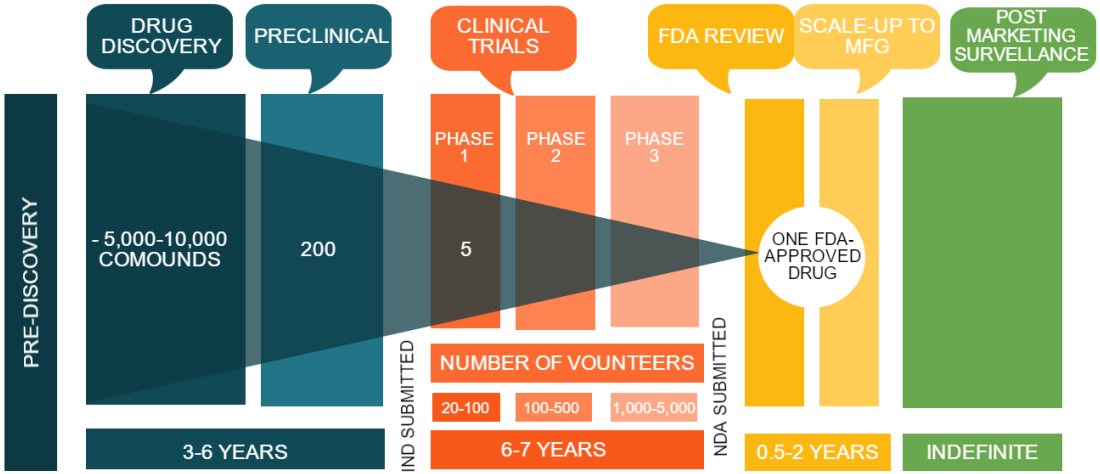
Examining medicines

Generic versus biologic

Patent term versus Data Protection

It takes an average of 12 years to develop a medicine



Only 1 in 6,000 compounds on average make it through the whole process

Only 12% of drug candidates entering clinical trials result in an approved medicine

Source: Shahza Somerville, Jessica Holden Kloda, Applied Clinical Trials, 2015

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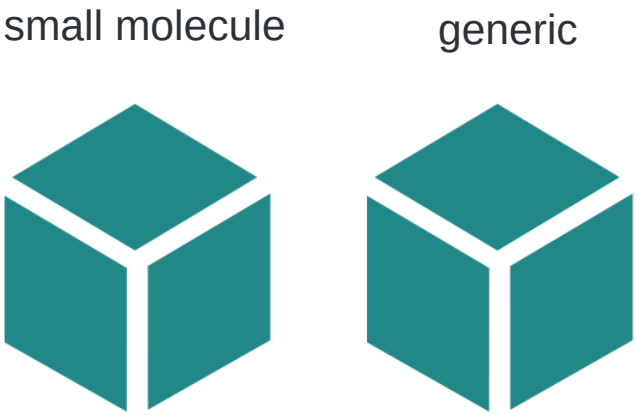
Small molecules and generics

