ASK

Attitude, Skills, and Knowledge in Oncology Biosimilars

Adapting to a changing landscape: switching to oncology biosimilars

Interactive discussion with:
Emma Foreman, Philippe Arnaud and Glenn Myers

Educational funding

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An interactive webinar: please participate

Questions for the panellists

- Throughout this session, **please pose your questions to the panellists in the Q&A box**
- Please note: you will **NOT** be able to ask questions via the chat function
- The speakers will look to incorporate your questions throughout the webinar to facilitate discussion

Interactive questions

- There will also be interactive questions displayed on the screen
- Please choose your answer by selecting the options when they appear on the screen

NOTE: If you are watching the archive footage, you will not be able to take part in any polls

Faculty

Chair: Emma Foreman

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Panellist: Glenn Myers

Clinical Pharmacist
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Faculty disclosures

All faculty are receiving a speaker honoraria for this ASK webinar

- PA has no relevant disclosures

Within the last 12 months:

- EF received speaking honoraria from Bristol Myers Squibb, Pfizer, Amgen, Astra Zeneca and Ipsen, and reports a relationship with Accord

- GM received fees from Merck, Eisai, Novartis, Apobiologix, AstraZeneca, Sanofi, Bristol Myers Squibb (BMS) and Ipsen, and reports commercial relationships with Amgen, Gilead, Roche and IMV Inc.

Learning objectives

At the end of this webinar, delegates should be able to:

- Recall effective strategies for ensuring patient safety and efficacy when switching between different brands of biologic pharmaceuticals, including pharmacovigilance requirements
- Describe key considerations across a multidisciplinary team when switching from an originator biologic to a biosimilar
- Discuss the potential savings and access to innovation opportunities created by switching from an originator biologic to a biosimilar

Oncology biosimilars

Biologic pharmaceuticals

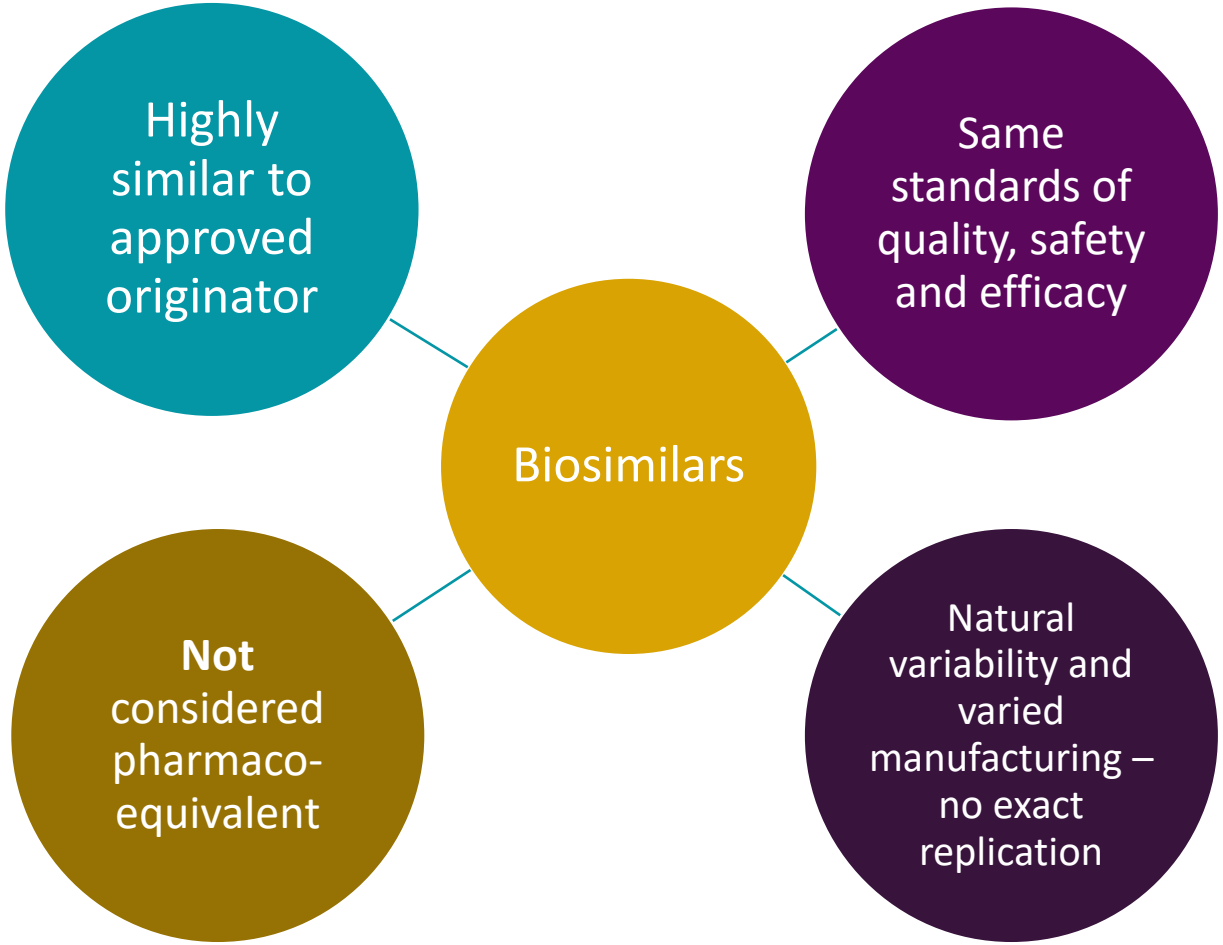
- A biologic is an active substance (e.g., drug, vaccine or anti-toxin) that is synthesized from living organisms or their products and used as a diagnostic, preventive or therapeutic tool

Example	Type	Nature
Bevacizumab[1]	Recombinant humanised mAb	Therapeutic – complex
Filgrastim[2]	Recombinant protein	Supportive – simple
Rituximab[3]	Chimeric mAb	Therapeutic – complex
Enoxaparin sodium[4]	Low molecular weight heparin	Supportive – simple

mAb, monoclonal antibody; VEGF, vascular endothelial growth factor.

