The scope of protection afforded by SPCs

and future perspectives for the SPC system

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Topics

1. UPC and proposed EU SPC reforms
2. Scope of protection of SPCs
3. New active substance status
4. Prodrugs, biologics and advanced therapies
5. UK SPCs and the Windsor Framework

Unified Patent Court and 'Unitary Patents'

- The Unified Patent Court (UPC) began operation on 1 June 2023

- The UPC Agreement applies only to SPCs protected by:
  - A European patent **(unless opted out)** or
  - A European patent with unitary effect ('Unitary Patent')

- Where not opted-out, UPC will have exclusive competence for:
  - Actions for actual or threatened infringement of SPCs
  - Actions for declarations of non-infringement of SPCs
  - Actions for provisional and protective measures and injunctions
  - Actions for declaration of invalidity of SPCs
  - Counterclaims for declaration of invalidity of SPCs

  …but 7 to 14-year transitional period in which national courts or authorities share competence (i.e. national litigation option)

- SPC cases will be heard before the Paris seat of the central division (26 June 2023 decision to amend UPCA)

Proposed EU SPC Reforms

Four proposals:

- Recast both existing SPC Regulations to include a **centralised examination route**

- Introduce two new SPC Regulations providing **unitary SPCs**

Third-party observations and pre-grant oppositions

- Observations within 3 mo of publication of application
- Opposition within 2 mo of publication of positive examination opinion

New recitals to codify case law

- Interpretation of Article 3
- Art. 3(a) Teva v Gilead
- Art. 3(d) Santen

Centralised examination by the EUIPO

- Mandatory for medicinal products with EP + EMA
- Optional for PPPs with EP
- EUIPO decision is binding on national offices

Unitary SPCs

- Optional for medicinal products with UP + EMA
- Optional for PPPs with UP + MA *applied for* in all states
- EUIPO invalidation

No unauthorised third-party SPCs

- Patent holder must have the consent of MA holder to obtain an SPC
- Also patent holders that are economically linked cannot obtain separate SPCs

Proposed EU SPC Reforms

Action points

- Obtain and preserve documentation showing consent of the authorisation holder for you to file SPC applications
- Centralised examination leading to a bundle of national SPCs is likely to be a safer route than pursuing a unitary SPC
- Competitor surveillance – be ready to take action with filing observations and/or pre-grant oppositions

Article 4 (subject matter of protection)

Within the limits of the protection conferred by the basic patent,

the protection conferred by a certificate shall extend only to the **product covered by the {authorisation/authorizations}** to place the corresponding {medicinal/plant protection} product on the market

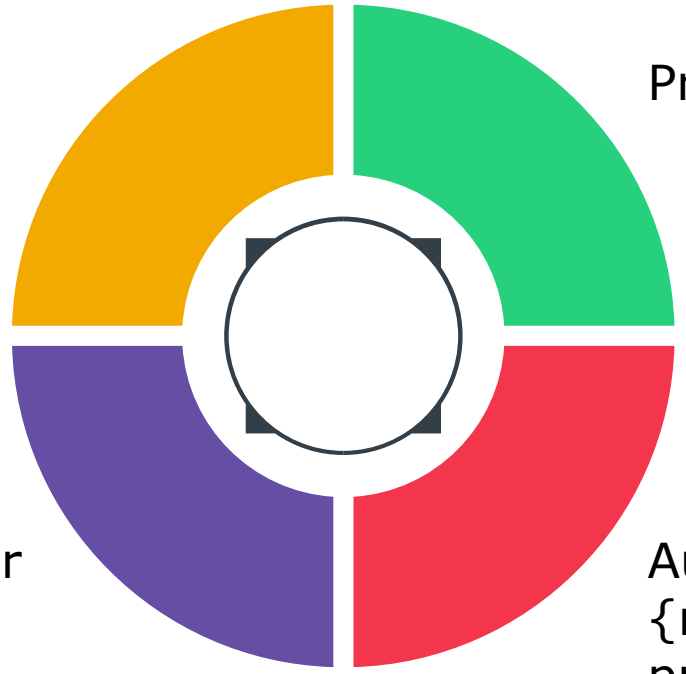
and for any use of the product as a {medicinal/plant protection} product that has been authorised before the expiry of the certificate.