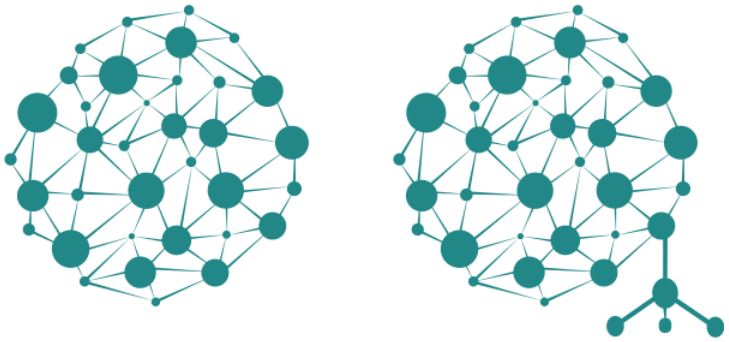


Source: Roche Products New Zealand 2015

Biologic and biosimilar

innovator

biosimilar



highly complex structure

different active ingredient

Source: Roche Products New Zealand 2015

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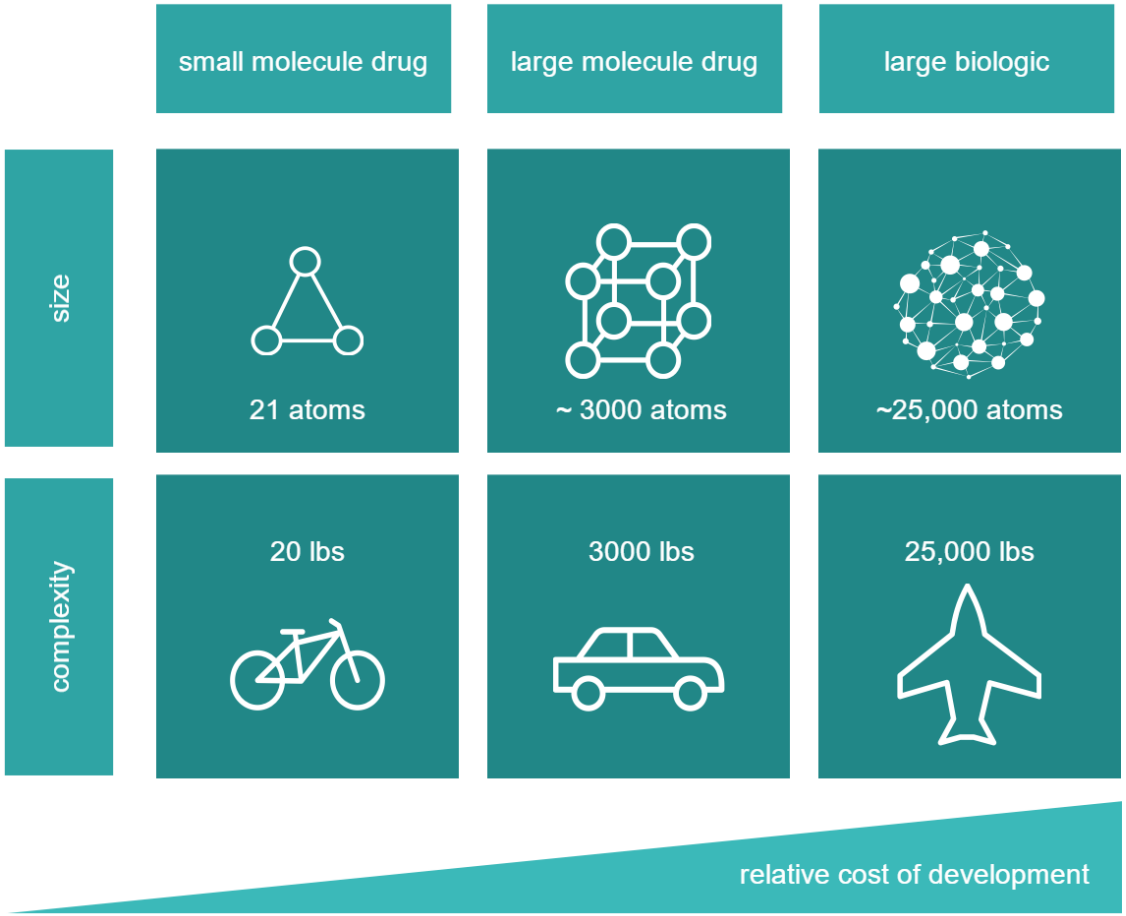
Comparing apples and oranges

