The Basics—Definitions

- **USAN**: A nonproprietary name selected by the USAN Council according to principles developed to ensure safety, consistency and logic in the choice of names.
  - By definition, nonproprietary names are not subject to proprietary trademark rights but are entirely in the public domain. This distinguishes them from the trademarked names that have been registered for private use.

- **INN**: International Non–proprietary name
  - An INN is not a substitute for a USAN; Globally recognized

- **CAS**: Chemical Abstracts Service

- **IUPAC**: International Union of Pure and Applied Chemistry
It is USAN policy that US pharmaceutical companies who intend to market their product(s) in the US, first apply for a nonproprietary name through their national nonproprietary naming commission, which in the US is the USAN Program.

- In requesting a USAN, the manufacturer gives permission to involve the INN Expert Group in creating a global name.
USAN process should begin after the IND is filed and during clinical trials, so that the USAN will be adopted before NDA is filed.

In practice, firms usually apply for a USAN when the investigational therapy is in Phase I or Phase II clinical trials.

By then the manufacturer's patents or intellectual property covering the substance are in place, and it is early enough in clinical trials that the risk of not having a name for the NDA is low.
When to Apply

- Names should be coined, whenever possible, using the list of existing USAN stems and, for salts and esters, the list of names for organic radicals and anions.
- Before submitting an application, need to take into consideration Chemical Abstracts Service (CAS) requirements and trademark screening.
Typical timeline for USAN process

**IND Filing**
- Obtain IND number

**Phase 1**
- Earliest time that US firms may request a USAN, or non-US firms may request an INN

**Phase 2**
- Typical time for US firms to apply for USAN
  - When firm and USANC reach consensus, USAN Program files to obtain an INN on behalf of the firm
  - Planned trade names may be filed for review by FDA

**Phase 3**
- Many firms publish results of earlier clinical and preclinical studies and want the USAN at this time
  - USAN usually adopted and published
  - Non-US firms with an INN obtain USAN status for this name
USAN name: Development timeline

- At the time of NDA/BLA filing, USAN required for packaging and labeling negotiations, promotional materials.
- USP adds nomenclature information pertaining to dosage forms and delivery methods.
- Firm receives final approval of trade name from the FDA.
- Postmarketing
  - USAN required to market the drug in the US.
  - Continued safety data on the drug and names are collected.
  - Changes to generic or trade name require large-scale education of health care professionals, approval from the FDA.
  - USP publishes monographs determining drug standards, titled with the USAN.
New USAN application policy effective March 15, 2007

Because of changes in United States salt nomenclature policies, it is now a requirement to apply for USAN for both the active moiety (base, parent) of your compound and, if applicable, the salt forms, when you file the initial USAN application.

Current labeling requirements in the United States require that a USAN be obtained for the form of the compound that is to be marketed. Often this has necessitated filing a USAN application for the parent compound, followed by a separate USAN application for the modified (salt) form at a later date.
How to Apply—Application forms

- **Form A** is used to request a USAN for the parent compound and modified (salt) form of a new compound for which no USAN exists. Applicants will receive two separate USANs; one for the parent and one for the salt form intended for marketing. The fee associated with this application is $15,000.

- **Form B** is used to request a USAN for a single entity (active moiety, parent compound) for which no modified or salt form will be developed or marketed in the US. The fee is $10,000.

- **Form C** The USAN program assigns a USAN Modified (USANM) to a substance when another form of it has already received a USAN. If no related salt or parent species has a USAN, the manufacturer must apply for a new USAN. Firms that have already named a salt or its active parent may request a USANM for a second or additional substance using Form C. A $5,000 fee applies to USANM submissions.
How to Apply– Application Forms

- **Form D** The term USAN Revised (USANR) describes a revised adoption statement that allows a firm to change supporting information associated with a USAN. The USAN assigned to the substance does not change. The associated fee is $2,500.

- **Form E** is used for contact lens materials. The fee for new contact lens materials is $10,000. Form E is also used for USANM and USANR contact lens applications.
How to Apply—Contents of the application

1. Suggested names
   - Applicants should propose one to three nonproprietary names for the substance. Refer USAN Rules for coining names.
   - The suggested name for the active moiety of a drug should be a single word. If sponsor already has an INN, that name should be provided.

2. Chemical name
   - Usually two chemical names are listed for each substance.
   - First name that is coined by CAS, the CA index name.
   - The second name should be developed in accordance with IUPAC nomenclature rules. Because the IUPAC name is established by an independent chemical reviewer it may differ from those names the firm lists on the application. Occasionally the USAN Program will accept and list a third chemical name if a firm requests it.
   - In submitting a USAN application, the manufacturer acknowledges that the USANC Secretariat will secure an IUPAC chemical name for the compound.
3. CAS Registry number

- A CAS number and name is required for all USAN submissions.
- Include proof of CAS information, provided as a copy of the firm's CAS correspondence or the results of a database search. In submitting the application form a firm grants the USAN Program permission to publish the chemical information.
- This information is needed for adoption and publication.

