

RSA for GMP Process-comparable and Clinical-grade AAV Vector Production

Section II AAV VECTOR STUDY INFORMATION

Do not exit your browser without saving your RSA information using one of the save buttons at the bottom of the page!
Do not use the forward/back browser buttons to navigate between RSAs; open a new browser window to access another RSA!

* Denotes Required Fields

Select Vector Type you are requesting at this time: Full GMP-grade vector (required for clinical trials)
 GMP process-comparable vector (for pharmacology/toxicology or other studies)

Note: 'GMP process-comparable' indicates vector prepared using similar cell culture and purification processes as GMP material, but for which some GMP requirements (such as raw materials qualification, manufacturing facility environmental monitoring, and in-process monitoring of process intermediates) are not fully implemented. In addition, characterization and release testing of this material is less extensive than for full GMP-grade material.

Study Title (maximum 250 characters):*

Study Abstract (maximum 4000 characters): *

(If GMP process-comparable vector is requested, describe pharmacology/toxicology study and briefly describe planned clinical trial)

Rationale for Conducting the Study (maximum 2000 characters):*

Summarize Study Endpoints (maximum 2000 characters):*

Summarize Study Design (maximum 2000 characters):*

Select Disease Category: * Heart Lung Blood Other - Please specify disease* _____

Targeted Disease: (Please Select One) ▼

Target organ(s), tissues, cell, etc.

Gene/Vector Name:

Route of administration:

Indicate the type of study in which this plasmid or vector will be used:

- Pharmacology/Toxicology Studies in animal model(s)
- Clinical Phase I
- Clinical Phase I/II
- Clinical Phase II
- Bridging Study

Attach clinical protocol document and informed consent here (Required if RSA is for full GMP-grade vector; If available, provide draft protocol when RSA is for GMP process-comparable vector):

<input type="text"/>	<input type="button" value="Browse"/>	<input type="button" value="Upload"/>
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Note: To save and upload a document, the upload button must be pressed.

If you have submitted other RSAs that relate to this study, select them from the list below:

List of submitted RSAs	RSAs related to this study
<i>This box displays the RSA numbers and titles that the investigator has already initiated. The investigator can select and add them to the far box using the blue Add button or remove them using that button.</i>	<i>RSAs that the investigator selects from the list on the left will appear here.</i>
<input type="button" value="Add"/> <input type="button" value="Remove"/>	

If you are the sole investigator and your institution is the only institution involved with this study, please indicate such by checking this box.

Sole Investigator and Institution

Co-investigator Collaboration:

List all investigators, companies/institutions that will be involved with this study (maximum 4000 characters):

<input type="text"/>

Have all of the investigators listed agreed to participate in this study and abide by GTRP Policies?

Yes No

If no, please provide an explanation:

<input type="text"/>

Please provide letters of collaboration:

<input type="text"/>	<input type="button" value="Browse"/>	<input type="button" value="Upload"/>
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Section III
AAV VECTOR REGULATORY INFORMATION

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Answer 1a or 1b below as applicable.

(1a) Have you discussed pharmacology/toxicology issues with the FDA (pre-IND meeting or other)?
(Question applies to RSAs for GMP process-comparable vector.)

Yes No

If yes, provide the following information for one meeting at a time:

Meeting date: _____ [mm/dd/yyyy] Meeting Type: Phone Face-to-Face

Meeting Summary: (maximum 2000 characters)

ADD Meeting

Click on the Add Meeting button above; your meeting information will be displayed in a table and the fields above will be cleared allowing you to enter a second, third meeting with the FDA, if needed.

Upload any FDA communications and other FDA documentation here

	Browse	Upload
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Note: To save and upload a document, the upload button must be pressed.

(1b) Have you discussed the proposed clinical study with the FDA (formal pre-IND meeting or other)? (Question applies to RSAs for full GMP-grade vector.)

Yes No

If yes, provide the following information for one meeting at a time:

Meeting date: _____ [mm/dd/yyyy] Meeting Type: Phone Face-to-Face

Meeting Summary: (maximum 2000 characters)

ADD Meeting

Click on the Add Meeting button above; your meeting information will be displayed in a table and the fields above will be cleared allowing you to enter a second, third meeting with the FDA, if needed.

Upload any FDA communications and other FDA documentation here

	Browse	Upload
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Note: To save and upload a document, the upload button must be pressed.

