**Form F**

**USAN Application for Proteins, High-Molecular Weight Peptides and Oligonucleotides, Monoclonal Antibodies, Gene Therapies, Cellular and Non-Cellular Therapies, and other substances for which a BLA is planned**

**6-21**

UNITED STATES ADOPTED NAMES COUNCIL

AMERICAN MEDICAL ASSOCIATION

330 N. WABASH AVENUE SUITE 39300

CHICAGO, IL 60611

**Email this form and all supporting documents to usan@ama-assn.org**

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| **REQUEST FOR A UNITED STATES****ADOPTED NAME (USAN) FOR A BIOLOGIC SUBSTANCE** (for USAN staff use only) |  |
| File No. (Single Entity):  | Acknowledged: |
| INN Status: | WHO No.: |

**SUGGESTED NAME(S) IN ORDER OF PREFERENCE:**

(Please attach verification of the absence of conflicts with existing generic names and trademarks.)

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**SYSTEMATIC NAME(S) OR DESCRIPTION:**

(Chemical Abstracts Service Index Name must be supplied, any other systematic names for the substance may also be listed.)

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**SEQUENCE:**

(Please attach as a word document.)

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**MOLECULAR FORMULA:** (Not required for cell therapies, for glycosylated peptides or proteins, please list the molecular formula for the peptide component, if known. If calculated, please indicate the types of calculations used.)

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**MOLECULAR WEIGHT:** (Please indicate whether this is theoretical/calculated or measured. If measured, please indicate the type of measurement(s) used, if calculated, please indicate the type(s) of calculations used. Not required for cell therapies.)

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**CHEMICAL ABSTRACTS SERVICE (CAS) REGISTRY NUMBER:**

(CAS Registry number must be supplied. A copy of the CAS search results for your compound should be submitted as an MS-Word document with your application. A CAS registry number is not required for cellular or non-cellular therapies.)

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**UNique Ingredient Identifier (UNII) NUMBER** (One will be assigned if a UNII is unknown or not available.)**:**

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**CODE DESIGNATION(S):**

(Please list all previous and current codes)

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**TRADEMARK(S):**

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**TRIVIAL NAME(S):**

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**MANUFACTURER(S):** (Please list the company sponsoring development of the drug in the US.)

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**PRINCIPAL THERAPEUTIC USE(S):**

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**PHARMACOLOGIC ACTION:**

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**DOES THE SUBSTANCE BIND TO A RECEPTOR, ENZYME, OR OTHER TARGET? YES\_\_\_\_ NO\_\_\_\_**

(If yes, please list all full names and abbreviations used to refer to the targets to which the substance binds. If this substance binds to more than 1 target, please provide binding constants or indicate the relative selectivity for each target, if known.)

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**US firms that have a US IND number are expected to file for a USAN first, rather than requesting a nonproprietary name directly from the INN Programme. If you are requesting a name that is already an INN, please list the INN number, and explain why the INN submission was made first.**

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**1. The process of selecting a USAN should be initiated after clinical studies have begun.**

 **Please indicate the date Phase 1 clinical trials began:**

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 **IND Application Number(s):**

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**2. Please attach a copy of the CAS registry information for this substance. Permission is granted to USAN to utilize this information in USAN-generated publications.**

**3.** **Permission is granted for the USAN Council secretariat to secure an International Union of Pure and Applied Chemistry (IUPAC) or other systematic name for the compounds submitted. Please note that names appearing on the statement of adoption may differ from those submitted by the firm.**

**4.** **Permission is granted for the USAN Council secretariat to submit the negotiated nonproprietary name to the World Health Organization (WHO) Nomenclature Committee for consideration. A fee of $12,000 assessed by the WHO is payable to the WHO or via wire transfer; payment will be made when the name is forwarded to the WHO for consideration and wire transfer instructions will be provided upon request. If the name is already an International Nonproprietary Name (INN), permission is granted to forward it to WHO as a matter of information.**

**5. This submission is made with the understanding that insofar as is known, none of the suggested names are trademarked or the subject of pending registration. It is further understood that the adopted USAN will remain a free and unrestricted nonproprietary name that will not be trademarked. Furthermore, USAN stems should not be incorporated into trade names.**

**6. This submission is made with the understanding that names recommended by the USAN Council for this compound will be posted on the USAN website as "names under consideration."**

**7. The undersigned understands and acknowledges that because “names under consideration” and adoption statements are published on the USAN
 website, there is a possibility that unaffiliated third parties might register a
 name as an internet domain without the prior knowledge of the USAN Program.
 The undersigned waives all liability of USAN if this is to occur.**

**8. The undersigned understands and acknowledges that all information included on the USAN application and provided by the applicant throughout the USAN negotiation process is kept confidential and is only shared with USAN staff, the USAN Council and the INN Expert Group.**

**9. The undersigned agrees not to publicly use USAN name suggestions before receiving a Statement of Adoption from the USAN Council.**

**10. Please wire $18,000.00 as the appropriate fee-for-service. You can request USAN’s wire information by contacting** **AMA.treasury@ama-assn.org****.**

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|  | **Name for a new Monoclonal Antibody, Gene Therapies, Cellular and Non-Cellular Therapies** | **$18,000** |

 ***Please make sure to note that payment is for a USAN application and include code designations or other relevant reference information.***

 **Submitted by:**

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 **Applicant: (Name of firm, sponsor or legal representative)**

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 **Address:**

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**Telephone:** (Multiple phone number(s) may be listed. Please indicate whether this is a landline or a cell phone.)