- Patent covers A *per se*: First MA for A to treat cancer (sets SPC scope)
  Second MA for A to treat heart disease (SPC scope increases)
- SPC for A protects A in all authorised forms, including A + B combination product
- SPCs do not protect A outside of a {medicinal/plant protection} product, e.g. as a reagent

SPC scope summary

Scope of basic patent [maximum limits]

Product definition of SPC



Equivalent forms (e.g. salt or ester derivatives)
→ **PPP Recital 13**
→ ***Farmitalia (C-392/97)***

Authorised use(s) as a {medicinal/plant protection} product

Recitals about scope – EU proposed changes

PPP Regulation – Recital 13: The certificate confers the same rights as those conferred by the basic patent; consequently, where the basic patent covers an active substance and its various derivatives (salts and esters), the certificate confers the same protection.

PPP Regulation – Recital 14: The issue of a certificate for a product consisting of an active substance does not prejudice the issue of other certificates for derivatives (salts and esters) of the substance, provided that the derivatives are the subject of patents specifically covering them.

Proposed Recitals in both Regulations

To avoid overprotection, it should be provided that **no more than one certificate**, whether national or unitary, **may protect the same product** in a Member State. Therefore it should be required that the **product, or any {therapeutically equivalent} derivative** such as salts, esters, ethers, isomers, mixtures of isomers, or complexes **{or biosimilars / equivalent to the product from a phytosanitary perspective}, should not have already been the subject of a prior certificate**, either alone or in combination with one or more additional active ingredients, whether for the same {therapeutic indication / application} or for a different one.

To ensure balanced protection, however, a certificate should entitle its holder to **prevent a third party from manufacturing not only the product identified in the certificate but also {therapeutically equivalent} derivatives of that product**, such as salts, esters, ethers, isomers, mixtures of isomers, or complexes, **{as well as biosimilars / equivalent to the product from a phytosanitary perspective}**, even where such derivatives are not explicitly mentioned in the product description on the certificate. There is therefore a need to consider that the **protection conferred by the certificate extends to such equivalent derivatives, within the limits of the protection conferred by the basic patent**.

New chemical active substance

EMA Reflection paper indicates that the substance:

"*is from a chemical structure point of view* ***not related*** *to any other authorised substances…"*

"*Such substance is considered to be new in itself when the administration…* ***would not expose patients to the same therapeutic moiety*** *as already authorised active substance(s)…"*

Annex I of Chapter 1 of Volume 2A of the Notice to Applicants (NtA):

"*a chemical… substance* ***not previously authorised*** *in a medicinal product for human use in the European Union"*

or

"*an* ***isomer, mixture of isomers, a complex or derivative or salt*** *of a chemical substance previously authorised in a medicinal product for human use in the European Union but* ***differing significantly in properties with regard to safety and/or efficacy*** *from that chemical substance previously authorised"*

What about prodrugs and other derivatives?

Does it need to be a “new active substance”?

“*The different salts, esters, ethers, isomers, mixtures of isomers, complexes or* ***derivatives*** *of an active substances shall be considered to be the same active substances,* ***unless they differ significantly in properties with regard to safety and/or efficacy****.*” (Directive 2001/83/EC, Art. 10(2)(b))

→ Is there a different “therapeutic moiety”?

→ If not, for a derivative to be given “new active substance” status, there has to be a significant change in the safety/efficacy profile

→ Demonstrate a change in the pharmaco-kinetics of the therapeutic moiety, pharmaco-dynamics and/or toxicity

→ **Experimental evidence required to support the difference**

What about prodrugs and other derivatives?

Does it need to be a “new active substance”?

