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# Using Type 9 NDA Designation to Accelerate Multiple Approvals for Your Drug Product

Authors: Elaine B. Taylor and Vibha Kumar

## INTRODUCTION

Often companies submit their original New Drug Application (NDA) and wait for approval of that original NDA before submitting a supplemental NDA with data to support a new indication or claim. This sequential process results in a delay of at least six months (if expedited review) or longer depending on the time for review of the original NDA. The United States Food and Drug Administration (FDA) has a process whereby you can submit more than one original NDA for the same drug product, alleviating the need to wait for approval of the original NDA. One type of NDA that allows for submission prior to approval to the original NDA is the Type 9 NDA. Figure 1 depicts an actual timeline for approval of two NDAs using the Type 9 NDA process and a theoretical timeline to show potential delay if second NDA had been submitted after approval of first NDA.

**Figure 1**: Rozlytrek – comparison of actual Type 9 NDA and theoretical sequential submission


**Source**: Drugs@FDA

A Type 9 NDA allows a sponsor to submit an NDA for a new indication or claim for a drug product while that drug product is currently being reviewed under a different original NDA (the "parent NDA"), and the applicant does not intend to market this drug product under the separate NDA after approval. A Type 9 NDA can be submitted on the same day as the original NDA or months later. After approval of one of the NDAs and regardless of which was submitted first, the NDA still under review will be reclassified as a Type 9 NDA. After approval of the Type 9 NDA, it will be reclassified as a supplement to the NDA approved first, and the Type 9 NDA will be administratively closed.

Historically, a majority of NDAs for new molecular entities (NMEs) and new chemical entities (NCEs) are classified as Type 1, Type 2, Type 3, or Type 5. There is limited awareness of the Type 9 NDA submission process and the benefits associated with this type of submission. These benefits include shortened approval times and abbreviated submissions as the second (Type 9) NDA can be submitted while the first (original) NDA is still under review, and information provided in the original NDA (eg, product quality, nonclinical, and clinical pharmacology) may be cross-referenced. Data specific to the proposed indication being sought under the planned second NDA is required to be provided in that NDA (eg, clinical pharmacology data).

## NDA CLASSIFICATION CODES

The NDA classification code system was developed to enable identification and grouping of product applications received by the FDA. This classification is based on characteristics of the product in the application and their relationships to products already approved or marketed in the United States (Table 1). This code was previously referred to as a Chemistry Classification Code.

The NDA classification codes are not suggestive of the innovation or therapeutic value that a drug represents but provide support for FDA's workload management and consistency across review divisions while enabling analysis of trends.

The FDA will assign an NDA classification code on the filing date for a new application and will reassess the code at approval or post-approval. The reclassification is for administrative purposes only.

**Table 1:** New Drug Application Classification Codes

| Classification | Meaning |
|---|---|
| Type 1 | DP that contains a NME |
| Type 2 | DP that contains a new active ingredient but not an NME |
| Type 3 | New dosage form of an active ingredient that has been previously approved or marketed in a different dosage form |
| Type 4 | New drug-drug combination of two or more active ingredients |
| Type 5 | New formulation or other differences (except new dosage form) from a product previously approved or marketed (including combination products) |
| Type 6 | New indication or claim, same applicant (no longer used and is replaced with Type 9 and Type 10) |
| Type 7 | DP that contains an active moiety that has been previously marketed but without an approved NDA |
| Type 8 | DP for OTC marketing that has an active ingredient that has been previously approved for marketing by Rx |
| Type 9 | New indication or claim for a DP currently being reviewed under a different NDA, drug not intended to be marketed under Type 9 NDA after approval |
| Type 10 | New indication or claim for a DP that is a duplicate of either a pending or approved NDA, drug is intended to be marketed under a separate Type 10 NDA after approval |
| **Combination NDAs** | |
| Type 1/4 | Type 1, NME, and Type 4, New combination |
| Type 2/3 | Type 2, New active ingredient, and Type 3, New dosage form |
| Type 2/4 | Type 2, New active ingredient, and Type 4, New combination |
| Type 3/4 | Type 3, New dosage form, and Type 4, New combination |
| Type 4/5 | Type 4, New combination, and Type 5, New formulation or New manufacturer |

