Product Quality Test for Pharmaceutical products (USP 40)

ภญ. ศศิดา อยู่สุข

สำนักยาและวัตถุเสพติด

กรมวิทยาศาสตร์การแพทย์

15 พฤศจิกายน 2560

Product quality tests, general

- To ensure that drug products are safe and effective at the time of release and over their shelf life
- Reference : **<1151> PHARMACEUTICAL DOSAGE FORMS (USP 40)**

Identification

- establish the identity of the drug substance(s) present in the drug product
- discriminate between compounds of closely related structure that are likely to be present
- be specific for the drug substances

Assay

- A **specific and stability-indicating test** should be used to determine the strength (API content) of the drug product

Impurities

- **API and excipients :** Process impurities, synthetic byproducts, and other inorganic and organic impurities
- from degradation of the drug substance
- from the drug-product manufacturing process
- Residual solvents

Uniformity of Dosage Units

- The variation in the drug substance content of each dosage unit be accurately controlled throughout the manufactured batch or compounded lot of drug product.
- demonstrated by one of two procedures: content uniformity or weight variation

Physicochemical properties

- pH
- Specific Gravity

Particle Size

- have a significant effect on dissolution rates, bioavailability, therapeutic outcome, and stability
- Aerosols, Nasal Sprays, Metered-Dose Inhalers, and Dry Powder Inhalers <601>

Dissolution

- to measure release of the drug substance(s) from the drug product such as tablets, capsules, suspensions, granules for suspensions, implants, transdermal delivery systems

Water content

- A test for water content is included when appropriate

Antimicrobial Preservative Content

- Acceptance criteria for preservative content in multidose products should be established.
- based on the levels of antimicrobial preservative necessary to maintain the product's microbiological quality at all stages throughout its proposed usage and shelf life

Antioxidant Content

- If antioxidants are present in the drug product, tests of their content should be performed.

Microbial Limits

- The type of microbial test(s) and acceptance criteria are based on the nature of the drug substance, method of manufacture, and the route of administration

Sterility

- Depending on the route of administration—e.g., ophthalmic preparations, implants, and solutions for injection

Leachables

- When evidence exists that leachables from the container-closure systems (e.g., rubber stopper, cap liner, or plastic bottle) have an impact on the safety or efficacy of the drug product, a test is included to evaluate the presence of leachables.

Other Tests

- alcohol content
- redispersibility
- particle size distribution
- rheological properties
- endotoxins/pyrogens
- particulate matter
- functionality testing of delivery systems
- osmolarity

<2> PRODUCT QUALITY TESTS FOR ORAL DRUG PRODUCTS

- (1) **universal tests** that are applicable to all oral drug products and should be included in the monograph, and
- (2) **specific tests** should be considered for inclusion for specific types of oral products.

Universal tests for Oral Drug Products

- **Universal tests**
  - **Identification** : The results of the identification test must be compared to the results obtained from a similarly prepared, suitable reference standard.
  - **Assay**
  - **Impurities** : degradation of the drug substance or from interactions between the drug substance and excipient(s)

Specific Tests for Tablets

- depending upon the nature of the drug substance and formulation
- **Volatile content** :
  - **Loss on drying** determines the amount of volatile matter of any kind that is driven off under the conditions specified
  - **Water determination** For substances appearing to contain water as the only volatile constituent (either are hydrates or contain water in adsorbed form)
- **Uniformity of dosage units**

Specific Tests for Powders

- Oral powders should indicate: “For Oral Use Only”.
- **Minimum fill**
- **volatile content**
- additional tests may apply, including **pH** in an aqueous solution, **powder fineness**, **microbial limits**, and others.