New active substance status itself is not a requirement for an SPC, but makes it easier to distinguish over the prior active substance

If the marketing authorisation includes new active substance status, it should also have its own INN and it is likely to be easy to satisfy Article 3(d) *[the MA is the first for that product]*

Even if the authorising body has not granted NAS status, the Patent Office/Court can independently assess whether there are enough data to show that the product is sufficiently different from previously-authorised active substances that it can be deemed a **different active ingredient/substance**

Biologics

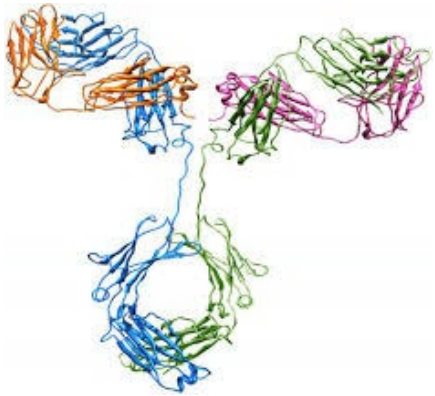
Proteins and polypeptides

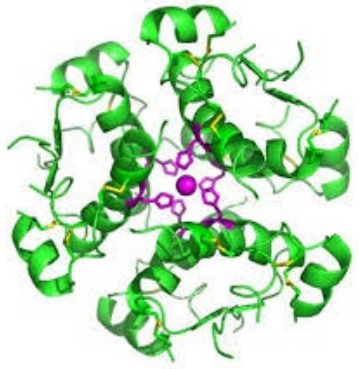
→ incl. derivatives and conjugates

→ produced by recombinant or non-recombinant cell-culture expression systems

Viral vaccines

Therapeutic antibodies





Therapeutic proteins

The **manufacturing method** is important to the authorisation and to the resulting product

Biosimilars are generally products with the same amino acid sequence but made by a different manufacturing method

→ SPCs should prohibit biosimilars from entering the market or being manufactured for export (unless under the terms of the manufacturing waiver)

New biological active substance

EMA Draft Reflection paper indicates that the substance:

"*is from a structure point of view **not related** to any other authorised substances…*"

"*Such substance is considered to be new in itself provided that the administration… **would not expose patients to the same therapeutic moiety** as already authorised active substance(s)*"

Annex I of Chapter 1 of Volume 2A of the Notice to Applicants (NtA):

"*a… biological… substance **not previously authorised** in a medicinal product for human use in the European Union*"

or

"*a biological substance previously authorised in a medicinal product for human use in the European Union, but **differing significantly in properties with regard to safety and/or efficacy** which is due to differences in one or a combination of the following:*

in molecular structure,
nature of the source material
or manufacturing process"

"*Proteins showing **substantial** differences in the amino acid sequence… would likely be considered NAS*"

