settings and locations where the data were collected	9
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were	9, 10,
		actually administered	Appendix
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	10
	6b	Any changes to trial outcomes after the trial commenced, with reasons	None
Sample size	7a	How sample size was determined	Not applicable
	7b	When applicable, explanation of any interim analyses and stopping guidelines	9
Randomisation:			
Sequence	8a	Method used to generate the random allocation sequence	Not applicable
generation	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Not applicable
Allocation	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers),	Not applicable
concealment mechanism		describing any steps taken to conceal the sequence until interventions were assigned	
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Not applicable

Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Not applicable
	11b	If relevant, description of the similarity of interventions	Not applicable
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	10
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	11
Results			
Participant flow (a	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and	Fig. 1
diagram is strongly		were analysed for the primary outcome	
recommended)	13b	For each group, losses and exclusions after randomisation, together with reasons	Fig. 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	5
	14b	Why the trial ended or was stopped	5
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Tab. 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was	Fig. 1,
		by original assigned groups	Appendix
Outcomes and	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its	5-7, Appendix
estimation		precision (such as 95% confidence interval)	
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Not applicable
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Not applicable
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	5, Tab 2
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	8, 9
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	8, 9
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	7-9
Other information			
Registration	23	Registration number and name of trial registry	11
Protocol	24	Where the full trial protocol can be accessed, if available	11
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	11

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.