The practical issues around interchangeability in relation to future nanomedicines and nanosimilars

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FIP Development Goals

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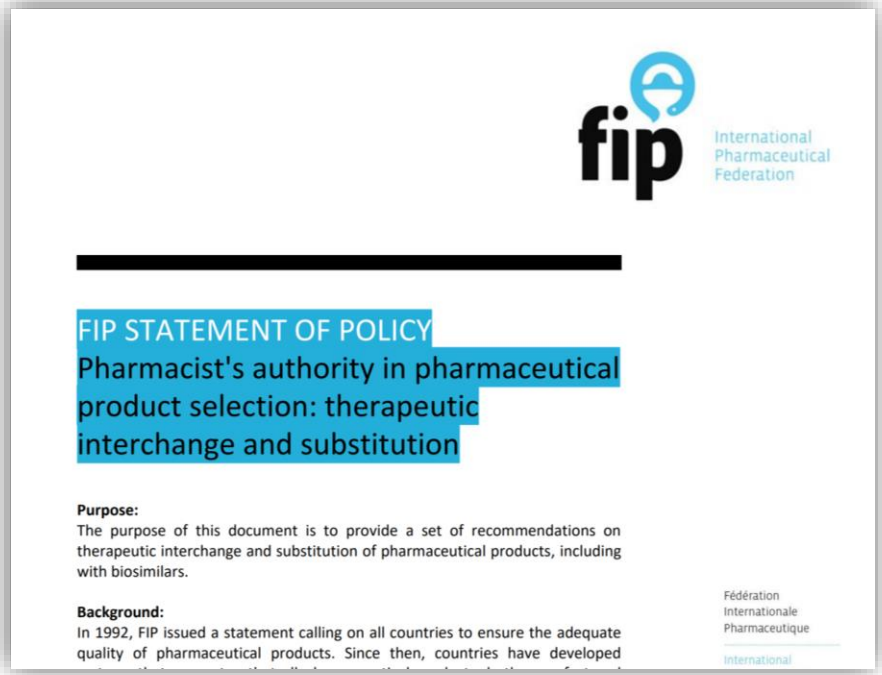
The FIP Development Goals are a key resource for transforming the pharmacy profession over the next decade globally, regionally and nationally. They align with FIP's mission to support global health by enabling the advancement of pharmaceutical practice, sciences and education and are set to transform pharmacy in alignment with wider global imperatives underpinning the UN Sustainable Development Goals (SDGs).

Policy on therapeutic interchange



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FIP STATEMENT OF POLICY

Pharmacist's authority in pharmaceutical product selection: therapeutic interchange and substitution

Purpose:

The purpose of this document is to provide a set of recommendations on therapeutic interchange and substitution of pharmaceutical products, including with biosimilars.

Background:

In 1992, FIP issued a statement calling on all countries to ensure the adequate quality of pharmaceutical products. Since then, countries have developed

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Therapeutic interchange is a collaborative action between the prescriber and the pharmacist designed to achieve maximum therapeutic benefit for the patient and to ensure the safest, most effective and economic use of pharmaceutical products.