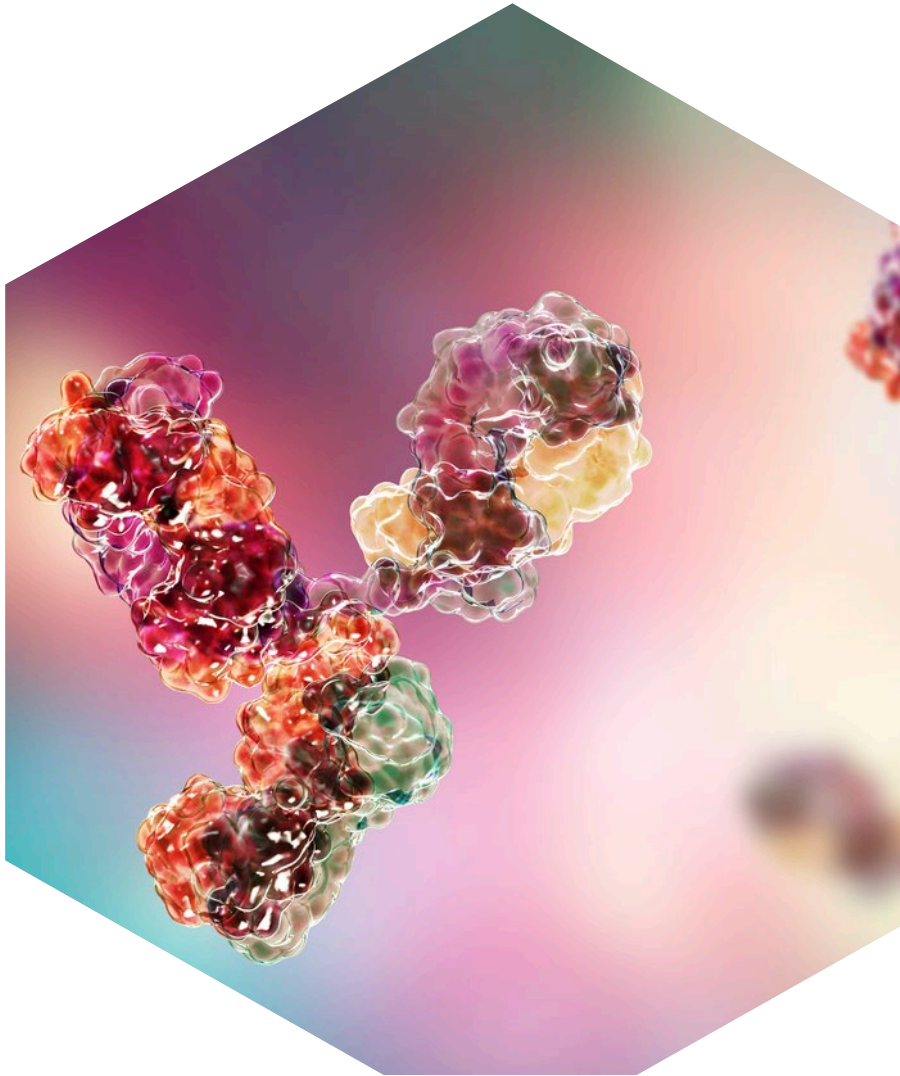
What about a new glycosylated form?

Does it need to be a "new active substance"?

Like for chemical active substances, NAS status is helpful although not strictly required

For biologics, NAS determination includes evaluating effects of differences in molecular structure and manufacturing process

> *"…where a molecular structure with the same basic structural element is produced but has additional post-translational modifications, such a structure would likely be considered as 'known active substance' unless it can be shown that these modifications have a* ***significant clinical impact in terms of safety and/ or efficacy****"*
>
> *"Meaningful changes… (****e.g. complete afucosylation*** *of a monoclonal antibody instead of the presence of both fucosylated and afucosylated forms) could be considered sufficient to justify the granting of NAS status, if it is substantiated that it translates in significant difference (e.g. in afucosylation) in terms of efficacy and/or safety"*



What about a new glycosylated form?

Does it need to be a "new active substance"?