1. Roche Products Ltd. 2021. Available at: https://www.medicines.org.uk/emc/medicine/15748/SPC/Avastin+25mg+ml+concentrate+for+solution+for+infusion/#gref [Accessed October 2021]. 2. Amgen Ltd. 2021. Available at: https://www.medicines.org.uk/emc/product/608/smpc [Accessed October 2021]. 3. Roche Products Ltd. 2021. Available at: https://www.medicines.org.uk/emc/product/3801/smpc. [Accessed October 2021]. 4. Aventis Pharma Limited. 2021. Available online: https://www.medicines.org.uk/emc/medicine/10054#PACKAGE [Accessed November 2021].

Patent expiration for ‘originator’ biologics has permitted the development of biosimilars[1,2]

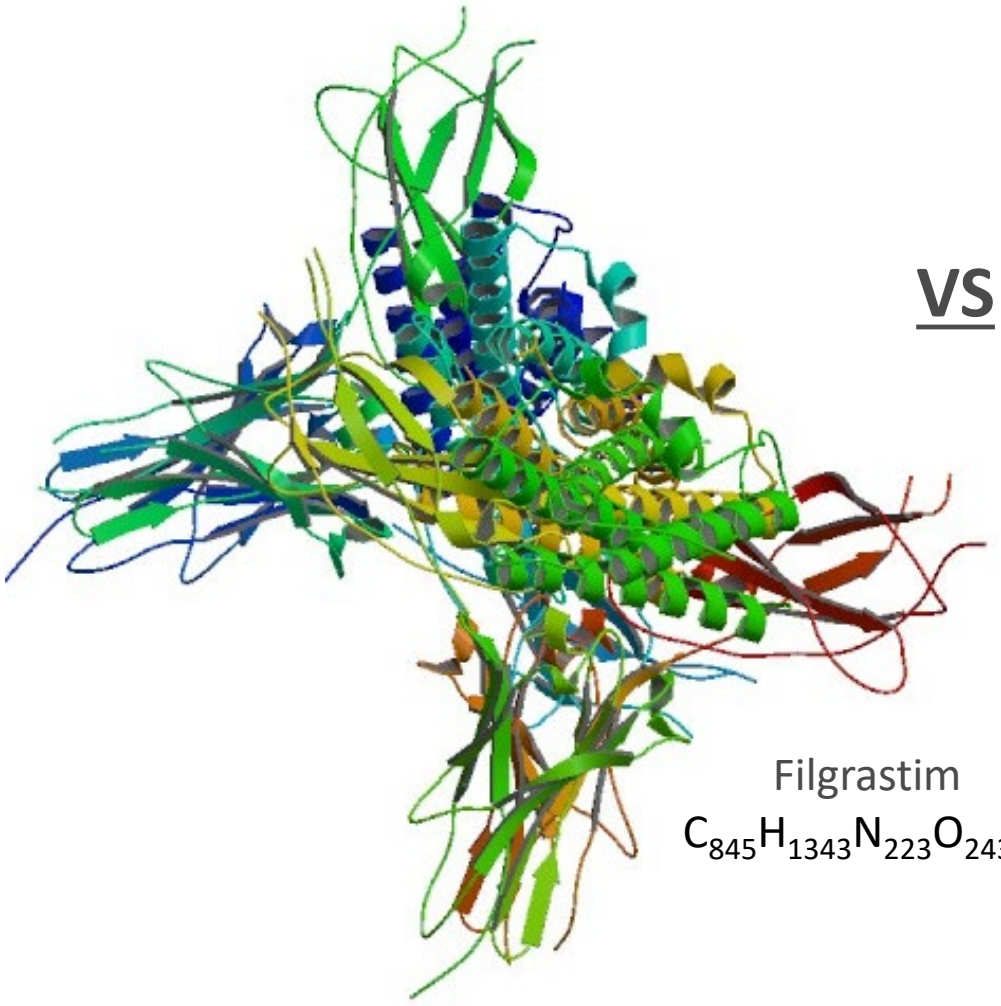


1. European Medicines Agency. 2021. Available at: https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines-overview [Accessed June 2021]. 2. European Medicines Agency. 2019. Available at: https://www.ema.europa.eu/en/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf. [Accessed June 2021].

Biosimilars ≠ Generics[1]

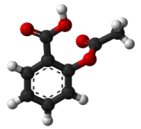
It is not possible to produce an exact copy of a biologic drug owing to:

- Size/complexity of the molecules
- Natural variability (e.g., post-translational modifications)
- Complex manufacturing – use of living cells rather than chemical components



Filgrastim
$C_{845}H_{1343}N_{223}O_{243}S_9$

VS



Aspirin
$C_9H_8O_4$

1. European Medicines Agency. 2021. Available at: https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines-overview [Accessed June 2021].

Why switch to a biosimilar?

- **Competitive pricing** – biosimilars are typically priced at a significantly discounted rate compared to the reference biologic; often between 10% and 50% discount[1,2,3]
- Can allow **improved patient access** at lower cost and provide **alternative options** to the reference biologic[4]
  - More patients receiving timely treatment
  - Improved drug access during national or international shortages – controls risk of supply disruption
  - Improved access to more rare non-formulary indications (e.g., bevacizumab for gliomas)
- Money saved can be invested in service improvements and other resources to improve healthcare efficiency
- Drives innovation (e.g. alternative formulations → subcutaneous administration)[5]

1. Tesar et al. *Front Public Health* 2020;8:431. **2.** Greener et al. *Prescriber* 2017;28(4):34–38. **3.** Faculty insight. **4.** Cuellar et al. *Am J Health Syst Pharm* 2019;76(21):1725–1738. **5.** Kim et al., *MABS* 2021;13,(1):e1868078.

