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## Variability of Drug Attributes in the US Market (RxNorm) compared to selection of Worldwide Market (RxNorm Extension)

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### Abstract

*We present details about RxNorm Extension, an international drug coding system that has the same structure as RxNorm, but covers product available in non-US markets: Canada, France, Germany, the UK, Australia. RxNorm Extension is used together with RxNorm as a single system to support the expansion of the OHDSI research network beyond the US. Here, we study the distribution of attributes for drugs in the different markets and their trends and differences.*

### Introduction

The OHDSI approach to systematic and standardized analytic of large-scale observational data is based on a common data model with a harmonized representation of clinical events: the OMOP Standardized Vocabularies. OHDSI makes the standard reference concepts and mapping available to the community. Drugs are one dimension of clinical events. RxNorm is a public drug repository, created by the National Library of Medicine, is used as a core to represent drugs in the data. RxNorm fully normalizes attributes of drugs: their ingredients, dose form, brand name and strength.

However, RxNorm is only available for drugs marketed in the United States. Products not sold in the US are therefore missing from RxNorm. We created a heuristic to create RxNorm Extension, a new drug repository, which is built from national drug repositories. Existing drugs as defined by their attributes are mapped and new ones are added. Attributes are mapped or introduced if missing as following:

- Active Ingredients not approved for marketing in the US are added (e.g. Pipradrol) as well as traditional medicines and herbal extracts
- RxNorm covers most of the conventional Dose Forms, except some exotic ones such as medicated nail polishes or those that those that are usually categorized as devices, such as intrauterine drug delivery systems
- Brand Names not used in the US are added (ImmuCyst, Kanuma, Loceryl etc.).

The RxNorm and RxNorm Extension vocabularies together form a comprehensive Drug Domain able to codify the local drug market of any country and therefore the patient data containing the drug exposure in these markets.

### Results

Here, we present trends and difference in the attributes of drugs in RxNorm and RxNorm Extension. There are much more ingredient combinations available worldwide. RxNorm has 4522 (54.3%) drugs containing single active ingredient and 3916 (45.7%) drugs contain several ingredients, but worldwide marked contains 7548 (30.1%) single-ingredient drugs and 17514 (69.9%) drugs with several ingredients. Overall, single-ingredient drugs in worldwide markets exceed multi-ingredient set more than twice, and

this number is likely going to increase further the addition of national drug repositories. The growth is mostly driven by an equal doubling of brand names and dosages, while ingredients grew by 10%. The basic attribute of any drug is the active ingredient, which is formulated into a specific strength, a dose form and may or may not be sold under a brand name. We will discuss the distribution of these attributes for each ingredient and compare between the US market, the world market, and selection of drugs that are prescribed in large-scale clinical data:

**Table 1. Average number of attributes per ingredient in different markets.**

Ingredients	Market	Dose Forms	Brand Name	Drug strength
Single	US	2.27	3.89	6.58
	World	3.15	9.8	11.71
	Actual data	2.94	7.69	5.58
Combo	US	1.44	3.44	3.5
	World	1.29	1.85	2.58
	Actual data	1.37	1.99	1.73

There are a number of trends comparing the various drug markets:

1. Single-ingredient drugs have a lot greater variety of dose forms than combos.
2. In non-US markets, multi-ingredient products are less often branded than single-ingredient products whereas in RxNorm they are more equally distributed..
3. The same trend is visible in drug strength variety, albeit not as pronounced.

### **Conclusion**

The worldwide market is different from the US market and RxNorm Extension provides a proper and accurate representation of various country-specific data.