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 **Name of Contact Person:**

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Optional: Please tell us your preferred pronouns or how you would like to be addressed in correspondence: [\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_]

 **Title:**

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 **Email Address:**

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 **Signature:**

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 **Date:**

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**USAN Application Checklist for Form F**

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| **Checklist of Required information for Biologics. The following items must be supplied with the USAN application form when the firm files a request for a USAN.** |
| **\_\_ CAS registry information (Acceptable forms of CAS information below, not required for cell therapies or non-cellular immunotherapies)*** Letter from CAS showing the CAS registry number
* Electronic document (MS-Word and/or PDF document preferred) showing results of a CAS search for the CAS registry number listed on the USAN application
* Sequence and structural information should be UNMASKED in the CAS database

**\_\_ Proof of payment*** PDF copy of the wire transfer confirmation, showing banking information

**\_\_ Sequence and Structural information, All Proteins and Peptides (MS-Word Document required)*** Complete mature amino acid sequence AS EDITABLE TEXT in a [Microsoft Word document](https://www.ama-assn.org/sites/ama-assn.org/files/corp/media-browser/public/usan/sequence-request-format-other-proteins_0.doc): single letter codes for each amino acid, in groups of 10 characters with 5 groups per line and a number indicating the position of the last amino acid at the end of each line
* Complete precursor nucleotide sequence
* A list of any mutations/amino acid differences with the native sequence (for gene and allele) (e.g. mutations introduced to alter receptor binding or change the isoelectric point, to prevent C1q binding, enhance FcRn binding, etc.)
* Positions of all disulfide bridges and post-translational modifications should be listed after the sequence
* Glycosylation patterns, including site, type of sugar, etc.
* For recombinant proteins: expression system and comparison with native sequence
* If available, the three-dimensional structure in Protein Data Bank format or the Protein Data Bank accession code
* For conjugated proteins: the ratio is the mean numbers of molecules of the conjugated part (indicated by range, thus integer numbers) per molecule of protein

**\_\_ Sequence and Structural Information, monoclonal antibodies, antibody fragments, multi-specific antibodies, antibody-drug conjugates (MS-Word document required)*** All information required for proteins and peptides
* [CDR-IMGT and sequence analysis of the variable regions showing percentage of human content](http://www.imgt.org/)
* CDR-Kabat (sequence and residue range)
* IG class and subclass, IG format
* Species or taxonomy related structure (chimeric, humanized, etc.)
* Name and/or structure of targeted antigen
* Expression system
* Clone name(s) and laboratory code name(s)
* If appropriate, the closest human V, J, and C genes and alleles (results obtained with IMGT/DomainGapAlign tool)
* If the terminal lysine is absent in the heavy chain amino acid sequence, a statement confirming that indeed there is no lysine codon in the nucleotide sequence (if not the lysine should be added in the amino acid sequence mentioning the posttranslational modification clipping)
* NEW! A list of all engineered mutations in the constant region, their locations, and their purpose

\_\_ **Antibody-drug conjugates*** All information required for monoclonal antibodies
* Editable ChemDraw file of the linker/payload combination, showing which parts of the molecule are the linker and which are the payload
* Sites of attachment of the linker to the monoclonal antibody included in the MS-Word sequence document

Mandatory information for USAN selection and publication for nucleic acid-based substances including gene therapy substances and oligonucleotides. Please note that incomplete requests will not be considered) **(MS-Word Documents Required)**\_\_**Nucleic Acid-based substances (e.g., oligonucleotides, gene therapy substances)** * The full nucleotide sequence of the substance in the following format: 50 nucleotides per line, in blocks of 10, with numbering at the end of each line in a format that can be copied (Word or in the text of an e-mail). The nucleotide sequence should be annotated to delineate relevant parts of the sequence (e.g., coding regions, control regions).
* A table of features providing an overview of the relevant parts of the sequence (not required for short oligonucleotides). The table should contain the annotation, a description of the annotation, the position and the color code used in the sequence. Where a new vector is derived from an existing one, a sequence alignment and table of comparison should be provided.
* A schematic map of the entire nucleic acid showing inserted/deleted gene(s) and relevant functional parts (not required for short oligonucleotides). For cell-based gene therapy substances, please consult the “Cell-based therapies” information sheet.