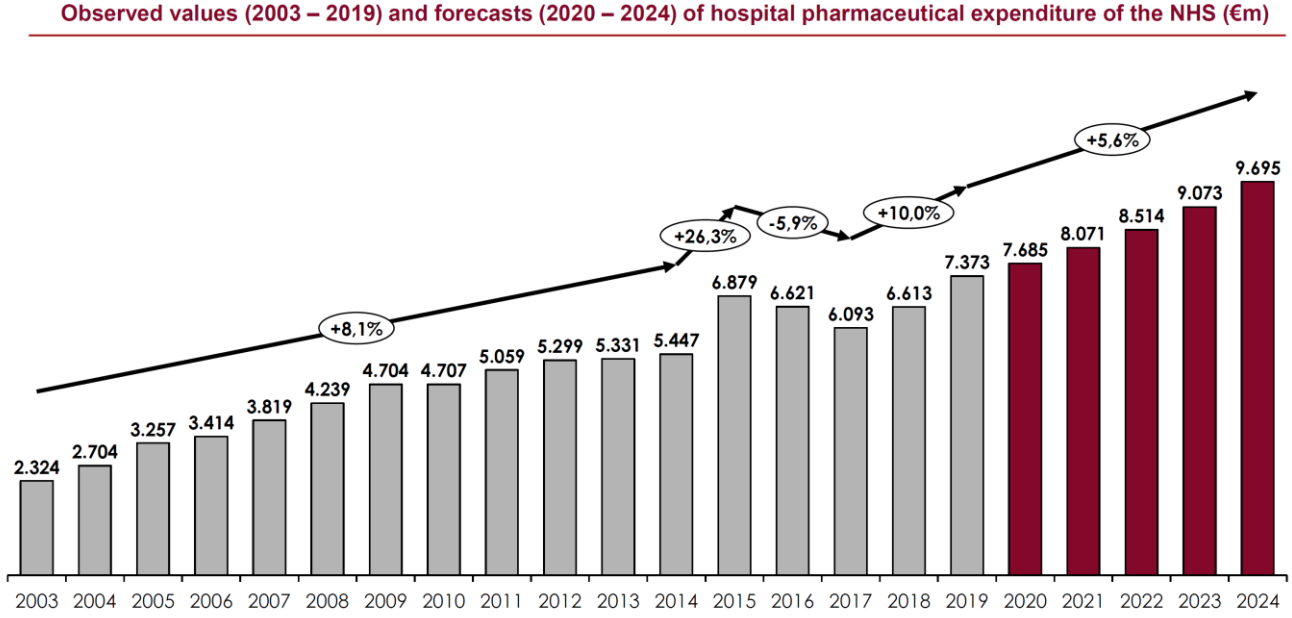
It is in accordance with a protocol previously established and agreed between the prescriber and the pharmacist, or after individual prior consultation with the prescriber. Therapeutic interchange may be within or outside a formulary system.

The concept of therapeutic interchange, as defined above, using the relevant expertise of the pharmacist and the prescriber, should be promoted, when this provides the best outcome for the patient. Such circumstances may occur during medicine shortages.

https://www.fip.org/file/2086

Hospital pharmaceutical spending has increased steadily over the period 2003-2019 and is expected to continue growing in the coming years (2020-2024)

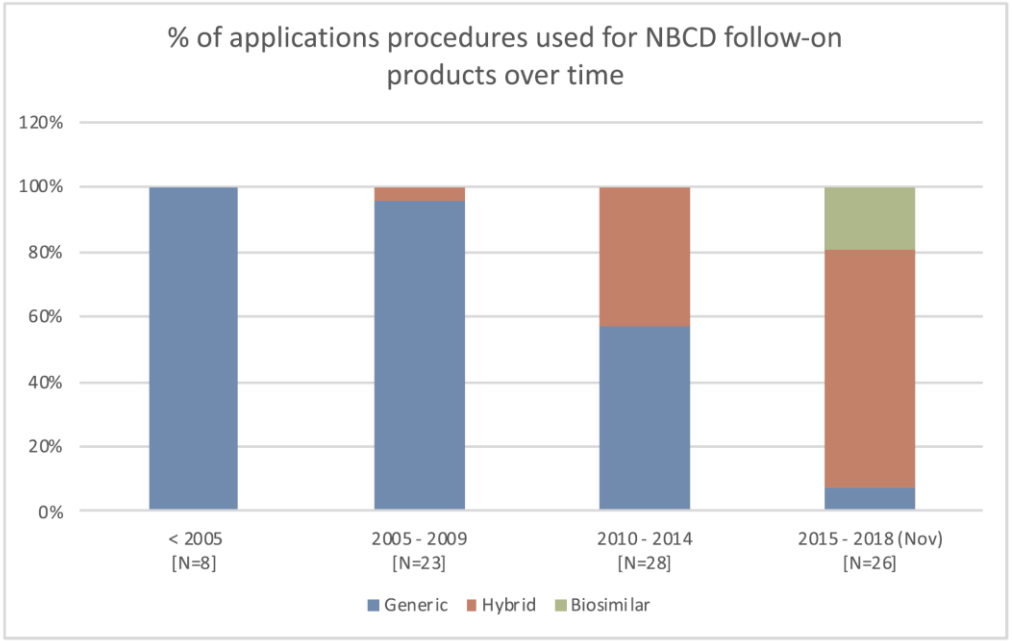
(Spain)