To obtain CAS registry numbers and CA index names, contact CAS at the following:

Chemical Abstracts Service
P.O. Box 3012
Columbus, OH 43210
800–848–6538 (North America)
614–447–3600 (worldwide)
help@cas.org
http://www.cas.org/support/custcare.html
4. **Structural Formula**
   - A structural formula is necessary for the USANC to determine if a USAN or INN already exists. The structure is also needed to compare the drug to chemically related compounds. Chemical information should be as complete, current and accurate as possible, including information on stereochemistry, if known.

5. **Molecular Formula**
   - A one-line molecular formula constructed in accordance with accepted chemical practices should be supplied, if possible. If the compound to be named is a salt or ester, the molecular formula information should be supplied for both the salt or ester and the compound from which it is derived. For salts, the active and other species should be listed separately, e.g., $\text{C}_8\text{H}_{13}\text{N}_5\text{O}_4 \cdot \text{HCl}$. If no molecular formula is available, such as for gene or cell therapies, this may be left blank.
6. Molecular Weight
   Molecular weight should be calculated in accordance with the most recent guidelines for standard atomic weights of the elements recommended by the IUPAC Commission on Atomic Weights and Isotopic Abundances. If no molecular weight can be calculated, this may be left blank, but approximate molecular weights should be listed if they are known.

7. Code Designations
   Any company code designation that has been assigned to the compound, particularly if this code has been used in published scientific papers, should be entered. The listed code designation must be specific for the chemical entity being developed. If the compound was licensed or acquired from another firm, former codes should be listed.
How to Apply—Contents of the application

8. Trivial names
   - The USANC should be made aware of such names but requests that manufacturers not create, use or encourage the creation of trivial names. The fact that a trivial name has become entrenched in the literature will NOT ensure its adoption as a USAN and may only cause confusion when one is adopted. In fact, many trivial names are not accepted because they do not conform to the USAN Program's Rules for Coining Names.

9. Manufacturer
   - The manufacturer listed should be the company now developing the drug. More than one company may be listed if necessary. The listed firm may or may not be the original innovator of the drug. The company listed as the manufacturer on the application is associated with the compound on the adoption statement if a name is selected.
How to Apply—Contents of the application

10. Principal therapeutic use(s)
   - The therapeutic category for the new compound may determine the stem selected. Pertinent reprints or other supporting evidence for the claimed indications must be included with the application.

11. Pharmacologic action
   - The pharmacologic action should be explained in detail since it may influence the stem selected. Pertinent reprints or supporting evidence are required.
12. Date clinical trials began
   ◦ The approximate date when clinical trials began should be listed.

13. IND number
   ◦ Ordinarily, the USANC will not review any request without an IND application on file or select a new name without the IND number.
**Review Procedure – Initial processing of application**

- USAN Program Secretariat verifies that the application is complete (payment must be received) and that the substance meets all prerequisites to apply. Two important requirements are that the substance has entered clinical trials and has an IND number. If the requirements are met the submission is considered a complete application. Each complete application is assigned a file number and a USAN staff member as the "negotiator."

- Applicant receives an acknowledgment letter, which confirms receipt of the submission and application fee and includes the USAN file number and the name of the assigned negotiator. The negotiator serves as the manufacturer's contact for all questions and correspondence.

- Before submitting an application to the USANC, the negotiator verifies that all the information required for the USANC to select a name is included and prepares a summary for the USANC.
Before most USANs are adopted, three parties (i.e., the manufacturer, the USANC and the INN Expert Group) must accept the name. After the USANC completes deliberation and recommends a name it is sent to the manufacturer for acceptance or rejection. Criteria for selection: usefulness to healthcare providers, patient safety, adherence to the nomenclature rules, absence of conflicts with existing names, suitability for use internationally, ease of pronunciation, and other factors. If manufacturer agrees, this leads to the INN Expert Group review or USAN adoption (depending on what has been submitted). At this time, after the USANC recommendation letter is sent to the applicant, the recommended name is published on the USAN site as a "name under consideration." If manufacturer disagrees, leads to a further round of balloting, which can add about six months to the timeline.

Upon receipt, the INN Expert Group evaluates suggested names following procedures somewhat similar to those of the USANC Council. The INN Experts review and accept the proposed name, or suggest an alternative. INN review criteria include conflicts with non-US trademarks or generic names, connotations in languages other than English, and conformity to international nomenclature schemes.

Following the INN review, and if all goes well with the proposed name, is the adoption of a USAN. A letter and adoption statement formally notifies the applicant that the negotiation has been completed and a USAN assigned. A firm may begin using a USAN when it receives an adoption statement. Upon publication the adoption statement is published on the USAN Web site and forwarded to both USP for inclusion in the *USP Dictionary of USAN and International Drug Names* and CAS for inclusion in their database.