2019 Global Drug Delivery & Formulation REPORT

Part One of a Four-Part Series

Part 1: A Review of 2019 Product Approvals

Part 2: Notable Drug Delivery and Formulation Product Approvals of 2019

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Introduction

The topline pharmaceutical product approval figures are in for 2019, and they largely reflect in terms of number and product types what was reported for 2018. It's hard to judge whether or not this is a positive indicator for the sector. It's always comforting to see continuation, but there is the suspicion that the environment is changing, and the industry may not be properly prepared to address the accompanying opportunities and challenges.

Any number of reviews and reports discuss the number and nature of US FDA product approvals. This four-part series starts with a review of the 2019 approval numbers focused on technologies and dosage forms, essentially the nuts and bolts underpinning these products and their therapeutic benefits.

To better identify trends related to drug delivery and formulation, the Global Drug Delivery & Formulation Report focuses on "innovative" product approvals. This is a mixed group of products that incorporate a new molecular entity (NME), provide a new dosage form of an NME or Previously Approved Active (PAA), or represent a new combination of NME or PAA actives. Multisource products, generics, and biosimilars are excluded.

This first article summarizes the 2019 product approvals in the three major world markets, the United States (FDA), Japan (PMDA), and the European Union (EMA). From a technology perspective, this represents a historical review. Given that innovative products take on average 8 to 10 years[1] to get through clinical development and regulatory review, the technologies underpinning these products were developed at least a decade ago.

What about multisource approvals, generics, and biosimilars? These products represent ancient history. Approved in 2019, these products are essentially copies of products approved a decade or more ago based on technology and formulation decisions made two decades ago.

This report tries to connect the past with the present to suggest what the future will deliver from a product and technology perspective.

Note: This first article examines approvals in 2019[2] for the United States (FDA), Japan (PMDA), and the European Union (EMA). The European Medicines Agency (EMA) approvals represent a subset of all approvals in Europe but represent only pan-European approvals. In the case of Europe, product approvals made only at the country level (RMS, CMS, UK, other) are not included in the report figures. In all tables, the figures exclude multisource (generic) and biosimilars unless explicitly stated.

NDA and BLA approval numbers and types in 2019 were little changed versus 2018

Table 1. FDA Therapeutics Approval Numbers by Classification[3] (2019)

BLA (CDER*, CBER*)		**26**
CDER	Biologic, 351(a) & 351(k)	22
	- 351(a) (Innovator)	12
	- 351(k) (Biosimilar)	10
CBER	Biologic Therapeutics, 351(a)	4
NDA (CDER)		**117**
Type 1	New Molecular Entity	39
Type 2	New Active Ingredient	7
Type 3	New Dosage Form	26
Type 4	New Combination	8
Type 5	New Formulation or New Manufacturer	32
Type 7	Previously Marketed, Unapproved	1
Type 1/4	New Molecular Entity and New Combination	1
Medical Gas	Medical Gas	3
ANDA (CDER)	Abbreviated New Drug Approvals (Generic, Multisource)	**962**

Source: PharmaCircle Pipeline & Products Intelligence and FDA Products Modules

* CDER (Center for Drug Evaluation and Research), CBER (Center for Biologics Evaluation and Research)

- Total 2019 Biologic approvals, 351(a) and 351(k), fell short of 2018's 33 approvals.
- Biosimilar approvals in 2019 edged ahead of 2018, with 10 versus 9. Both years were well ahead of 2017's 5 approvals.
- 2019's 40 non-biologic novel drug approvals, including single active and combination products, fell just short of 2018's 41. Both were well above 2017's 34 approvals.
- New Dosage Form approvals (Type 3 and Type 3,4) totaled 26 in 2019, a little behind 2018's 28 approvals. These products incorporated previously approved actives (PAA) and generally offered improved convenience or addressed additional indications.
- New combination approvals incorporating PAA and novel actives totaled 9 in 2019. This fell well short of the 20 approvals in 2018.
- New Formulation or New Manufacturer (Type 5) approvals totaled 32 in 2019, a little short of 2018's 40 approvals. These approvals are often injectable multisource products not eligible for ANDA review.

Table notes: Multisource injectables are approved through the NDA rather than the ANDA regulatory process and can unintentionally skew the new drug approval figures. Type 5 approvals are not considered in the analyses presented on the following pages.

Injection route approvals largely matched oral route approvals in Japan and the EU

Table 2. 2019 Approvals by Administration Route

Route of Administration	FDA (n=105)	EMA (n=47)	PMDA (n=60)
Inhalation	**2**	**1**	**4**
Injection	**38**	**21**	**25**
Infusion, SCF	-	-	1
Infusion IM	-	2	-
Infusion IV	11	6	9
Infusion IV, SC	-	-	1
Infusion IV, Injectable IV	-	-	1
Injectable IM	4	2	3
Injectable IV	4	-	2
Injectable SC	14	8	8
Injectable IV, IM	1	-	-
Injectable IV, SC	1	1	-
Injectable IV, IM, SC	-	1	-
Injectable Intravitreal	2	-	-
Intralesional, Infusion IV	-	1	-
Implantation	**1**	**1**	-
Intrauterine	**1**	**-**	-
Nasal	**4**	**2**	**-**
Ophthalmic	**3**	**1**	**3**
Oral	**52**	**20**	**25**
Topical	**3**	**1**	**-**
Transdermal	**1**	**-**	**3**

Source: PharmaCircle Pipeline & Products Intelligence module

- As was the case in 2018, Oral products in 2019 represented the largest proportion (50%) of approvals in the U.S. followed by Injection products.
- Injection and Oral product approval numbers were almost balanced in the EU and Japan. In the case of the EU this largely reflects the EMA regulatory focus which only approves new products and dosage form improvements if they fall into a relatively limited range of therapeutic indications. Products that simply offer improved oral dosage forms are often approved through more localized regulatory pathways.
- Nasal products showed an upsurge in approvals in 2019, led by the high-profile approval in the U.S. of Janssen's Spravato (nasal ketamine).
- Transdermal approvals also experienced a bit of a bump in 2019, at least in the U.S. where Hisamitsu's Secuado (asenapine) daily patch was approved for the treatment of schizophrenia.
- 2019 saw the absence of sublingual approvals in the three territories following several years of multiple approvals.