Specific Tests for Liquids

- **Deliverable volume** : applicable for the liquid formulation is packaged in a multiple-dose container
- **Alcohol determination**
- **pH**
- **Antioxidant :** Release testing should be performed
- **Extractables** : rubber stopper, cap liner, plastic bottle
- **Volatile content** : applicable for powders and granules for reconstitution
- **Water determination** : for Lyophilized oral products

<3> Product Quality Test for Topical and Transdermal Drug Products

- **Specific tests**
    - **Uniformity of Dosage Units :** applicable for TD and for topical dosage form intended for systemic delivery or packed in single-unit containers such as packets
    - **Antimicrobial preservative content** : for multiple-unit products
    - **Antioxidant content** (if present)

Specific tests for Topically applied semisolid drug products

- **Minimum fill**
    - Single- and multiple-unit container must meet minimum fill requirements.
    - For single-unit containers where the test for <905> is applied, minimum fill is not required.

<1> INJECTIONS AND IMPLANTED DRUG PRODUCTS (PARENTERALS)—PRODUCT QUALITY TESTS

- Parenteral drug products include both injections and implanted drug products
- Parenteral dosage forms include solutions, suspensions, emulsions, sterile powders for solutions and suspensions (including liposomes), implants (including microparticles), and products that consist of both a drug and a device such as drug-eluting stents.
- The chapter is divided into three main sections: (1) universal product quality tests that are applicable to parental dosage forms; (2) specific product quality tests, which are tests that should be considered in addition to Universal Tests; and (3) product quality tests for specific dosage forms

Product Quality tests Common to Parenteral Dosage Forms

Universal Tests

- Identification
- Assay
- Impurities
- Foreign and Particulate matter
- Packaging Systems

Specific tests

- Uniformity of Dosage Units
- Vehicle and Added Substances
- Antimicrobial Preservatives
- Water Content
- Completeness and Clarity of Solutions

<771> OPHTHALMIC PRODUCTS-QUALITY TESTS

- **Universal Tests**
  - **Identification**
  - **Assay**
  - **Impurities**
  - **pH**
  - **Osmolarity**
  - **Particulate and Foreign matter**
  - **Antimicrobial preservative : applicable for multiple-unit products**
  - **Uniformity of dosage units : applicable for product packed in single-unit containers**
  - **Container contents (Minimum Fill)**

<771> OPHTHALMIC PRODUCTS-QUALITY TESTS

- **Specific Tests**
  - **Viscosity**
  - **Antioxidant content**
  - **Particle size and Particle size distribution**
  - **Resuspendability/Redispersibility**
  - **Drop size**
  - **Added substances**

Nevirapine Oral Suspension (USP40)

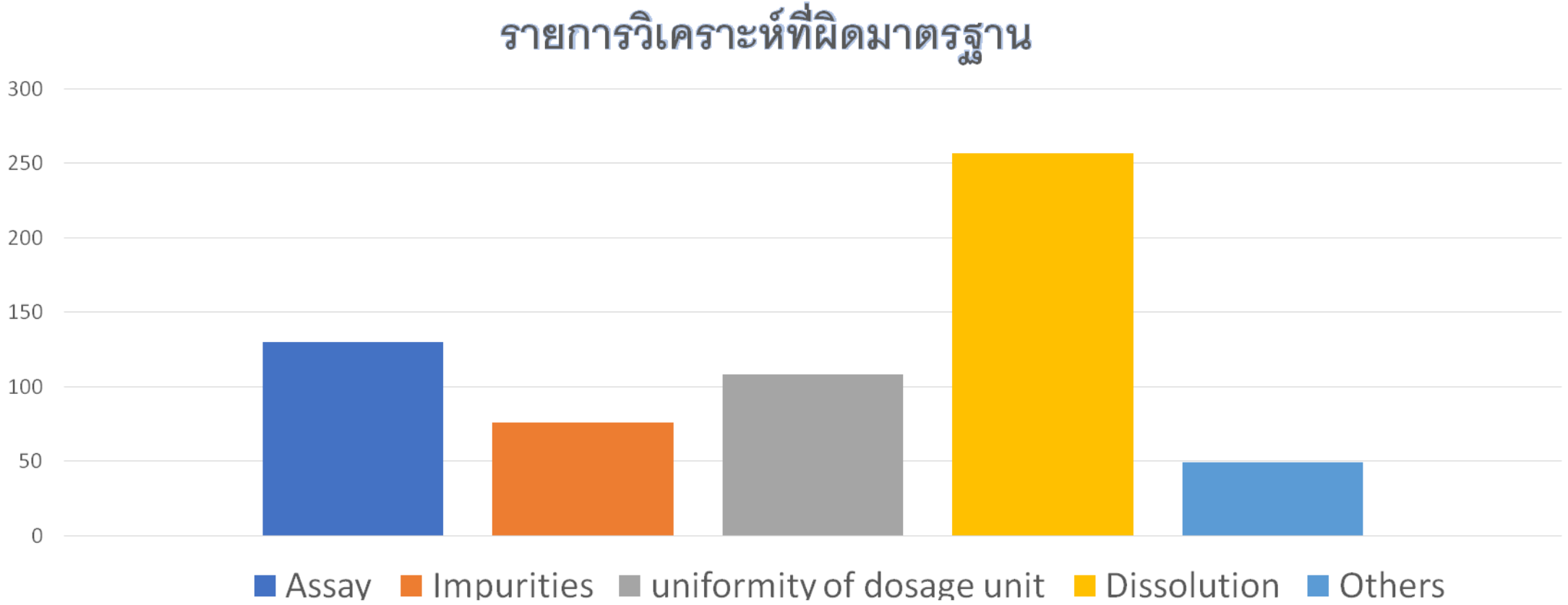
- **IDENTIFICATION**
- **ASSAY**
- **PERFORMANCE TESTS**
    - **Dissolution ⟨711⟩**
- **IMPURITIES**
    - **Organic Impurities**
- **SPECIFIC TESTS**
    - **Microbial Enumeration Tests ⟨61⟩ and Tests for Specified Microorganisms ⟨62⟩**