Patient safety considerations

Risk assessment[1]

- Clinician acceptance[1]
- Rare (≥ 1 in 10,000 and < 1 in 1000)[2] or very rare (< 1 in 10,000)[2] adverse events in pharmacovigilance[1]
- Supply chain reliability[1]
- Clinically significant differences from innovator[3]
- Patient acceptance[1]
- Nurse acceptance[1]

Image: FreePik.com

1. NHS Commissioning Support. Available online: https://www.sps.nhs.uk/wp-content/uploads/2018/07/AGA_7962_Biosimilar-Adalimumab-Toolkit-Interactive-PDF_v10.pdf (accessed November 2021). **2.** National Institute for Health and Care Excellence. Available online: https://bnf.nice.org.uk/guidance/adverse-reactions-to-drugs.html (accessed November 2021). **3.** Cancer Vanguard. Available online: http://cancervanguard.nhs.uk/wp-content/uploads/2017/03/UK_MKT_SDZ_17_0027d-Vanguard-Introduction-Training-Slide-Set-for-website-FINALii-1.pdf (accessed November 2021).

Pharmacovigilance considerations[1,2]

- Clear delegation of responsibility
- Depending on country of licence
- Manufacturer risk-management plan
- Pharmacovigilance
- Real-world data post-marketing
- Patient/product registries
- Traceability – product and batch
- Periodic safety update report

Real-time information, where possible

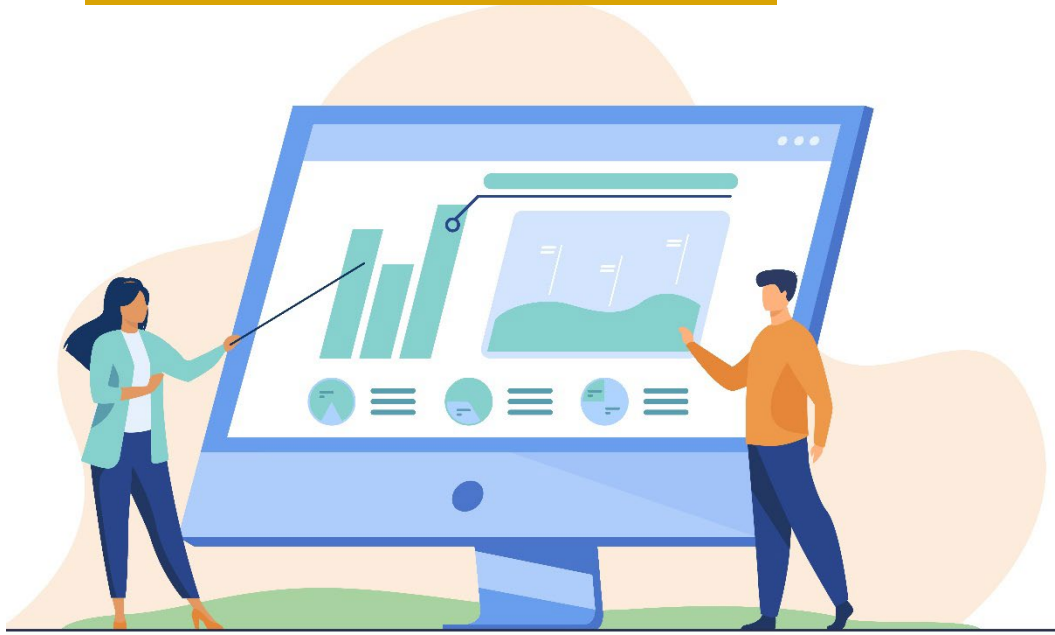
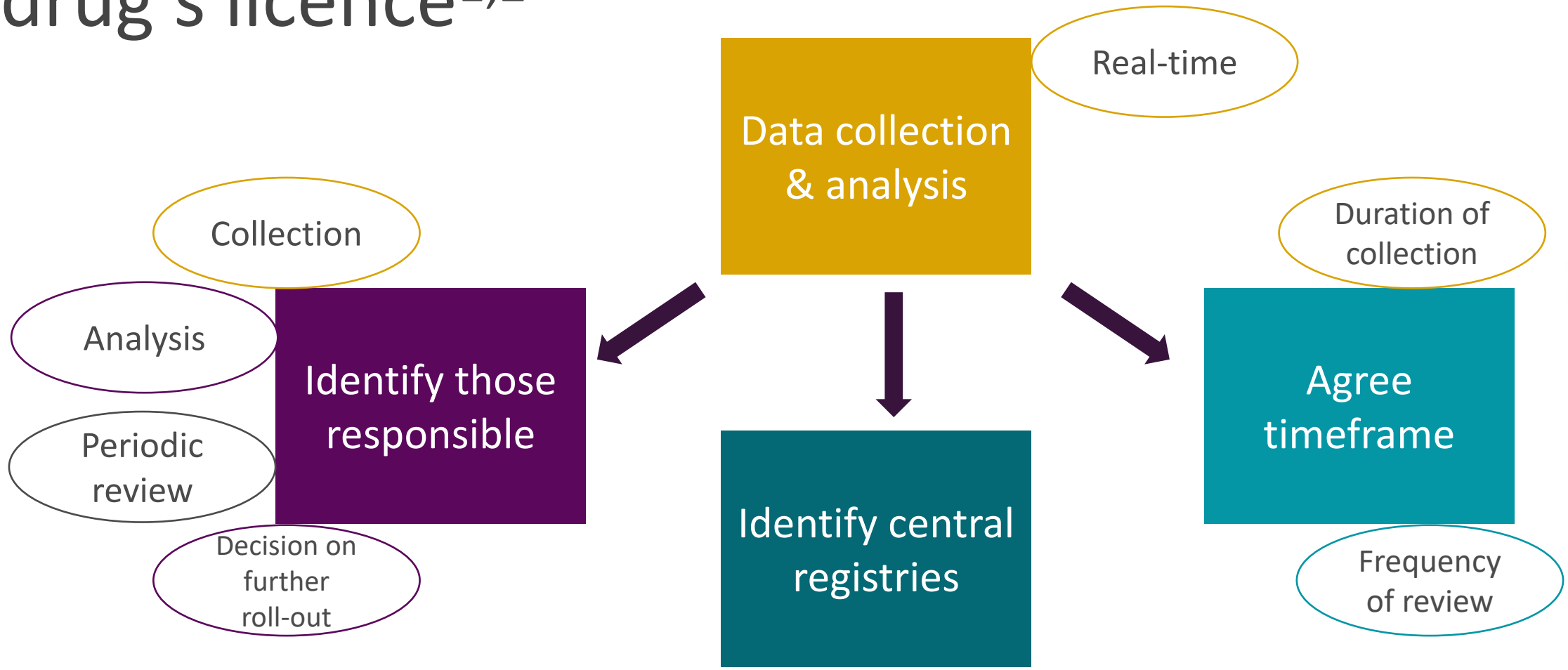