\_\_**For pegylated nucleic acid-based substances*** The details of pegylation: the end group and the polymer chain with the average number of repeat units (to 2 significant figures).
* The details of the linker (not the reagent used): where the linker is attached to the active moiety, and, ideally, if multiple sites are involved, in what proportion they are modified. For conjugated nucleic acid-based substances: The mean numbers of molecules of the conjugated part, and if known, positions where the conjugate is attached.

**\_\_ Cell Therapies (MS-Word document required)*** Laboratory code name(s) and/or other code name used in publications and clinical trials
* Cell source or tissue of origin
	+ Where a cell therapy product or substance is prepared from a cellular source, a description of the starting cell material should be provided, for example, isolation from peripheral blood or apheresis material, with some characterization of the cellular subpopulations within the starting material.
	+ Where a starting cell material is derived from a Cell Bank, information on its derivation and characterization should be provided.
	+ Where a substance is initially extracted from tissue, a description of the starting tissue material should be provided, as well as the process for extraction of the cells.
	+ Where there is no further processing or manipulation of the cells, section 3 must still be completed.
* Outline the key steps of the manufacturing process, including any manipulations
	+ Describe any cell enrichment or purification/selection of the starting material or performed on the cells at any step at in the preparation of the drug product or substance.
	+ Provide a list and details of any in vitro culture conditions, including those used during genetic modification of the cells, cell activation and differentiation, number of passages and/or population doublings.
	+ Describe any in-process holding steps and the finished product storage conditions, if applicable.
* Characterization/description of the substance
	+ A detailed description of the substance should be provided. This includes, but is not limited to the cell identity, purity (identifying all major cell populations), activation state of the critical cell type(s), if they have been antigen loaded, and potency (if appropriate). The identity of the main cell populations should be described at both the phenotypic level (cell surface expression profile, using a minimum of 2 cell surface markers) and functional level, where available.
	+ Where the substance is claiming to be a stem cell to act therapeutically, additional in vitro and/or in vivo information must be provided to demonstrate that the cells are capable self-renewal, are unspecialized, and the population can give rise to a number of specialized cell types.
	+ Where the substance is claiming to be composed of stem or progenitor cells to act therapeutically, additional in vitro and/or in vivo data must be provided to demonstrate the claimed cell functionality/ies.
	+ Where the substance is claiming to be composed of stromal cells to act therapeutically, additional in vitro and/or in vivo data must be provided to demonstrate the claimed cell functionality/ies. It is up to the applicant to decide the best analytical methods and markers used to characterize the substance. Justification of the phenotype should be carefully considered.
* If genetic manipulation exists: the detailed description of the vector and insert should be provided
	+ The full nucleotide sequence of the substance in the following format: 50 nucleotides per line, in blocks of 10, with numbering at the end of each line in a format that can be copied (Word or in the text of an e-mail). The nucleotide sequence should be annotated to delineate relevant parts of the sequence (e.g. coding regions, control regions).
	+ A table of features providing an overview of the relevant parts of the sequence. The table should contain the annotation, a description of the annotation, the position and the color code used in the sequence. Where a new vector is derived from an existing one, a sequence alignment and table of comparison should be provided.
	+ A schematic map of the entire nucleic acid showing inserted/deleted gene(s) and relevant functional parts.
	+ If the manipulation has an impact on the characteristics of the cell population (e.g. modification of a known gene function or cell de-differentiation), this should be described in line with the section on ‘characterization/description’.

**\_\_ Verification of the Absence of conflicts (recommended)*** Trademark search results (WIPO database)
* Analysis of suggested names using the FDA’s POCA online tool
* Google search

**\_\_ Cover letter (recommended)*** Explanation of the action and use of your substance
* Explanation of why the USAN stem suggested was chosen for your substance

**\_\_ Additional information to support the choice of stem and document action of the compound (recommended)*** Pharmacokinetic data/binding constants showing strength of binding with intended target(s)
* Nonclinical pharmacology section or executive summary of the investigator’s brochure
* Publications related to the substance to be named

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***Please note:***

*This checklist lists USAN requirements for submission. INN has separate requirements, and failure to meet those requirements may delay INN review. If we will be filing an INN application on your behalf, requirements for the INN submission must also be included in the MS-Word document that includes structural information for the substance:*

* All Proteins <https://extranet.who.int/tools/inn_online_application/INN_online_application_files/20_481_Annex_INN_Form_Proteins_20200518.pdf>
* Nucleic acid-based substances

<https://extranet.who.int/tools/inn_online_application/INN_online_application_files/20_480_Annex_INN_Form_nucleic_20200518.pdf>

* Cell based therapies

<https://extranet.who.int/tools/inn_online_application/INN_online_application_files/20_478_Annex_INN_Form_cell_20200518.pdf>