Ritonavir Oral Solution (USP 40)

- **IDENTIFICATION**
- **ASSAY**
- **IMPURITIES**
    - **Organic Impurities**
- **PERFORMANCE TESTS**
    - **Deliverable Volume ⟨698⟩**
- **SPECIFIC TESTS**
    - **Alcohol Content**
    - **Microbial Enumeration Tests ⟨61⟩ and Tests for Specified Microorganisms ⟨62⟩**

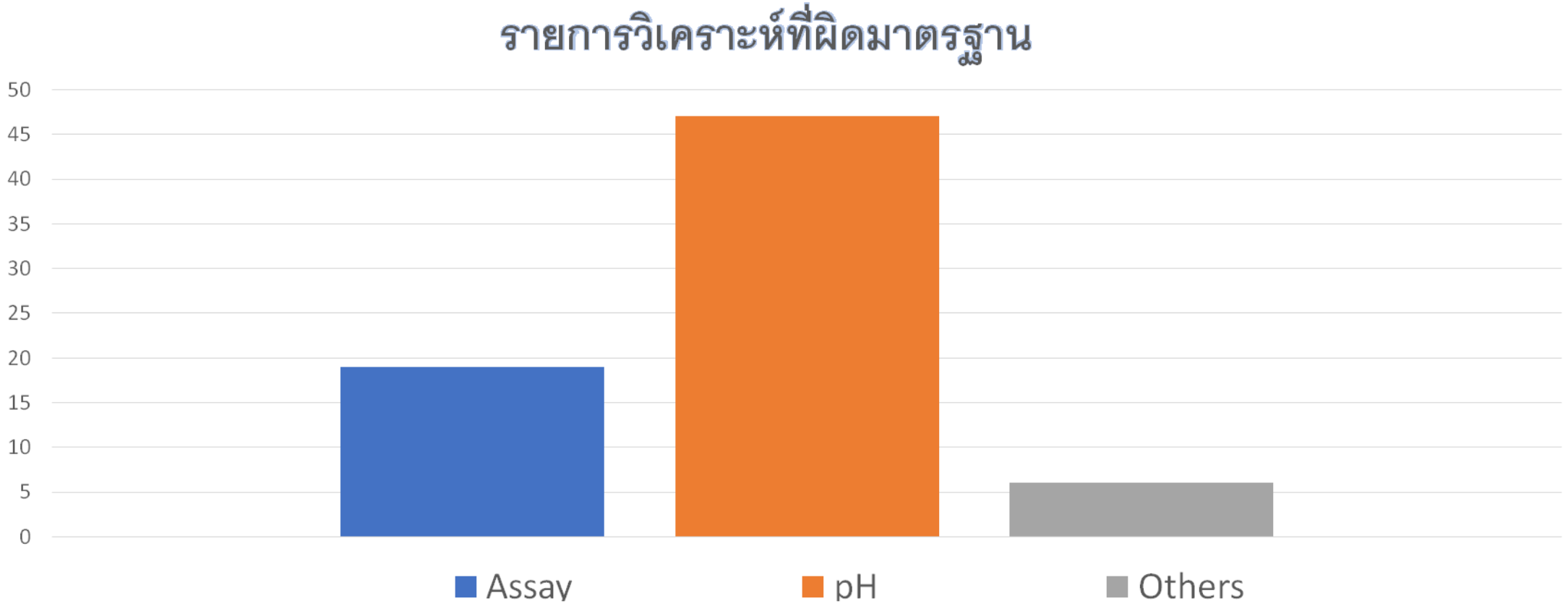
ข้อมูล Greenbook 2551-2559 : Oral solid drug products