Category	Small molecule drugs	Biologics including biosimilars
Size & Stability	25-100 atoms	2500 – 25000 atoms
Molecular Complexity	5 QC testing parameters	25 QC testing parameters
Value (sales per g)	Cents	US$300-5,000
Production principle & steps	Chemical synthesis ; ca. 4 steps	Recombinant tech ; > 15 steps
Raw materials	< 5	> 50
Scalability	Easy-medium exceeding 100 KL	Medium to difficult up to 20 KL
CAPEX (100 KL facility)	<US$ 40 million	Ca. US$400 mill
Labour	X-trained, less skilled	High tech and specific roles
Supply chain (storage & transport)	Ambient to years	Cold or frozen
Lifetime/expiry	Years	18-36 months

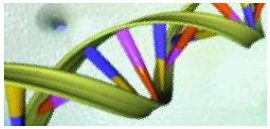
Source: McKinney & Co., 2014

Copying a biologic is not a simple task



Source: Roche Products New Zealand, 2015

The manufacturing process for biologics is highly complex



Establishment of genetically engineered cells that produce the desired product

Human gene

DNA vector

Cloning into DNA vector

Transfer into host cell

Bacterial or mammalian cell produces protein

Scale-up and production of large quantities

Fermentation

Downstream processing and purification

Formulation

The process is the product

Each stage of the complex manufacturing process confers unique properties on the resulting biologic product

Source: Roche Products New Zealand, 2015

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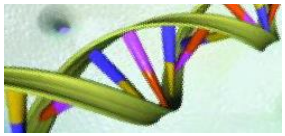
Biosimilars: *Different process, different product*



Same gene as innovator

Differences in the process

Human gene

DNA vector

Cloning into DNA vector

Transfer into host cell

Bacterial or mammalian cell produces protein

Fermentation

Formulation

Biosimilar that is not identical to the originator

Biogeneric term is not applicable

Even if a biosimilar uses the same human gene as its innovator, It will differ in other parts of the manufacturing process

Source: Roche Products New Zealand Ltd, (2015)

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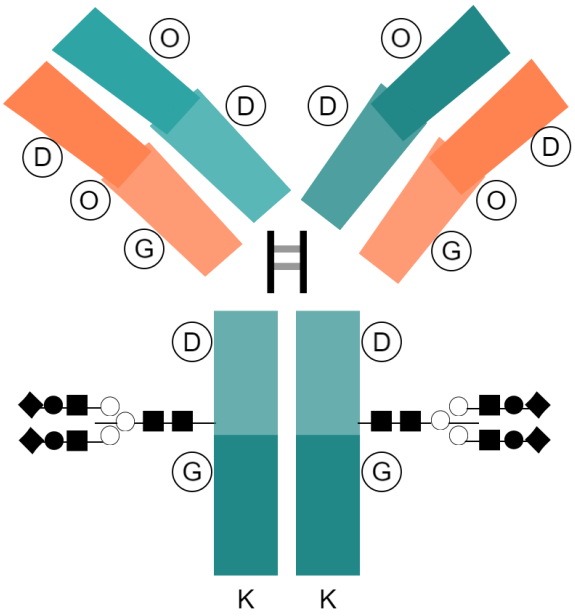
Immunogenicity and biologics
Examples of modifications: inherent or due to the manufacturing process



- Pyroglutamyl peptides
- Deamidation
- Methionine oxidation
- Glycation
- High Mannose. G0. G1. G1. G2
- Sialylation
- C-terminal Lysine

Modifications may result in approximately 10^8 potential variants

The human immune system may see a biologic and its biosimilar as significantly different

Safety and efficacy data are critical for any biological product

This data is protectable using Regulatory Data Protection, a form of IP rights recognised in the Trade-Related Aspects of Intellectual Property Rights (TRIPS), article 39.3