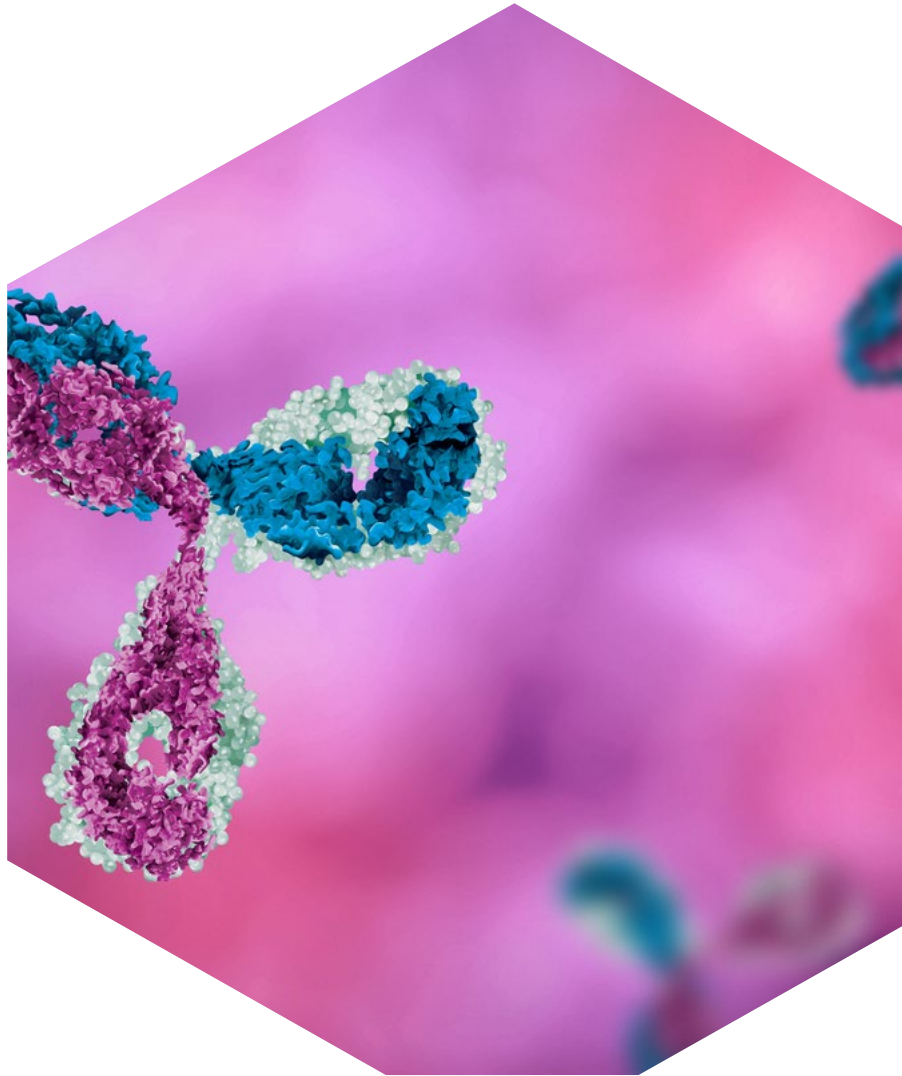
Even if the authorising body has not granted NAS status, the Patent Office/Court can independently assess whether there are enough data to show that the product is sufficiently different from previously-authorised active substances that it can be deemed a **different active ingredient/substance**

→ **UKIPO Decision BL O/552/14** (Icahn School Med)

- → Was it permitted to have two SPCs to agalsidase-alfa [Replagal®] and agalsidase-beta [Fabrazyme®], both of which are forms of secreted human α-galactosidase A?
- → Data showing glycosylation of agalsidase-alfa and agalsidase-beta affected clinical efficacy (bioavailability)
- → Concluded they were different products

"…***compelling non-clinical data*** *may support relevant substantial differences in safety and/or efficacy*"

"*Generation of clinical data is not required*"



Products containing micro-organisms

- Approval is usually at the strain level (accession number), which identification should be used in the product definition