(5,742 ตัวอย่าง)

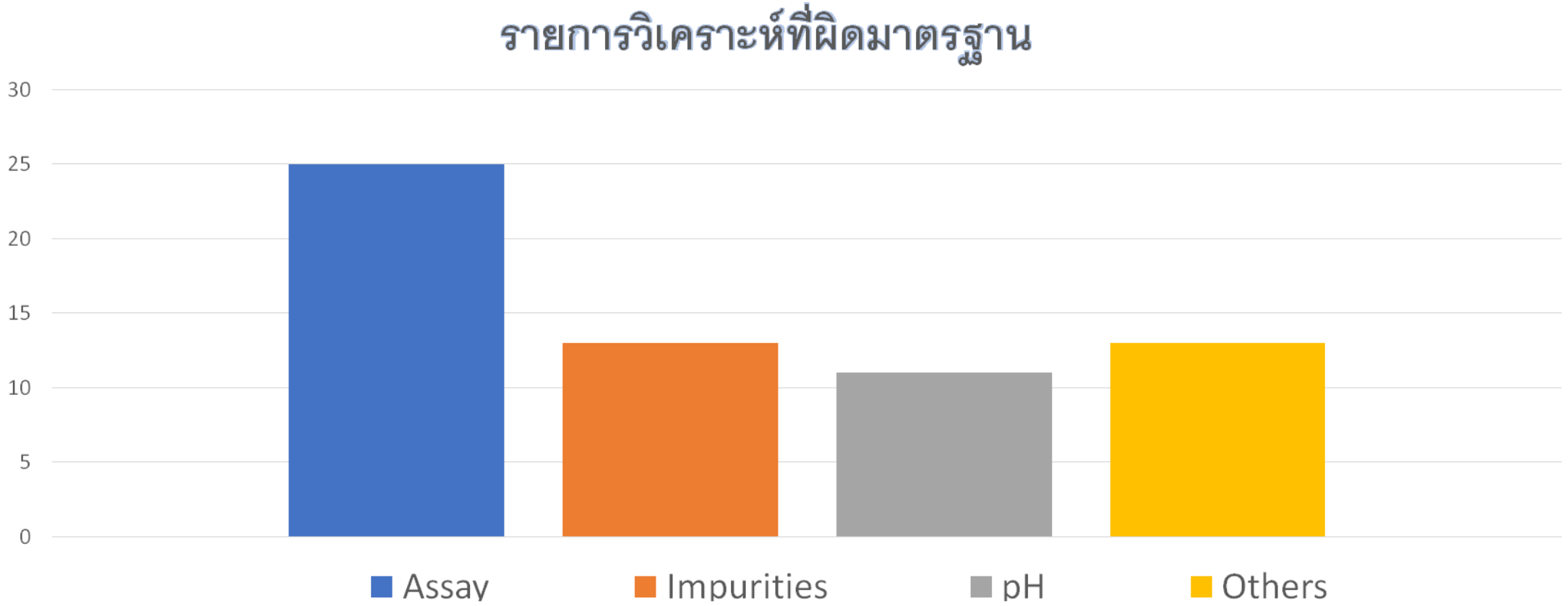


ข้อมูล Greenbook 2551-2559: Oral liquid drug products

(722 ตัวอย่าง)