Source: Adapted from Steven Kozlowski; FDA

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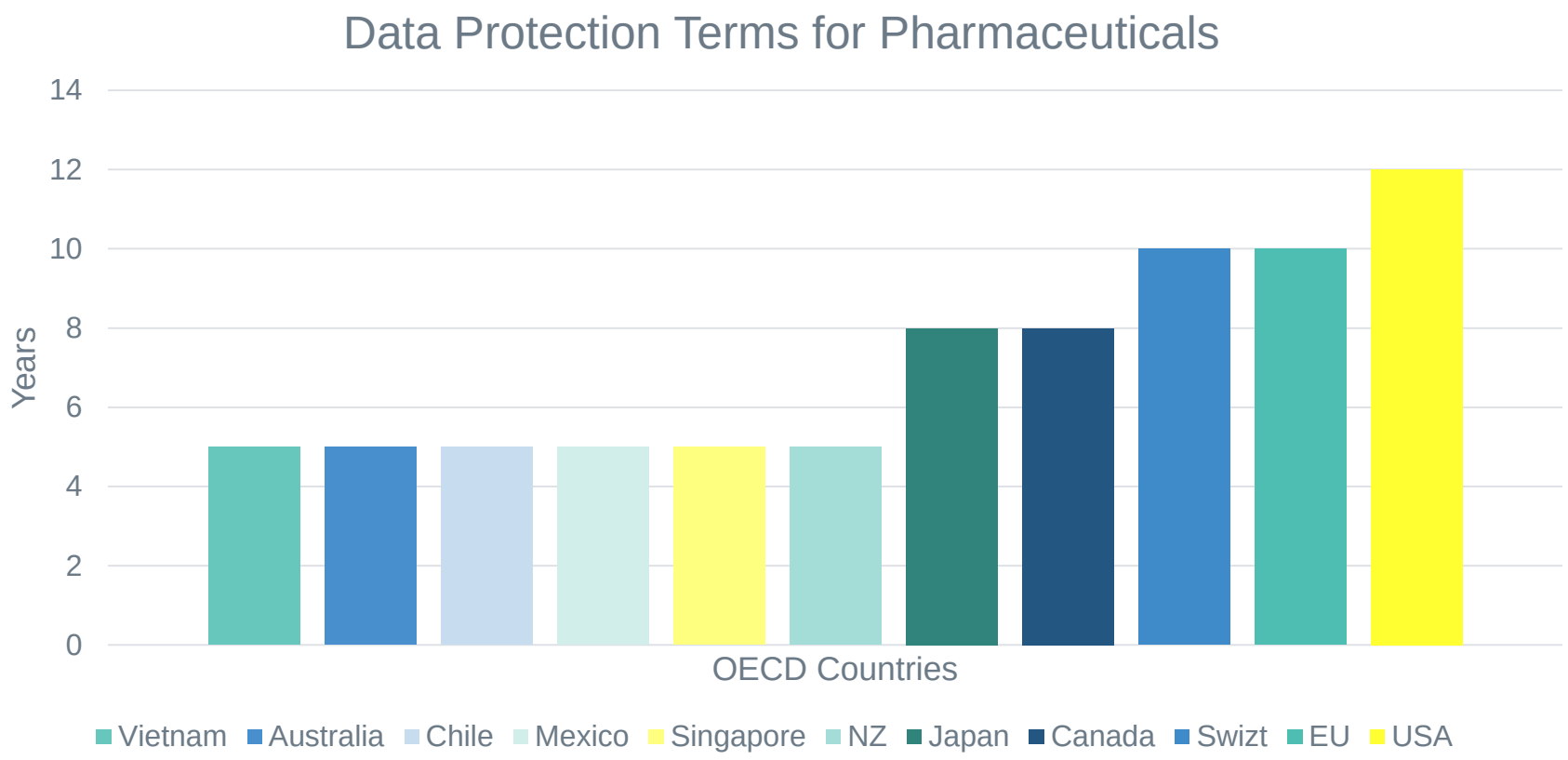
Comparison of data protection and patents