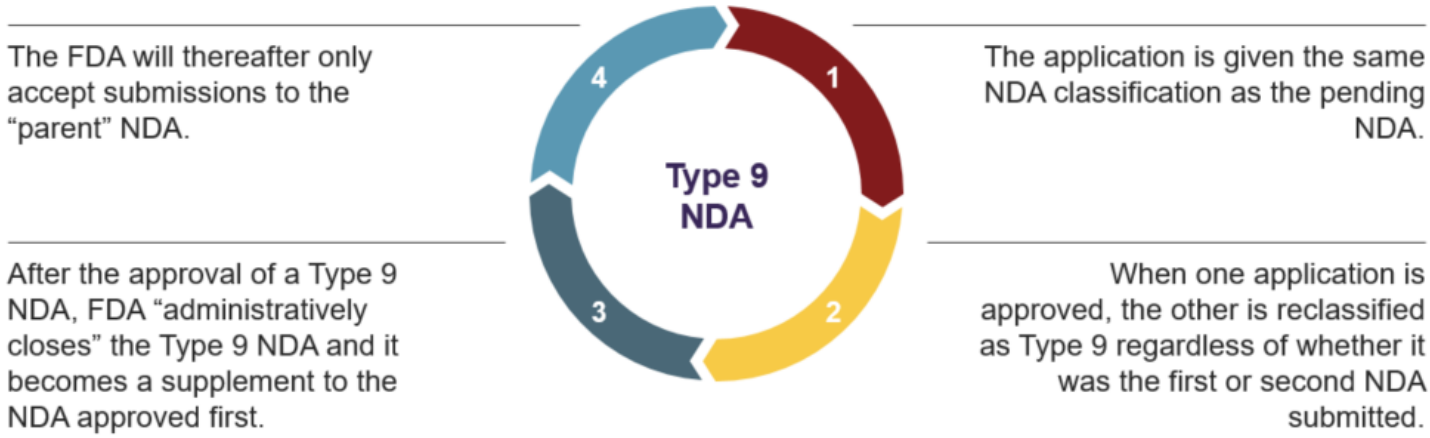
**Source:** FDA CDER Manual of Policies and Procedures (MAAP 5018.2). 2015
DP=drug product; NDA=new drug application; NME=new molecular entity; OTC=over the counter; Rx=prescription

The FDA Center for Drug Evaluation and Research Office of Pharmaceutical Quality issued a Manual of Policies and Procedures (MAPP) effective date 04 November 2015. FDA's policy regarding NDA classification codes is outlined in MAPP 5018.2 and is stated in the MAPP as follows:

- FDA tentatively assigns an NDA classification code by the filing date for a new application and reassesses the code at the time of approval. The reassessment will be based upon relationships of the drug product being approved to products already approved or marketed in the United States at the time of approval. FDA may also reassess the code after approval.
- FDA can tentatively determine a classification code for an investigational new drug (IND) prior to submission of a marketing application. This can be useful particularly with regard to whether or not the active ingredient in the IND may be considered to contain a NME. Any determination of the chemical type during the IND stage is performed as part of review and may be revised when the marketing application is submitted, or upon approval, or after approval.
- When two or more NDAs for the same active ingredient tentatively considered as an NME are submitted by the same applicant and approved at the same time, the classification is changed for all but one NDA. In this case, the decision as to which NDA should be coded Type 1 may depend on factors other than timing. For example, the NDA with the bulk of the efficacy data could be coded Type 1 and the other NDA(s) reclassified, generally as Type 3 or Type 5.
- Generally, only one NDA classification code should be assigned, except that more than one code may be assigned to combination products (Type 4 and Type 5).

Generally, a Type 9 NDA is submitted as a separate NDA to comply with the guidance for industry on Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees. Figure 2 depicts the FDA procedure when a Type 9 NDA application is submitted to FDA.

**Figure 2**: FDA procedure when a Type 9 NDA application is submitted




**Source:** FDA CDER Manual of Policies and Procedures (MAAP 5018.2). 2015.

## EXAMPLES OF TYPE 9 NDAS AND FDA REVIEW & APPROVAL

Several sponsors have submitted Type 9 NDAs under differing circumstances. We searched the FDA-approved drugs database for drugs approved from January 2017 to June 2020 and found five approved NDAs that were classified as Type 9 NDAs (Table 2). We reviewed the approval information available on Drugs@FDA for these Type 9 NDAs. These Type 9 NDA submissions included adding (1) a new indication and/or (2) safety or dosing information in the labeling. For two of the drug products (Rozlytrex and Rybelsus), the sponsors submitted their original and Type 9 NDAs on the same day. For the other three drug products, the Type 9 NDA submissions were staggered by 3 to 7 months after the original NDA submission.