Proposals in the field of hospital pharmacy

- Evaluation, Access and review ⇨ pharmacotherapeutic guides (therapeutic interchange)
- Rational use of medicines ⇨ Use of biosimilars (and nanosimilars?)
- Procurement and purchasing ⇨ Is there competition?
- Logistics and dispensing ⇨ Mesures to manage supply problems

Application procedures involved in the approval of non-biological complex drugs (NBCDs)



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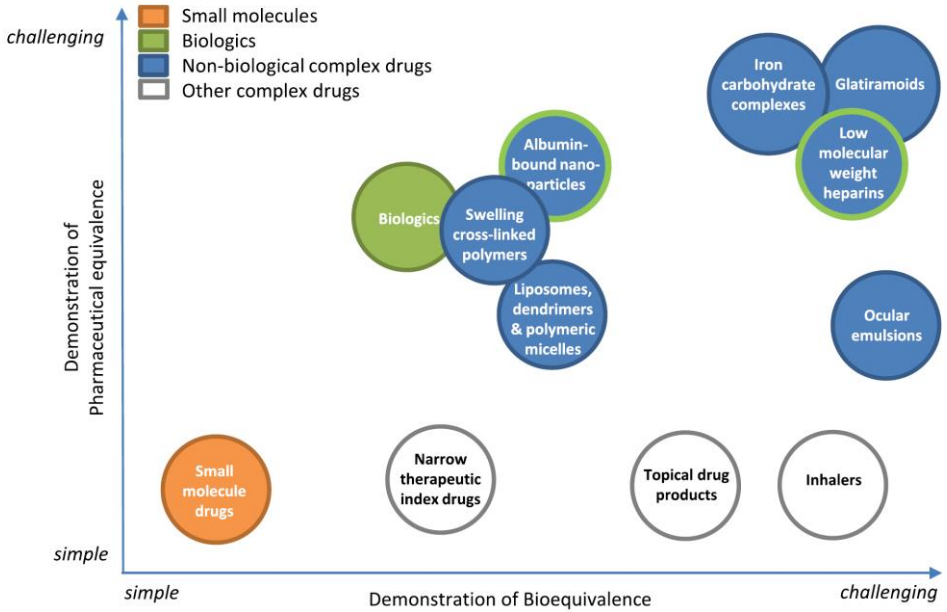
Eur J Pharm Sci. 2019 May 15;133:228-235. doi: 10.1016/j.ejps.2019.03.029.

The complex drug landscape



Ann N Y Acad Sci. 2017 Nov;1407(1):39-49. doi: 10.1111/nyas.13347.