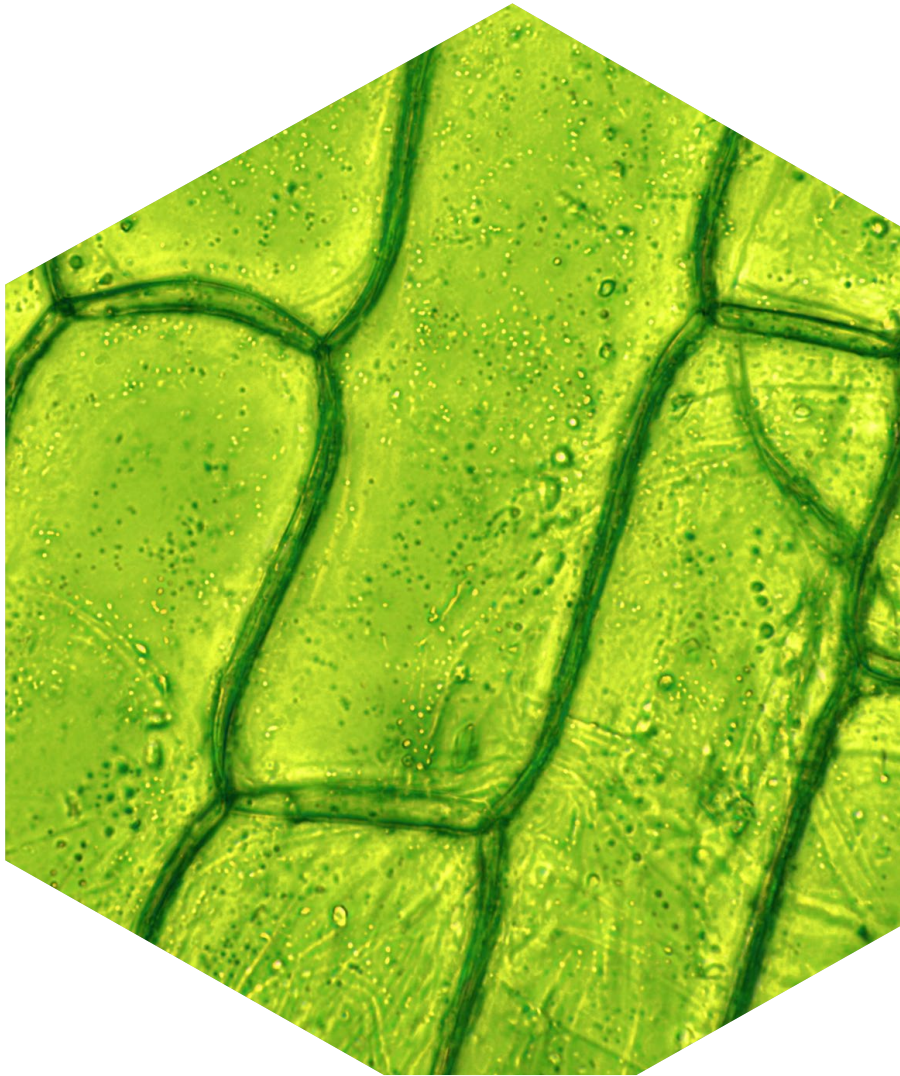
  e.g. "*Bacillus Firmus strain I-1582*"
  "*A live attenuated human rotavirus, strain RIX4414*"
  "*Leptospira interrogans serogroup Australis serovar Bratislava, strain MSLB 1088*"

- The correct regulatory procedure must be used to be eligible for SPCs:

  → **UKIPO Decisions BL O/610/20** and **BL O/732/21** (Erber Aktiengesellschaft)

  → "*microorganism DSM 11798 of the Coriobacteriaceae family*" was approved as an additive in animal feed to reduce contamination by mycotoxins

  → Found not to satisfy Art. 3(b) / Art. 3(1)(b) of either of the SPC Regulations



What is the scope for a biologics SPC?

Pharmaq v Intervet (E-16/14)

- Intervet authorised product: SAV1 vaccine (as an inactivated virus)
- Intervet SPC product definition, based on the claims of the basic patent, recited the inactivated deposited SAV1 virus **or closely related strains which share similar genotypic and/or phenotypic characteristics to said deposited virus strain**
- Pharmaq product: SAV3 vaccine (a molecular variant of SAV1)
- EFTA Court determined that the SPC only covers a strain that constitutes the **same active ingredient** as what was authorised, with therapeutic effects within the authorised indications

  → SPC is invalid if granted with a product definition having a wider scope than the MA **i.e. it should be limited to the International Nonproprietary Name (INN) / strain**

- Norwegian Court of Appeal decided that SAV3 was significantly more efficacious than SAV1 → **not the same active ingredient**

  → Consider whether it is feasible to file a 'third-party SPC' based on your patent and a competitor's MA *[not expected to be possible after SPC reforms – consent requirement]*

What is the scope for a biologics SPC?

EU proposed changes to SPC Regulations

> "*For **biological products**, the application of the rules, both as regards the conditions for grant and the effects of a certificate, should take into account the fact that **minor differences may be unavoidable** between a subsequent biosimilar and the product initially authorised, given the nature of biological products*"
>
> (Explanation of new SPC proposals)

Proposed Recitals in both Regulations (paraphrased)

MEDICINAL PRODUCTS

→ **Therapeutically equivalent** derivatives or biosimilars will be protected, within the limits of the protection conferred by the basic patent

PLANT PROTECTION PRODUCTS

→ **Derivatives equivalent to the product from a phytosanitary perspective** will be protected, within the limits of the protection conferred by the basic patent

Article 2, Protocol on Interpretation of Article 69 EPC

"For the purpose of determining the extent of protection conferred by a European patent, due account shall be taken of any element which is equivalent to an element specified in the claims"

- But less likely to cover independent, unrelated antibodies directed to the same target

Advanced therapy medicinal products e.g. cell therapies

How are they awarded NAS status?