**Table 2:** Type 9 NDAs approved Jan 2017 – Jun 2020

| Drug | NDA # | Date submitted | Date approved | Indication |
|---|---|---|---|---|
| Austedo | 208082 | 29 May 2015 | 03 Apr 2017 | Treatment of chorea associated with Huntington's disease |
| | 209995 (became 208082/S-001 upon approval) | 30 Dec 2016 | 30 Aug 2017 | Treatment of tardive dyskinesia |
| Verzenio | 208716 | 5 May 2017 | 28 Sep 2017 | Treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer |
| | 208855 (became 208716/S-001 upon approval) | 15 Aug 2017 | 26 Feb 2018 | Allowed for use of Verzenio in combination with an aromatase inhibitor as initial endocrine-based therapy for the same indication as NDA 208716 |
| Rozlytrex | 212725 | 18 Dec 2018 | 15 Aug 2019 | Treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are ROS1-positive |
| | 212726 (became 212725/S-001 upon approval) | 18 Dec 2018 | 15 Aug 2019 | Treatment of adult and pediatric patients 12 years of age and older with solid tumors that have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion with a known acquired resistance mutation |
| Rybelsus | 213051 | 20 Mar 2019 | 20 Sep 2019 | Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus |
| | 213182 (became 213051/S-001 upon approval) | 20 Mar 2019 | 16 Jan 2020 | Same - added cardiovascular data to labeling |
| Tazverik | 211723 | 23 May 2019 | 23 Jan 2020 | Treatment of adults and pediatric patients aged 16 years and older with metastatic or locally advanced epithelioid sarcoma not eligible for complete resection |
| | 213400 (became 211723/S-001 upon approval) | 18 Dec 2019 | 18 Jun 2020 | Treatment of adult patients with relapsed or refractory (R/R) follicular lymphoma (FL) whose tumors are positive for an EZH2 mutation and who have no satisfactory alternative treatment options |

**Source:** Drugs@FDA

## DISCUSSION

Using the Type 9 NDA submission process will allow the FDA to begin review of your second application prior to approval of the first (original) application thereby reducing the time to approval for your second application. For example, Austedo's original NDA was under FDA review for approximately 23 months before receiving approval, and at Month 19, a Type 9 NDA was submitted for a new indication. By submitting the Type 9 NDA for a second indication during review of the original application, the overall time to market for the second indication was reduced by 4 months – a key advantage for both the company and the patients that will have earlier access to the drug. For drugs that generate $100 million in annual sales, four months earlier to market may produce an additional $33 million in sales.

Earlier approval may also result in first to market which has several advantages. McKinsey evaluated 492 drug launches over a 27-year period and found that first-in-class players on average achieve a greater-than-fair market share of 6% over later entrants. In addition, McKinsey noted that expansion of indications faster than later entrants can result in 13% above fair market share (McKinsey 2014).

One consideration for this process are the NDA fees. Under the Prescription Drug User Fee Amendments (PDUFA) VI, which took effect in 2018, supplements will no longer incur a fee but since both the original and Type 9 are considered NDAs at the time of submission, they may both be assessed the standard NDA fees. The fees will be dependent on several variables and you will want to verify the fees at the time of your NDA submissions.

A risk associated with submitting prior to approval of your original NDA is that you are not certain that the key sections in the original NDA will be considered approvable by the FDA. There may be chemistry, manufacturing, and control (CMC), clinical, nonclinical, or other deficiencies that the FDA identifies in your original application that affect the approvability of your Type 9 application. You avoid these potential issues when you wait for your original NDA to be approved. This risk may outweigh the gain in the timeline and should be evaluated for each individual product prior to use of the Type 9 NDA process.

The Type 9 NDA process has the potential to reduce the timeline from submission of an original application to the submission and ultimate approval of an additional indication or other claim. An assessment of timing, cost implications, and any risks should be evaluated to determine the feasibility of using a Type 9 NDA for your drug product program.

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## About the Authors

Elaine Taylor
Vice President, Regulatory Strategy and Policy,
Synchrogenix, a Certara company

Elaine Taylor has more than 30 years of experience in the pharmaceutical industry and has extensive experience developing and providing strategic guidance and regulatory advice at all stages of product development. Currently, Elaine is Vice President of Regulatory Strategy and Policy at Synchrogenix, a Certara company, where she leads the Regulatory Strategy group. Her group provides global regulatory strategy, consulting, and submission support from early stage (preclinical) to post-marketing.

Vibha Kumar
Senior Regulatory Writer,
Synchrogenix, a Certara company

Vibha Kumar has over 15 years of experience in the pharmaceutical industry as a regulatory affairs professional. She has supported CMC development and regulatory submissions for a variety of finished product dosage forms with emphasis on regulations and electronic Common Technical Document requirements. In her current role at Synchrogenix, a Certara company, as Senior Regulatory Writer, Vibha leads and writes regulatory documents ensuring they follow current regulations and guidances.

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