Image from FreePik.com

1. Isaacs et al. *Considerations in Medicine* 2017;1(1):3–6. **2.** Casadevall et al. *Expert Opin Biol Ther* 2013;13(7):1039–1047.

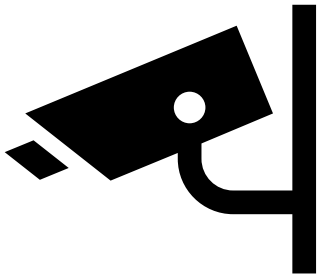
Clinical data collection may be part of the drug's licence[1,2]



ADA = anti-drug antibody

1. Cancer Vanguard. Available online: http://cancervanguard.nhs.uk/wp-content/uploads/2017/03/UK_MKT_SDZ_17_0027d-Vanguard-Introduction-Training-Slide-Set-for-website-FINALii-1.pdf (accessed November 2021)
2. NHS Commissioning Support. Available online: https://www.sps.nhs.uk/wp-content/uploads/2018/07/AGA_7962_Biosimilar-Adalimumab-Toolkit-Interactive-PDF_v10.pdf (accessed November 2021).

Monitoring for immunogenicity must be appropriate to the setting[1,2]



- Prescribing information rarely instructs on monitoring for anti-drug antibodies
  - Appropriate assays may not be available
  - How or when to monitor patients for anti-drug antibodies
    - Reactive therapeutic drug monitoring
    - Routine serum sampling

1. Cancer Vanguard. Available online: http://cancervanguard.nhs.uk/wp-content/uploads/2017/03/UK_MKT_SDZ_17_0027d-Vanguard-Introduction-Training-Slide-Set-for-website-FINALii-1.pdf (accessed November 2021)
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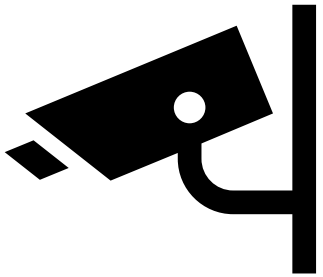

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    - Routine serum sampling

→

- Primary or secondary loss of response
- Hypersensitivity
- Injection site/other allergic reaction

1. Cancer Vanguard. Available online: http://cancervanguard.nhs.uk/wp-content/uploads/2017/03/UK_MKT_SDZ_17_0027d-Vanguard-Introduction-Training-Slide-Set-for-website-FINALii-1.pdf (accessed November 2021)
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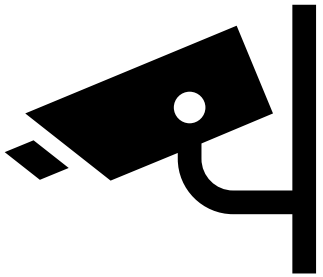

- Prescribing information rarely instructs on monitoring for anti-drug antibodies
  - Appropriate assays may not be available
  - How or when to monitor patients for ant
    - Reactive therapeutic drug monitoring
    - Routine serum sampling

- Primary or secondary
- r

- Sometimes collected for research purposes
- Can be used to monitor drug level and correlate with efficacy
- May be appropriate to enrol patients receiving biologics to serum registries

1. Cancer Vanguard. Available online: http://cancervanguard.nhs.uk/wp-content/uploads/2017/03/UK_MKT_SDZ_17_0027d-Vanguard-Introduction-Training-Slide-Set-for-website-FINALii-1.pdf (accessed November 2021)
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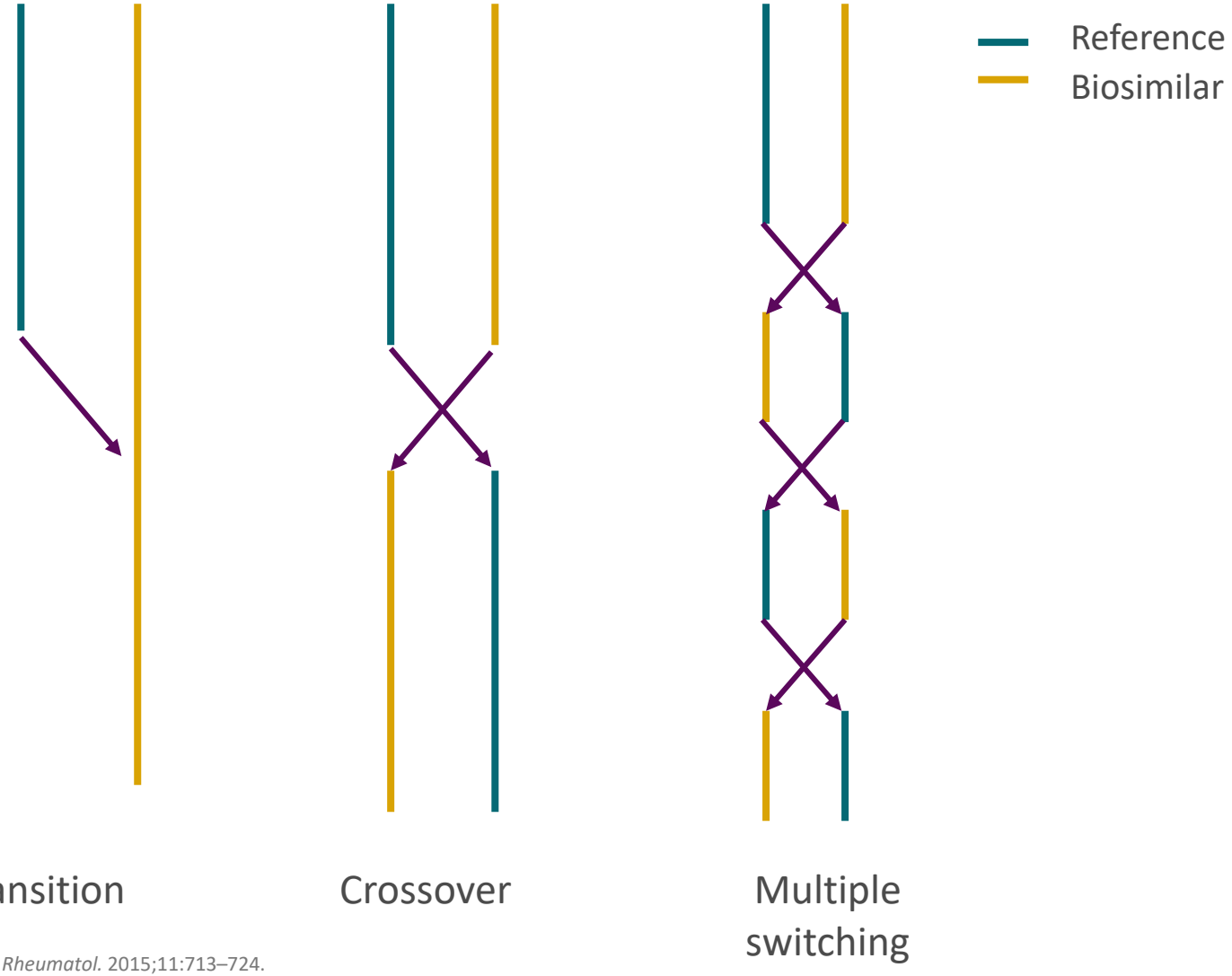
Building a case for switching