Metric	Patent	data protection
Coverage	Compound and analogues (and/or uses, formulations, synthetic processes)	Compound (and formulation) with market authorisation (MA).
Prevention of:	Manufacture and sale of product or product of a process by another copy Process use Indirect infringement	MA grant to another applicant based on originators data
Exempted Use	Private and non-commercial use Securing reg. authorization Experimental use	Any non-MA requiring use
Protection Period	20 years from application	Variable (5-12 years) from 1st MA.
Requirement	Novelty, inventive step, non-obviousness etc.	Demonstrated safety and efficacy

A range of data protection terms from 5 years to 12 years

OECD average 7-8 years



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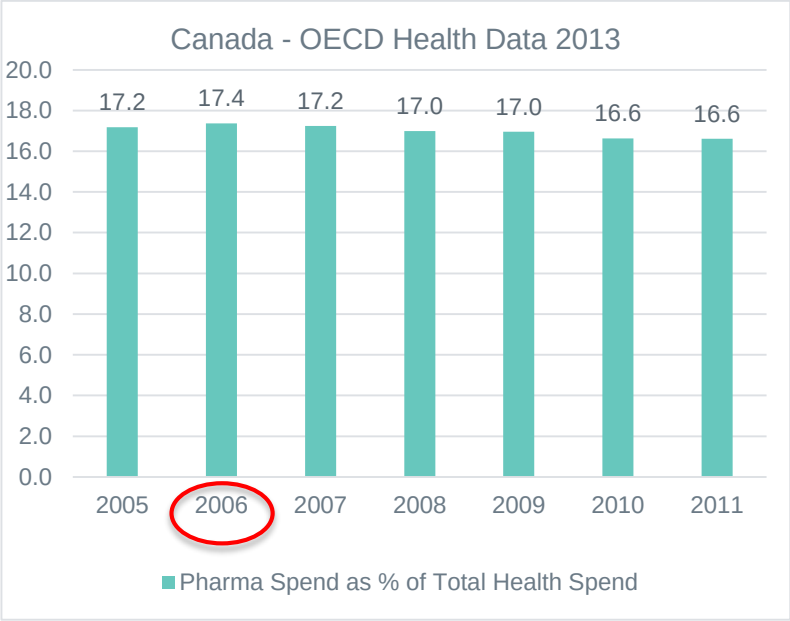
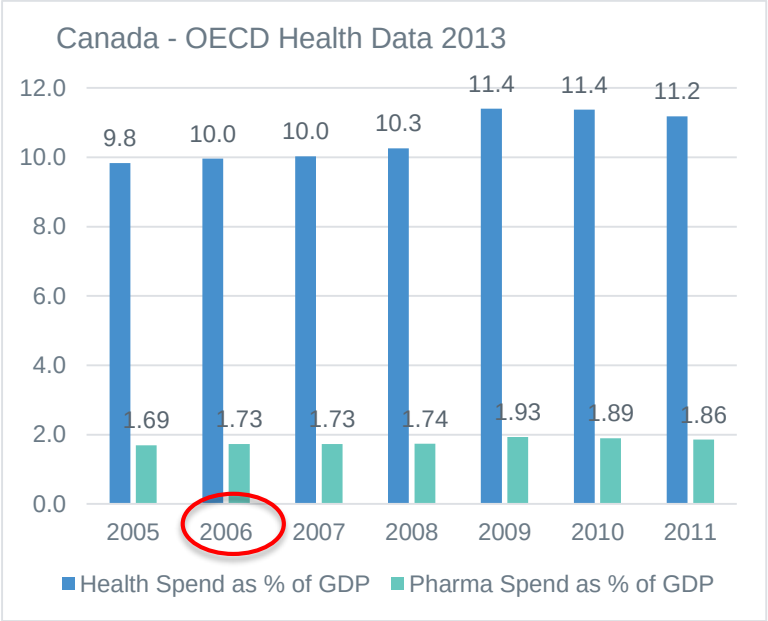
Increasing data protection term in Canada from 0 to 8: no effect on pharma spend