- NAS status is determined based on the same general criteria as for biological medicinal products.

> "*the NAS claim should be based on **differences in active substance**. Differences in process- and product-related impurities or extraneous agents are not considered*"

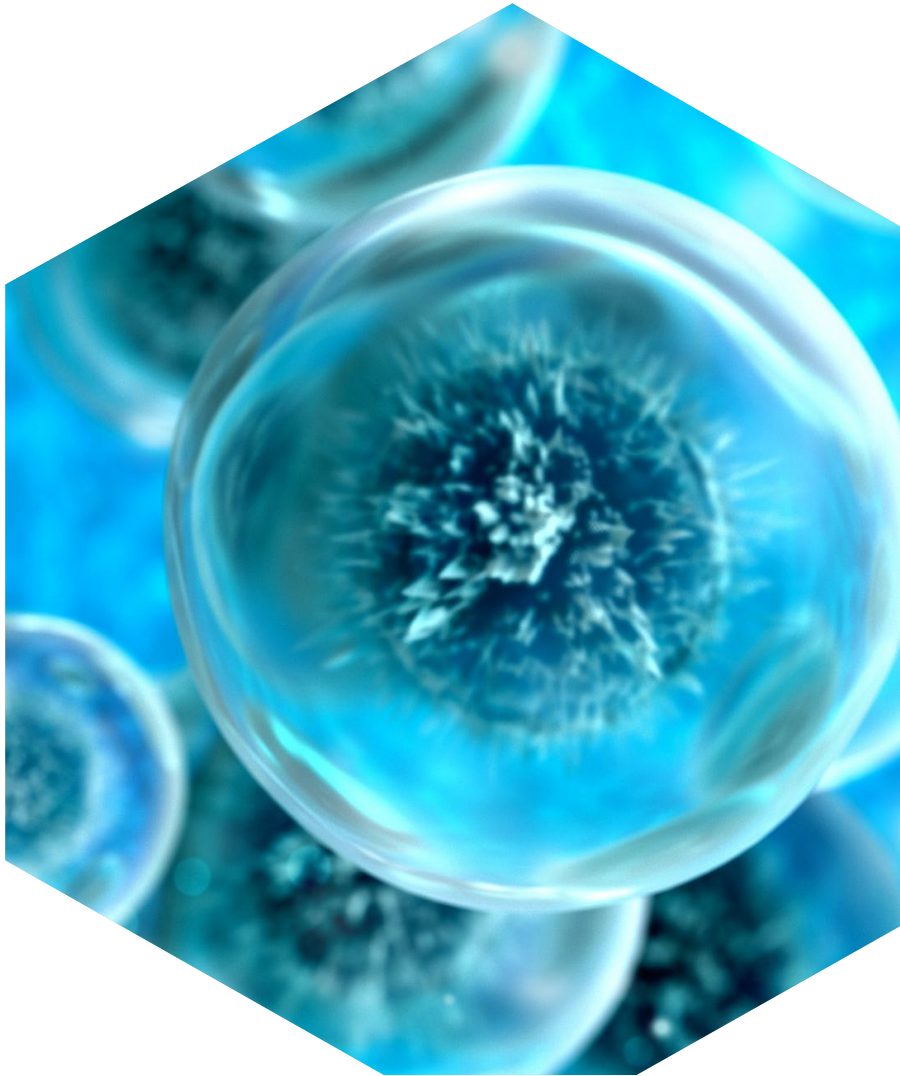
1. Can the **basic structural features** be identified (to check whether related to other authorised active substances)?

   e.g. mesenchymal vs haematopoietic stem cells;
   adenovirus vs AAV viral vectors for *in vivo* gene therapy;
   different therapeutic or regulatory sequences