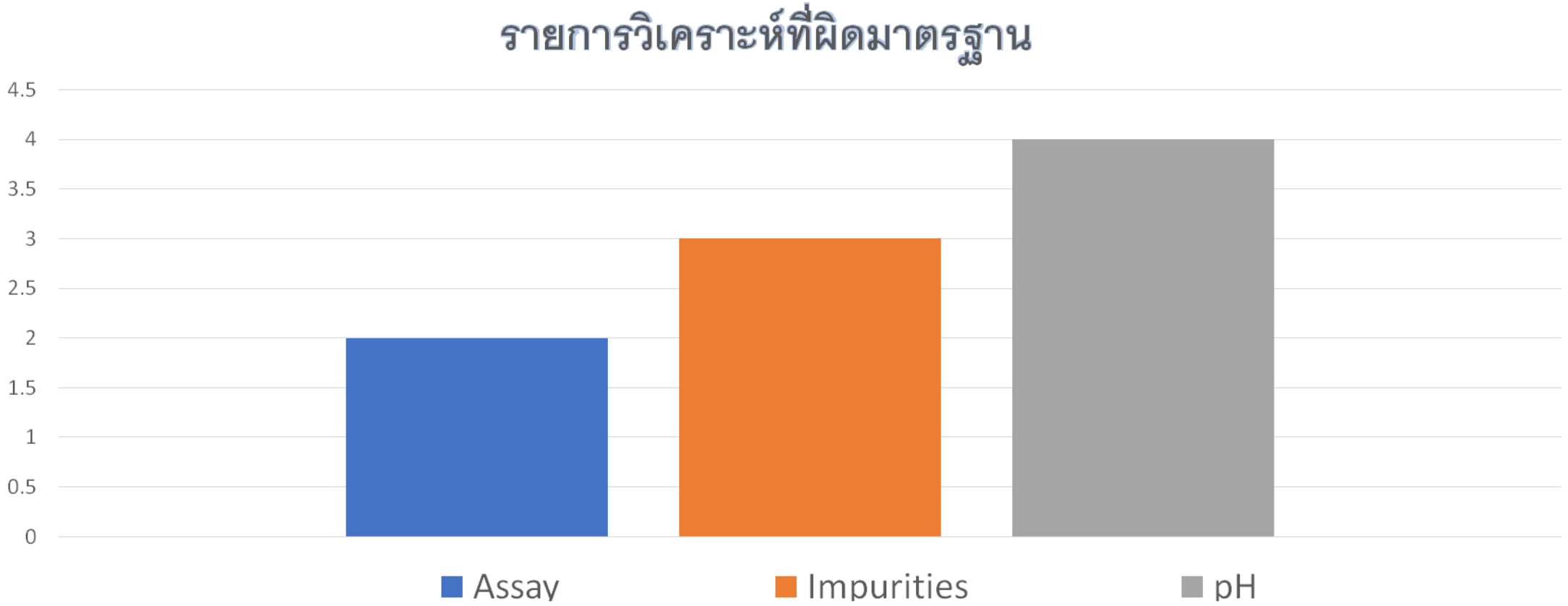


ข้อมูล Greenbook 2551-2559 : Injection drug products (1,292 ตัวอย่าง)



ข้อมูล Greenbook 2551-2559: Ophthalmic/Otic drug products

(139 ตัวอย่าง)



ข้อมูล Greenbook 2551-2559 : Topical drug products (556 ตัวอย่าง)


THANK
YOU