(2) Has the IND been filed for use of this vector construct in the submitted study? Yes No
(Question applies to requests for full GMP-grade Vector only.)

(3) Has the NIH Recombinant Advisory Committee (RAC) reviewed this study?
(Question applies to requests for full GMP-grade Vector only.)

Yes; Provide date of review:[mm/dd/yyyy] _____ No

Upload documentation:

	Browse	Upload
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Note: To save and upload a document, the upload button must be pressed.

(4) Has your Institutional Biosafety Committee (IBC) approved this study?

- Yes; Provide date of review:[mm/dd/yyyy] _____ No

Upload documentation:

Browse

Note: To save and upload a document, the upload button must be pressed.

(5a) Has your Institutional Review Board (IRB) provided provisional or final approval of the clinical protocol?

- Yes No

If Yes,

Provisional approval date: [mm/dd/yyyy] _____

Final approval date:: [mm/dd/yyyy] _____

(Question should be answered for requests for GMP process-comparable vector **and** requests for full GMP-grade Vector.)

Upload documentation:

Browse

Note: To save and upload a document, the upload button must be pressed.

(5b) Is a review scheduled with the IRB?

- Yes; Date of Review: [mm/dd/yyyy] _____ No

This RSA's ID Number is _____.

Section IV STUDY-SPECIFIC FUNDING SUPPORT

Do not exit your browser without saving your RSA information using one of the save buttons at the bottom of the page!
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**Please provide information on your current and pending funding for this research study.
Specify funding number(s), amount of funding, and funding period.**

Note:

- If any of the NIH or NHLBI grants funds are allocated for vector production, please indicate the amount.
- If your request at this time is for GMP process-comparable vector please delineate funds available for vector production as well as funds available to you to conduct your pharmacology/toxicology testing using the vector.

- NIH Funding (maximum 1000 characters):

- NHLBI Funding (maximum 1000 characters):

- Other (Institution, Industry, etc) (maximum 1000 characters):

- No Funding Secured

This RSA's ID Number is _____.

RSA-GMP Process-comparable and Clinical-grade AAV Vector Production
Web-based Form

Section V

AAV VECTOR REQUEST INFORMATION

Do not exit your browser without saving your RSA information using one of the save buttons at the bottom of the page!
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1. Vector Product Name 1:*

Note to Applicant Investigator:

¹ The Vector Product Name will appear on the final product label. It is recommended that the Vector Product Name conform to the following template: AAVX-Y..., where X indicates the AAV pseudotype, and Y...is an alpha numeric sequence (up to 8 letters/numbers) denoting the product.

2. Provide preclinical or background data on the AAV construct and activity if not described elsewhere in this application.

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Upload	

Note: To save and upload a document, the Upload button must be pressed. (maximum of 3 uploads)

3. Provide a list of recent and relevant references containing background information (e.g., vector structure and function, and characterization, etc.):

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Upload	

Note: To save and upload a document, the Upload button must be pressed. (maximum of 3 uploads)

4. Provide protocols used to generate (cell culture) and purify vector that has been used in relevant research and pre-clinical studies:

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Upload	

Note: To save and upload a document, the Upload button must be pressed. (maximum of 3 uploads)

5. Provide characterization data (titer, purity, activity, etc.) for vector used in relevant pre-clinical studies (maximum 2000 characters):

6. Provide average / typical yields for vector used in relevant pre-clinical studies (e.g., purified vector genomes recovered per prep; indicate size of prep):

7. Note to Applicant Investigator:

AAV cis-plasmid requirements for optimal vector quality, safety and yield:

- 1) Kanamycin resistance gene (to optimize safety of clinical vector product)*
- 2) ITR to ITR (transgene cassette) sequencing completed, and report available*
- 3) ITR to ITR sequence length < 5kb (i.e., within packaging limit of AAV)*
- 4) 'Backbone' sequence length > 6kb (to minimize reverse packaging)*

Is your AAV cis-plasmid available now? Yes No

If yes, amount of plasmid to be provided (must provide at least 100 ug): _____

If no, when will it be available? _____

8. Provide a detailed and accurate map of the plasmid showing (as appropriate) the AAV ITRs, promoters, transgene, polyadenylation region, and any other relevant features. Also, indicate restriction sites (e.g., SmaI, SnaBI, and PvuII and other relevant enzymes) and any unique sites.