2. If not, are there **substantial differences in biological characteristics and/or biological activity**?
3. Does the **starting material or manufacturing process** result in substantial differences in biological characteristics and/or biological activity?

   e.g. activation or stimulation of cells

4. Significant difference in **safety and/or efficacy**?



Advanced therapy medicinal products e.g. cell therapies

Considerations for the product definition

- The product definition should consist of, or at least include, the INN
  For some cell therapy and cell-based gene therapy medicinal products this may be a paragraph that defines the product, usually including some method language

- Where the INN is a one/two-word name, it may be acceptable (but not necessary) to add wording from section 2.1 of the authorisation for context, e.g. "*[INN], which is _____*"

Examples of authorised products with SPC applications (all defined by INN)

HOLOCLAR: "*ex vivo expanded autologous human corneal epithelial cells containing stem cells*"
[German SPC specified "*containing limbar stem cells*" based on the claim]

ZALMOXIS: "*Allogenic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV- TK Mut2) in all forms protected by the basic patent*"
– Approval withdrawn after unfavourable phase III trial results

ZOLGENSMA: "*onasemnogene abeparvovec*" or "*onasemnogene abeparvovec in all forms protected by the basic patent*"

KYMRIAH: "*tisagenlecleucel*"

Summary on scope of protection

- First, the scope of SPCs is fundamentally limited by the scope of the basic patent (Art. 4)
- Within that, SPCs cover the specifically authorised product, as a {medicinal product / PPP}
- This extends to various derivatives / equivalent forms, but it is likely that these must constitute the "**same active ingredient**" to be covered
    - Biosimilars are **therapeutically equivalent** forms with **no clinically meaningful differences**
    - 'Biobetters' are likely to be considered as **different active ingredients** and/or be granted NAS status
- The EU's proposed reforms would codify (1) a restriction on obtaining multiple SPCs to therapeutically equivalent active ingredients, and (2) the extension of scope to cover them (subject to the maximum scope of the basic patent)
- At least in the EFTA states (NO, IS, CH/LI), the product definition of an SPC should be chosen so that it does not cover more than the authorised product

Summary on scope of protection

Action points

- The product definition should consist of, or at least include, the INN for the product
- Consider adding wording to the product definition to expressly cover equivalents that would be deemed the "same active ingredient"
  e.g. "*and therapeutically equivalent variants thereof*"
  "*or a biosimilar thereof*"
- Consider filing further SPC applications based on any third-party authorisations where there is a question whether the new authorised product will fall within your SPC scope (e.g. biobetters), subject to Art. 3(a) considerations
- Look for creative solutions to obtain decisions that competitor products fall within your SPC scope, e.g. UK Court declaration or UK Patent Office opinion
- Don't forget that UPC opt-out requests can be withdrawn to allow you to use the UPC for streamlined litigation

UK SPCs and the Windsor Framework

How to obtain protection covering Northern Ireland?

Human medicinal products

- Current provisions require both GB and EU(NI) authorisations for full UK SPC coverage

- System from 1 Jan 2025 under the Windsor Framework:
  - MHRA solely responsible for authorisation throughout the UK
  - 'UK only' label on medicinal products; cannot move into ROI
  - Limited transitional provision allowing early entry of GB-authorised medicines into NI before 1 Jan 2025
  - Further guidance required from UKIPO about which authorisations can trigger the SPC filing deadline either side of 1 Jan 2025
  - In the meantime, if you expect to have the necessary documentation in place, be prepared to take action before 1 Jan 2025 based on a combination of GB and EU(NI) authorisations

UK SPCs and the Windsor Framework

How to obtain protection covering Northern Ireland?

Veterinary medicinal products

- Current provisions require both GB and EU(NI) authorisations for full UK SPC coverage
- Temporary grace period allows GB → NI movement
- No change under Windsor Framework; long-term solution still needed

Plant protection products

- Current provisions require both GB and NI authorisations (after European Commission prior approval of the active substance(s)) for full UK SPC coverage
- No change under Windsor Framework

Thank you

Any questions?

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