Cross-country comparison of hospital pharmacy substitution policies for generic, hybrid and biosimilar drugs

	Generic regulatory pathway 10(1)		Hybrid regulatory pathway 10(3)		Biosimilar regulatory pathway 10(4)
	✓	Legal obligatory substitution of originators with generics based on contracts with health insurance companies	✗	No well-established policy management for drugs approved via this pathway	✗	The *Gesetz für mehr Sicherheit in der Arzneimittelversor-gung (GSAV)* bill regulates exchange at pharmacy level Until 1 April 2022, the automatic substitution of a biological product is prohibited without the authorisation of the prescribing physician
	✓	Automatic substitution at a pharmacy level	✗	No well-established policy management for drugs approved via this pathway	✗	Automatic substitution of a biological product is forbidden without authorisation of the prescribing physician and patient acceptance
	✓	Automatic substitution if drugs are listed on the AIFA 'Transparency List' Regional/local recommendations or non-binding guidelines to steer generic substitution	✗	Hybrid management remains uncertain and the product may be treated either as biosimilar or generic	✗	Automatic pharmacy-level substitution of biosimilars is prohibited
	✓	*'Répertoire des Génériques'* is the substitution list for generics and originators	✓	Hybrid groups (drugs listed in an *arrêté*) are established and registered	🔍	*'La liste de référence des groupes biologiques similaires'* details which biosimilars can be substituted Substitution must be agreed with patient
	✓	Automatic, mandatory substitution, close to no possibility to prescribe branded products	🔍	Substitution is on a case-by-case scenario, based on clinical and safety evaluation and provision of additional data to prove therapeutic equivalence	✗	Pharmacists are prohibited from substituting with biosimilars; however, NHS guidance encourages physicians to substitute biosimilars with agreement of patient

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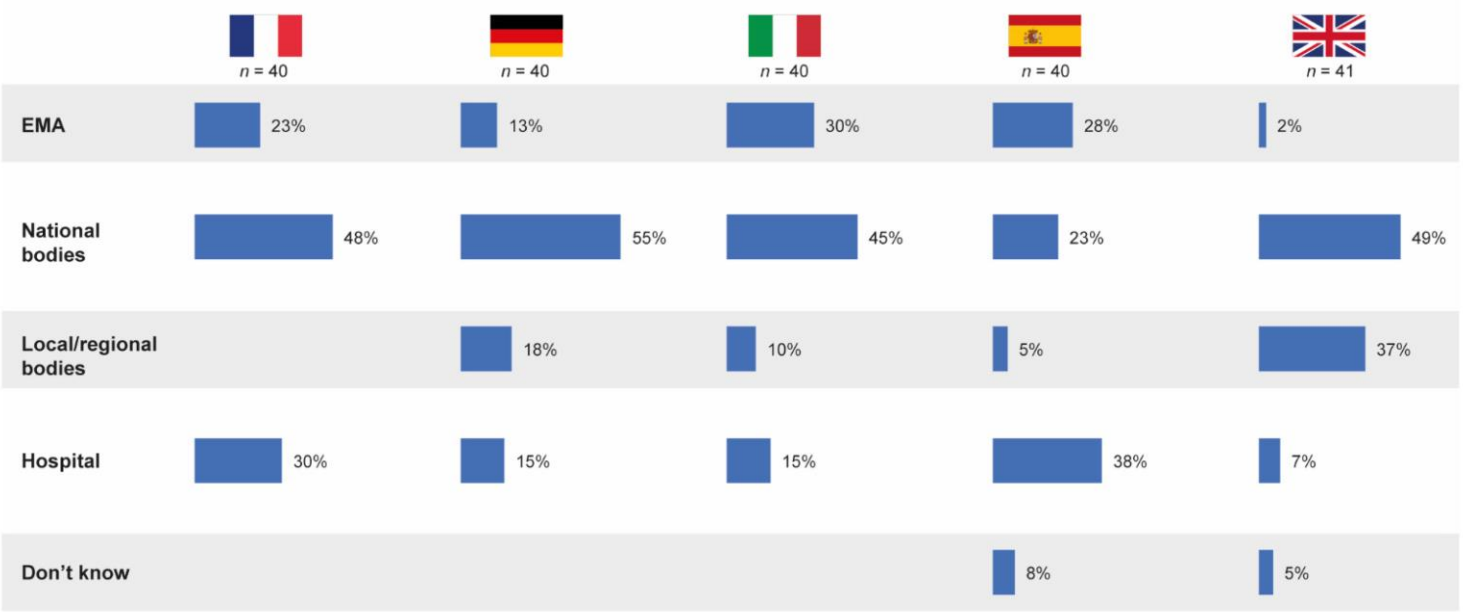
Pharmaceutics. 2021 Jul 2;13(7):1010.
doi: 10.3390/pharmaceutics13071010.