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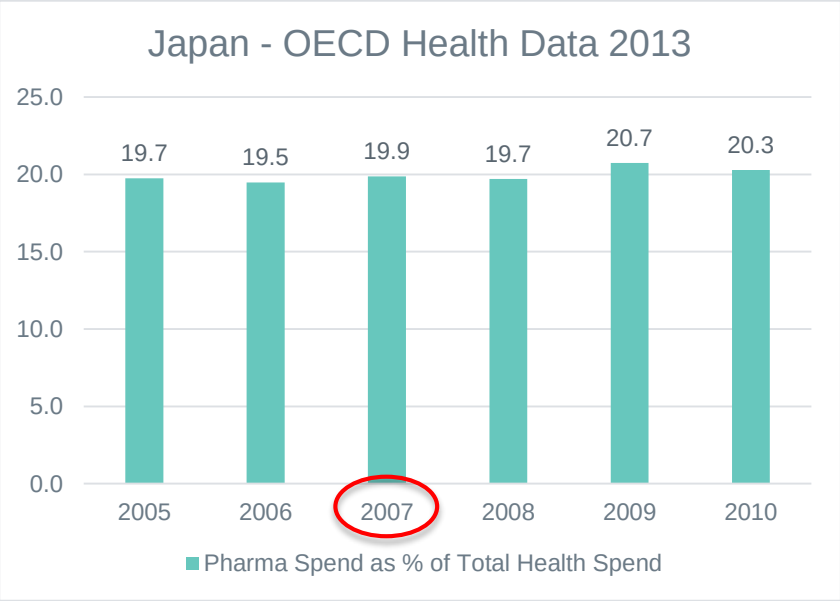
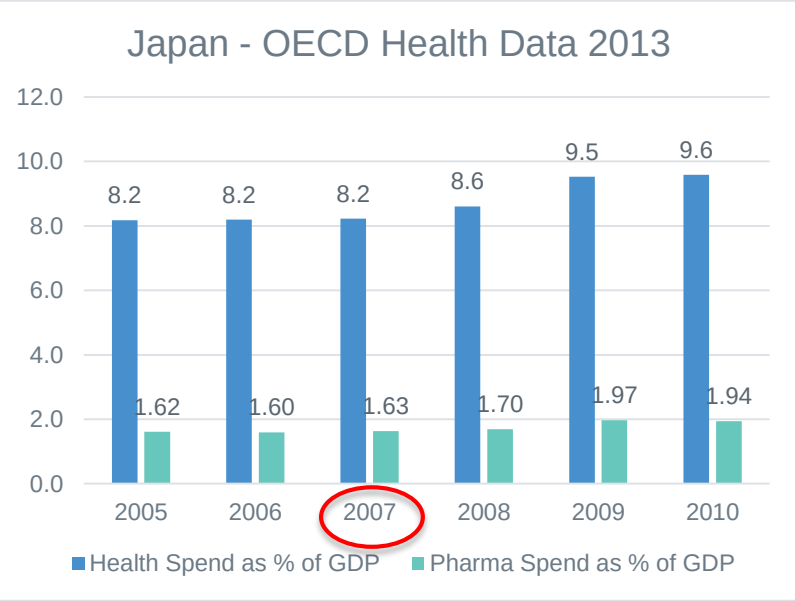
Increasing data protection term in Japan in 2007 from 6 to 8: pharma spend stayed in line with overall healthcare spend





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Data protection summary

- Range of data protection terms in Trans-Pacific Partnership negotiating countries ‘clusters’ (5 years, 8 years and 12 years)
- Data protection is more important for biologics which are very innovative and complex molecules compared to traditional medicines, meaning patents are not always effective form of IP protection
- As a result most OECD countries have extended data protection for biologicals to encourage investment in these important new medicines from between 8-12 years
- Historically no evidence of unfettered increase in pharmaceutical expenditure in Canada or Japan as result of ↑ data protection

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