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Upload	

Note: To save and upload a document, the Upload button must be pressed. (maximum of 3 uploads)

9. Provide a picture of a DNA gel showing the digestion pattern of the cis-plasmid with e.g. SmaI, SnaBI and PvuII, and other relevant enzymes.

	Browse
Upload	

Note: To save and upload a document, the Upload button must be pressed. (maximum of 3 uploads)

10. Provide sequencing data of the cis-plasmid if available:

	Browse
Upload	

Note: To save and upload a document, the Upload button must be pressed. (maximum of 3 uploads)

11. If the construct has not been sequenced, provide complete predicted sequence of vector expression cassette (ITR to ITR), as well as the cis-plasmid backbone:

	Browse
Upload	

Note: To save and upload a document, the Upload button must be pressed. (maximum of 3 uploads)

12. Provide a description of the titring method (e.g., dot blot hybridization, Q-PCR) that your lab has used previously for this vector (maximum 2000 characters):

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13. If Q-PCR has been used for titring, describe standards used to generate standard curves (e.g., linearized or supercoiled plasmid DNA) (maximum 2000 characters):

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Note to Applicant Investigator: The GTRP AAV Clinical Vector Core Laboratory will titer by Q-PCR using linearized standards for optimal accuracy and consistency.

14. Provide a description of method for assessment of vector functional activity (e.g. in vitro transduction of 'X' cells and assessment of transgene expression by 'Y' ELISA using 'Z' monoclonal antibody) (maximum 2000 characters):

--

15. Will you be providing the primers and probes specific for the vector? Yes No

16. Provide a summary of methods used by the Investigator to date for characterization of relevant pre-clinical vector. In particular, provide a description of any assays that you feel are unique / highly relevant to characterize the candidate vector (maximum 2000 characters):

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17. Serotype of *rep* and *cap*:

AAV2/2 AAV2/1 AAV2/5 AAV2/6 AAV2/7 AAV2/8 AAV2/9 Other *Indicate Other:* _____

18. Promoter driving the transgene expression:

19. Name of the transgene and its biological activity:

20. Localization of the protein it produces (membrane bound, cellular or secretory):

21. Any known toxicities (maximum 2000 characters):

22. Paper or manuscript describing the transgene/promoter, if available:

<input type="text"/>	Browse...
Upload	

Note: To save and upload a document, the Upload button must be pressed. (maximum of 3 uploads)

23. Are there any legal, contractual, or intellectual property constraints on the use of the vector? Yes No

If yes, please explain (maximum 250 characters):

Pharmacology / Toxicology Testing (question applies to RSAs for full GMP-grade vector):

24. Has Pharmacology and safety testing been completed? Yes No

Vector Production Requirements:

25. Estimate when you expect to initiate the planned studies:

GMP process-comparable vector (if applicable) _____

Full GMP-grade vector _____

26. Estimated amount of vector needed for pharmacology and safety testing studies (concentration required [vg/mL] and total vector genomes required) (question applies to RSAs for GMP process-comparable vector):

To denote an exponential number, use SHIFT 6 symbol. Example: 2×10^{14}

27. Estimated amount of vector needed for clinical study (concentration required [vg/mL] and total vector genomes required) (question applies to RSAs for both GMP process-comparable vector and full GMP-grade vector):

To denote an exponential number, use SHIFT 6 symbol. Example: 2×10^{14}

Formulation:

28. *Note to Applicant Investigator: The recommended formulation for the vector is 180mM NaCl, 10mM sodium phosphate, 0.001% Poloxamer 188, pH 7.3. This formulation has been characterized and optimized to maintain vector stability and consistency.*

Is this acceptable to the Investigator? Yes No

If No, provide an alternative requested vector formulation (maximum 500 characters):

29. Provide a value for the desired final product concentration (e.g. 1×10^{12} vg/mL):

30. Provide a description of the desired final product vialing configuration (e.g. 1mL product in 1.5mL cryovials, etc):

Storage:

31. *Note to Applicant Investigator: The recommended storage temperature for the final vector product is $< -60^{\circ}$ C. This condition has been demonstrated to maintain long term vector stability.*

Is this acceptable to the Investigator? Yes No

If No, please state alternative storage conditions requested:

Future Needs:

32. Describe potential future needs for production of this vector (maximum of 2000 characters):

Save and Submit Preliminary RSA

Submit Final RSA

This RSA's ID Number is _____.