Types of switching studies



Adapted from Dorner et al., *Nat Rev Rheumatol.* 2015;11:713–724.

Horizon scanning[1,2]

Ongoing task

Maintaining awareness of product launches

Requires regular review

Standing agenda item

Prevent repeat work

Use regional & national boards and working groups

Local, regional, national, international

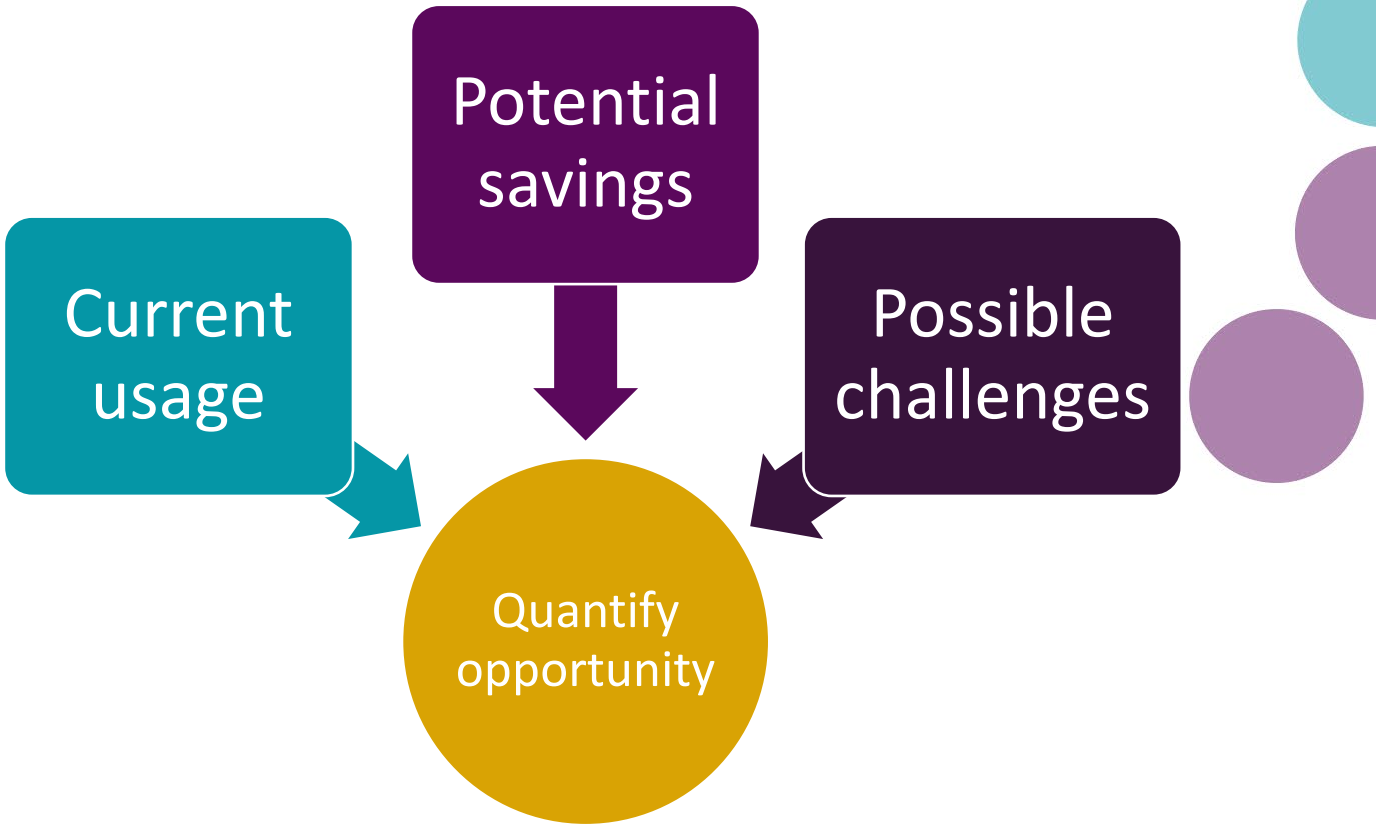
Done at all levels

Image from FreePik.com

1. Cancer Vanguard. Available online: http://cancervanguard.nhs.uk/wp-content/uploads/2017/03/UK_MKT_SDZ_17_0027d-Vanguard-Introduction-Training-Slide-Set-for-website-FINALii-1.pdf (accessed November 2021) **2.** NHS Commissioning Support. Available online: https://www.sps.nhs.uk/wp-content/uploads/2018/07/AGA_7962_Biosimilar-Adalimumab-Toolkit-Interactive-PDF_v10.pdf (accessed November 2021).