Stakeholders believed by pharmacists to be relevant in the definition of substitutability of follow-on products in the hospital formulary.



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Formulary selection criteria for nanosimilars

Pharmaceutical quality	Efficacy/safety	Manufacturer considerations	Product considerations	Hospital and patient factors
• Chemical composition • Identity • Quantity • Pharmacopial specifications • **Particle size and size distribution** • **Particle surface characteristics** • **Uncaptured pharmacological active moiety fraction** • **Storage stability**	• **Pharmacokinetics** – **Uptake** – **Distribution** • Clinical data • Range of indications • Immunogenicity • Potential for therapeutic interchange • Number of similar agents on formulary • Pharmacovigilance requirements	• Supply reliability • History of drug shortages • Supply chain security • Anti-counterfeit measures • Patient assistance programs • Reimbursement support • Manufacturer services, expertise	• Product packaging and labeling • Bar coding • Compatibility with CSTDs, robotics • Ready-to-use preparation and administration – **Stability for ready-to-use administration** • Storage requirements	• Economic considerations – Hospital – Payer – Patient • Transitions of care • IT and medication system changes • Educational requirements • Pharmacovigilance requirements

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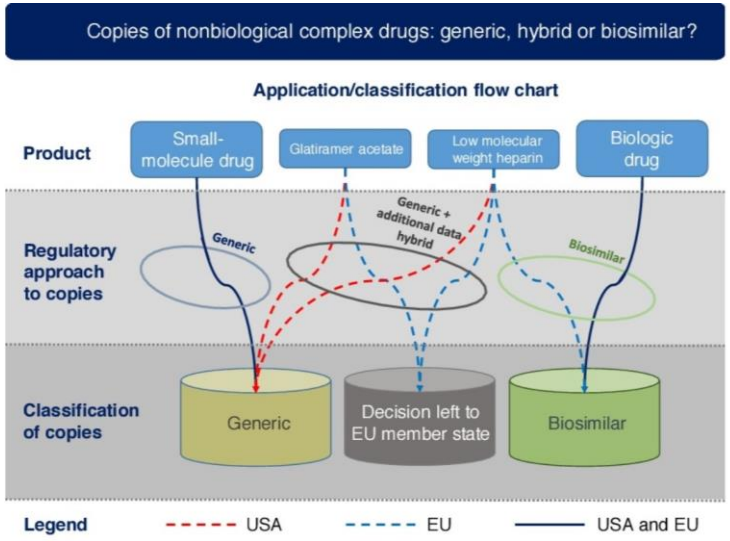
Am J Health Syst Pharm, Volume 78, Issue 12, 15 June 2021, Pages 1047–1056, https://doi.org/10.1093/ajhp/zxab048

The complex drug landscape

Example : glatiramoids



Example : teriparatide

Brand name	Type
Movymia®	Biosimilar
Duratil®	Generic
Livogiva®	Biosimilar
Terrosa®	Biosimilar
Forsteo®	Originator

Drug Discov Today. 2019 Jan;24(1):250-255. doi: 10.1016/j.drudis.2018.08.003

Concluding remarks

- Interchangeability of reference nanomedicines and their follow-on products is not supported by well-defined equivalence evaluations, with adverse clinical and cost implications with use of nanosimilars.

- For patient safety and benefit, regulatory approval processes for nanosimilars need to be better defined and standardized to support consistent evaluation of critical quality attributes as evidence of therapeutic equivalence to reference nanomedicines.

Thanks!

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