Table notes: The figures above include all formulations approved for each product. In a few cases, two or more formulations were approved for a single product. The figures above do not include FDA Type 5 Approvals or Biosimilars (all). These excluded approvals, generally injectables, are not subject to ANDA regulations but still effectively represent generics in terms of drug delivery and formulation.

Industry interest in formulation enhanced products has waned with attention turning to devices

Table 3. 2019 Approvals by Drug Delivery Category

Route of Administration	FDA (n=105)	EMA (n=47)	PMDA (n=60)
Inhalation			
Devices (Integral)*	2	1	3
Formulations	2	1	4
Injection			
Device, Injection Systems (Integral)*	5	4	4
Device, Pre-Filled Syringes	6	5	2
Formulations			
Conjugates	4	2	2
Viral Vectors	1	-	-
None	21	10	14
Implantation			
Formulations	1	1	-
Intrauterine			
Formulations	1	-	-
Nasal			
Devices	4	1	-
Formulations	3	1	-
Ophthalmic			
Device, Pre-Filled Syringes	1	-	-
Formulation	3	1	3
Oral			
Formulations	15	6	4
None	37	14	21
Topical			
Formulations	2	-	-
None	1	1	-
Transdermal			
Formulations	1	-	3

Source: PharmaCircle Pipeline & Products Intelligence Module

* Integral refers to devices that are integrally associated with a product. Examples would include auto-injectors and dry powder inhalers.

- Formulation enhanced oral products represent a notable minority of approvals in all three territories suggesting the increasing development of molecule optimized therapeutics and the relative lack of opportunity for simple formulation enhanced next generation products.
- Injection systems, while an increasingly popular option to encourage the use of outpatient injectables, represent a small proportion of total Injectable approvals.
- For the second year in a row there were no approvals of abuse resistant modified release opioids in the U.S. This is doubtless a function of heightened regulatory scrutiny and increased potential liability.
- Nasal product approvals saw an increase in 2019, with the majority, 4/5, employing some sort of formulation technology.

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Approvals continue to be associated with simpler dosage forms (Solutions & Tablets)

Table 4. 2019 Approvals by Dosage Form

Route of Administration	FDA (n=105)	EMA (n=47)	PMDA (n=60)
Inhalation			
Inhalation Powder	2	1	1
Inhalation Suspension	-	-	3
Injection			
Powder for Solution	1	-	
Solution	25	16	19
Suspension	4	1	1
Lipid Complex	-	-	1
Lyophilized Powder for Solution	7	4	3
Lyophilized Powder for Suspension	1	-	1
Nasal			
Powder	1	1	-
Solution	1	1	-
Spray Solution	2	-	-
Ophthalmic			
Ointment	1	-	-
Solution	2	1	3
Oral			
Bar	1	-	-
Capsule	9	3	4
Film	1	-	-
Pellet	2	-	-
Sachet, Granules	-	2	1
Soft Gel Capsules	3	-	-
Solution	3	3	-
Suspension	1	-	-
Tablet	32	12	20
Topical			
Cream	1	-	-
Foam	1	-	-
Lotion	1	-	-
Spray	-	1	-
Other			
Implant	1	1	-
Intrauterine Foam	1	-	-
Transdermal Patch	1	-	3

Source: PharmaCircle Pipeline & Products Intelligence module

- Oral Tablet and Capsule presentations, along with simple Injection Solution dosage forms, accounted for the majority, two thirds, of all dosage forms approved in 2019.
- Even Oral approvals, a longtime bellwether of dosage form innovation, saw only 30% of approvals associated with anything other than simple tablet and capsule presentations. A number of the non-tablet and capsule presentations were directed to pediatric applications.

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Approvals by Molecule Type were notably consistent across the major markets

Table 5. 2019 Approvals by Molecule Type

Molecule Type	FDA (n=105)	EMA (n=47)	PMDA (n=60)
Antibody	13	8	5
Carbohydrate	1	-	1
Cell Therapy	-	-	1
Gene Therapy	1	-	1
Oligonucleotide	-	1	1
Other (IgG)	-	-	1
Peptide	6	2	3
Polymeric	2	-	-
Protein	4	3	4
Protein Conjugate	1	3	2
SiRNA	-	-	1
Small Molecule	72	28	39
Stem Cell	-	1	-
Vaccine	4	1	1

Source: PharmaCircle Pipeline & Products Intelligence module

- Biologicals accounted for one third (71/212) of non-generic new product approvals in 2019, representing an insignificant change over the 2018 results.
- Antibody related approvals represent the largest proportion of biological approvals but seem on a downward trend in share, if not number, as newer molecule types are being developed and approved.

References

1. See Jan/Feb 2020 issue at www.drug-dev.com.
2. Summary reports of 2019 approvals in all three territories are available at www.pharmacircle.com/rc/.
3. NDA Classification Codes. https://www.fda.gov/media/94381/download.

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