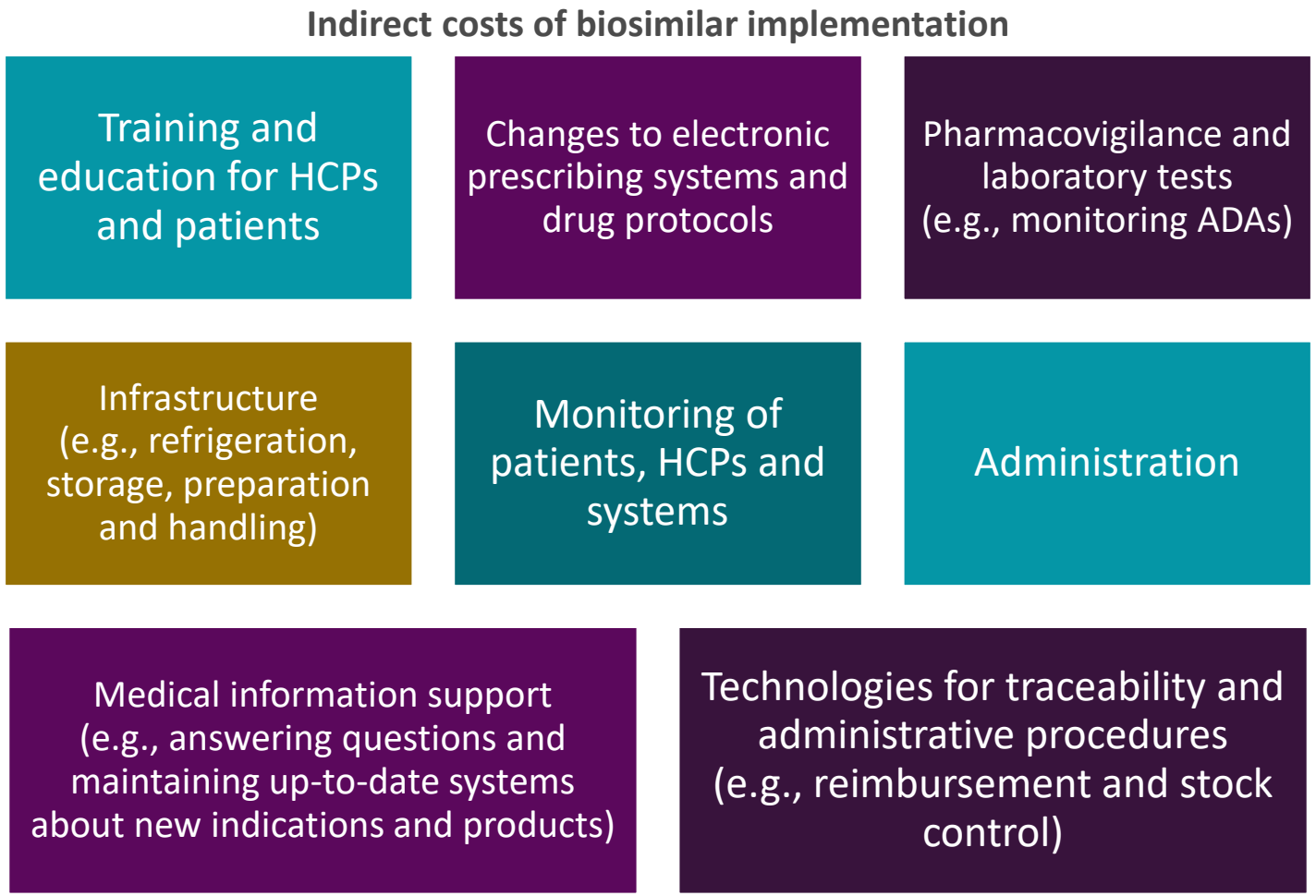
Cost – a key consideration in some settings

- Resources can be limited
  - When adding products to the formulary, cost reduction can be a key consideration[1]
    - Not always the case, e.g., in France – less of a concern[1]
  - Tendering, usually at hospital level, for supplier contracts ensures adequate supplies and high quality, while containing spending[2]
    - Switching can also occur at a national level



1. Speaker insight. **2.** Simoens & Cheung. *J Mark Access Health Policy* 2019;8:1705120.

Cost of implementation not limited to acquisition[1,2]



ADA, anti-drug antibody; HCP, healthcare professional.

1. Cuellar et al. *Am J Health Syst Pharm* 2019;76(21):1725–1738. **2.** Zlatkus et al. *Drugs Context* 2020;9.

Other considerations when evaluating biosimilars[1]

Mindful of differences in…

Administration	Storage	Packaging & Labeling
• Delivery system • Routes of administration • Amount of pharmacy technician time required • Timing of administration • Patient experience	• Shelf life • Light sensitivity • Chance of dispensing error	• Clarity of information on the labels • Clear differences between the two products • Handling warnings

1. Griffith et al. *Hosp Pharm* 2014;49(9)813–825.

Who to switch and when?

Switching all patients[1,2]

- Avoid confusion
- Maximise cost reductions

Starting new patients only[1,2]

- Gain experience & comfort with efficacy and safety before switching established patients
- Rare adverse events more apparent after larger numbers of patients treated[3,4]

Discussion with **clinicians** and **patient advocacy groups** to understand patient needs[2]

1. Cancer Vanguard. Available online: http://cancervanguard.nhs.uk/wp-content/uploads/2017/03/UK_MKT_SDZ_17_0027d-Vanguard-Introduction-Training-Slide-Set-for-website-FINALii-1.pdf (accessed November 2021). **2.** Faculty insight. **3.** Cuellar et al. *Am J Health Syst Pharm* 2019;76(21):1725–1738. **4.** Braun et al. *Biologicals* 2016;44(4):257–266.

Practical aspects of switching

Early engagement is key to success[1]

- Work in partnership with clinicians and patient groups, encouraging patient-centred care approach
  - Interacting at the individual patient level also required
- Identify a switch lead within the pharmacy – clearly identified roles
- MDT steering group with agreed roles – ensure collaboration
- Review case studies of previous biosimilar launches
- Look for regional and national boards and working groups – avoid duplication of work or reproducing similar toolkits

1. NHS Commissioning Support. Available online: https://www.sps.nhs.uk/wp-content/uploads/2018/07/AGA_7962_Biosimilar-Adalimumab-Toolkit-Interactive-PDF_v10.pdf (accessed November 2021).

Use an agreed process

Traceability/brand names[1]

Electronic prescribing implications[1]

Which patients?[2]

Types of monitoring[2]

What indications?[1]

Stocking & storage[1]

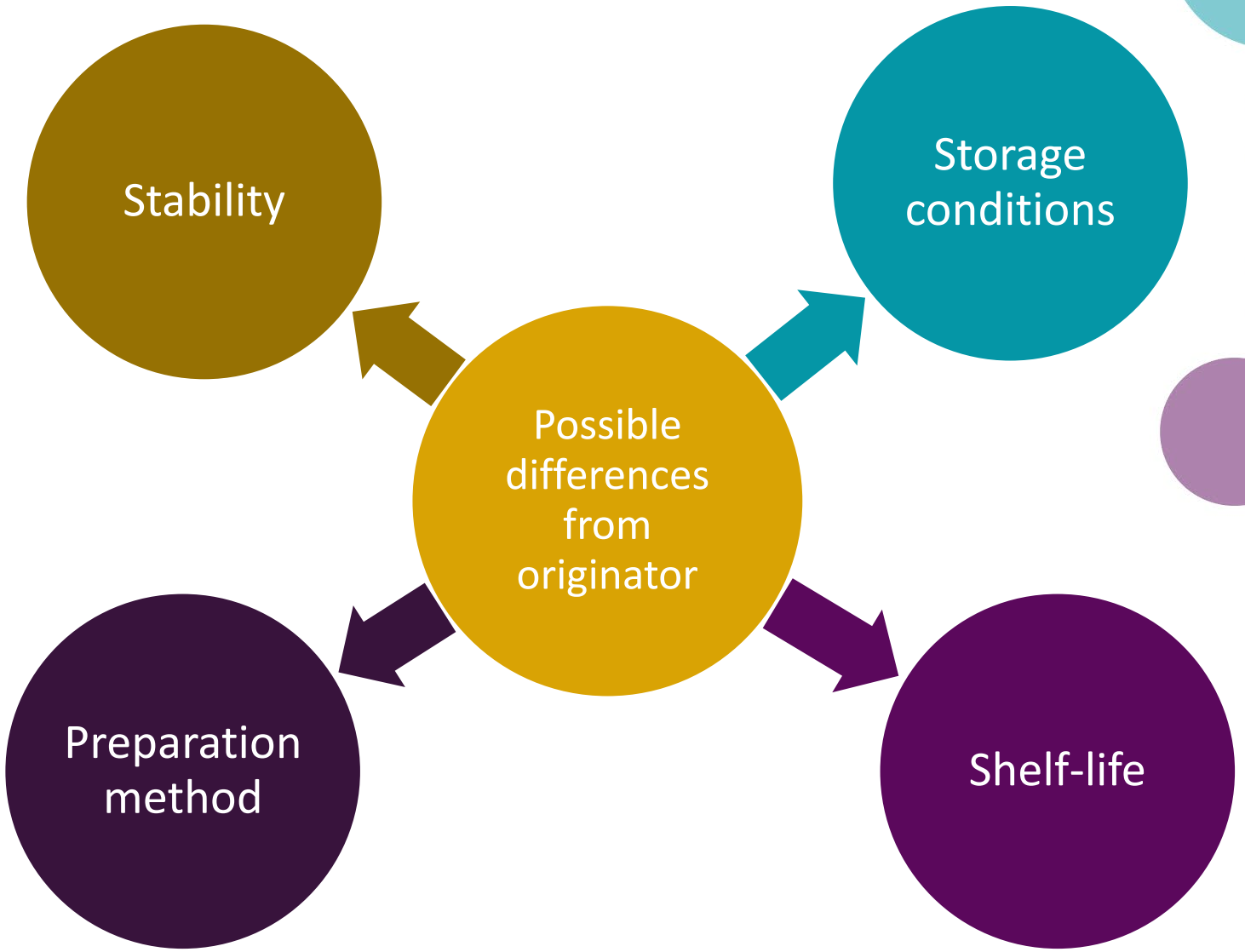
Communication[1]

Early preparation[1]

1. NHS Commissioning Support. Available online: https://www.sps.nhs.uk/wp-content/uploads/2018/07/AGA_7962_Biosimilar-Adalimumab-Toolkit-Interactive-PDF_v10.pdf (accessed November 2021). **2.** Cancer Vanguard. Available online: http://cancervanguard.nhs.uk/wp-content/uploads/2017/03/UK_MKT_SDZ_17_0027d-Vanguard-Introduction-Training-Slide-Set-for-website-FINALii-1.pdf (accessed November 2021).

Pharmacy considerations[1,2]

- Any changes to preparation method/storage to be flagged
- Education – prevent inadvertent mishandling
- Separate storage and clear labelling essential of biosimilars and originators



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Administrative considerations

Accurate tracking and tracing

- Essential for linking AEs to specific products
- Unique names required, e.g., brand name or INN
- Could require updates to IT systems, e.g., electronic medical records[1,2]

Feasibility

- Existing resources sufficient?
- Offset predicted resources against predicted savings – true cost
- Data collection

Redirecting savings[3]

- Utilize some of the savings from using the biosimilar to hiring a dedicated pharmacist for biosimilar implementation[3]

1. Cuellar et al. *Am J Health Syst Pharm* 2019;76(21):1725–1738. **2**. Zlatkus A, et al. *Drugs Context* 2020;9. **3.** Faculty insight.

Differences between products can affect uptake

Educate **all** stakeholders

Dosing

Container

Administration

Cuellar et al. *Am J Health Syst Pharm* 2019;76(21):1725–1738.

Training the MDT is crucial[1]

- Robust staff education improves confidence of staff and patients
- Targeted small group training specific to needs of the role
  - feedback from team
- Resources for MDT training widely available:
  - biopharmaceutical manufacturers
  - licensing authorities
  - medical societies/organisations

1. NHS Commissioning Support. Available online: https://www.sps.nhs.uk/wp-content/uploads/2018/07/AGA_7962_Biosimilar-Adalimumab-Toolkit-Interactive-PDF_v10.pdf (accessed November 2021).

Review safety data regularly[1,2]

- Data associated with biosimilars is different from that of the reference molecule
- Not every indication of the reference molecule needs to be studied

Timing of new data releases

Ongoing studies

Studies of new indications

Manufacturer periodic safety updates

Involvement in professional registries

1. Cancer Vanguard. Available online: http://cancervanguard.nhs.uk/wp-content/uploads/2017/03/UK_MKT_SDZ_17_0027d-Vanguard-Introduction-Training-Slide-Set-for-website-FINALii-1.pdf (accessed November 2021) **2.** NHS Commissioning Support. Available online: https://www.sps.nhs.uk/wp-content/uploads/2018/07/AGA_7962_Biosimilar-Adalimumab-Toolkit-Interactive-PDF_v10.pdf (accessed November 2021).

Access to innovation

Money saved can be invested or reinvested[1]

- Dedicated resources – specific biosimilar pharmacists/nurses
- Improved treatment options
- Innovative medicines
- Novel devices

1. Faculty insight.

Competition drives innovation

Manufacturers need to compete

Originators must adapt

Trastuzumab biosimilars drove development of SC formulation by originator

SC = subcutaneous

Patient communication

Hearing the patients' voices[1]

- Must be included in the decision to switch
- **Patient panels, forums or advocacy groups**
- Listen for areas of concern
- Discuss any potential impacts on patients

Patient acceptance can improve uptake

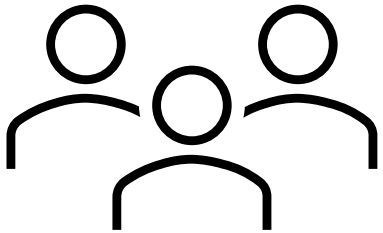
Consistent approach to education – receiving the same message from all team members

Prioritise information from societies and expert groups – no commercial bias

1. NHS Commissioning Support. Available online: https://www.sps.nhs.uk/wp-content/uploads/2018/07/AGA_7962_Biosimilar-Adalimumab-Toolkit-Interactive-PDF_v10.pdf (accessed November 2021).

Ideal patient communication[1,2]

- Keep it simple
- Mixture of written and oral information
- Involve patient groups or advocates when developing materials
- Well-informed and approachable staff
- Build an existing rapport with patients
- Invite patient feedback



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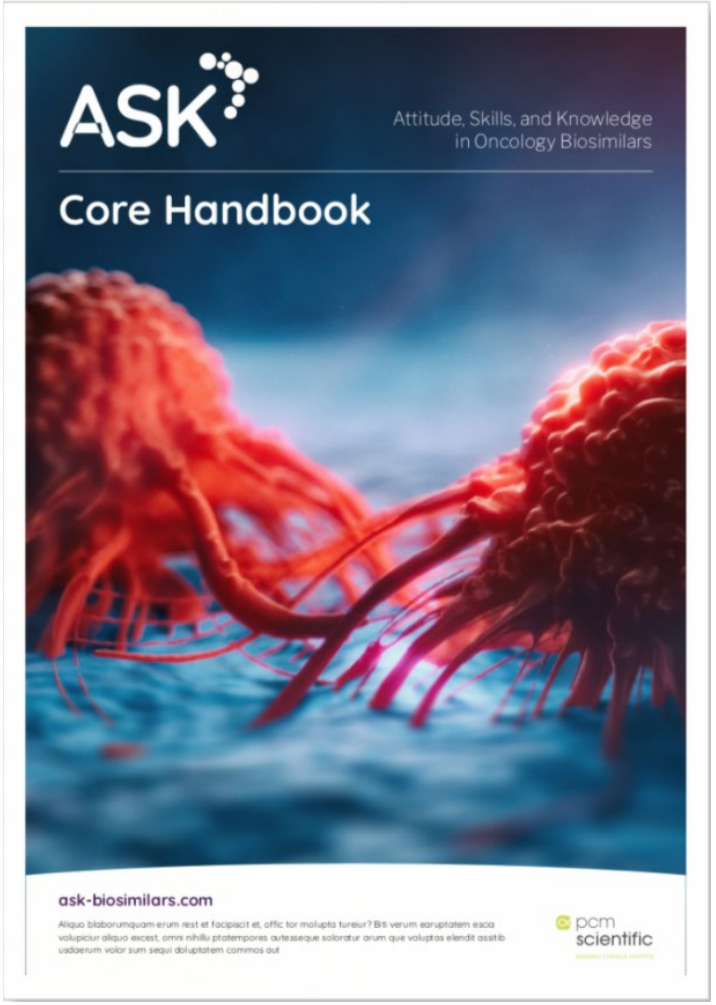
Closing remarks

Free learning resources available

- Handbook
  - English version available now
  - Coming soon in French, German, Italian, Japanese and Spanish
- Learning chapters – coming soon
- Abstract library – available now
- National guideline summary documents – coming soon
- Subtitled webinar archive footage – coming soon

Find out more via the website:

ask-biosimilars.com



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Thank you for joining this webinar!