When an Excipient Is Not an Active Ingredient: The Halozyme Opinion and the Future of SPC Strategy in Europe

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The pending **Halozyme** case before the Court of Justice of the European Union ("CJEU") may soon provide another important clarification about the interpretation of the Regulation (EC), on the Supplementary Protection Certificates ("SPCs") for medicinal products in Europe. In particular, the case concerns the interpretation of Article 1(b) of Regulation (EC) No. 469/2009, which defines a "product" as "*the active ingredient or combination of active ingredients of a medicinal product*".

The dispute originates from national proceedings, **Halozyme** seeks a Supplementary Protection Certificate (SPC) for a combination medicinal product consisting of the therapeutic monoclonal antibody trastuzumab co-administered with recombinant human hyaluronidase (rHuPH20).

Halozyme argues that the product contains two active ingredients: *(i)* the therapeutic monoclonal antibody, which exerts the primary disease-targeting effect, and *(ii)* recombinant human hyaluronidase, which enzymatically degrades hyaluronic acid in the extracellular matrix, thereby increasing tissue permeability and enabling efficient subcutaneous delivery and absorption of the co-administered drug.

According to Halozyme, both substances qualify as active ingredients because each performs a specific and essential pharmacological function contributing to the overall therapeutic effect of the medicinal product. In particular, hyaluronidase is not merely ancillary but plays an indispensable and active role by facilitating the mechanism through which the therapeutic agent achieves its intended efficacy.

On this basis, Halozyme argues that recombinant human hyaluronidase should not be classified as an excipient, notwithstanding its designation in the marketing authorisation.

The Advocate General has proposed a rather strict and formal interpretation: whether a substance qualifies as an "active ingredient" for SPC purposes must be determined by reference to the classification contained in the marketing authorization ("MA") relied upon in support of the SPC application. In practical terms, if a substance is expressly classified as an **excipient** in the MA, it should not be reviewed as an active ingredient in subsequent SPC proceedings.

This interpretation gives central importance to the regulatory classification made during the MA process. It also limits the possibility for applicants to argue, before national patent offices, using complex scientific argumentations on whether an ancillary or facilitating substance may have a therapeutic contribution of its own. The Advocate General's reasoning appears to favor legal certainty, administrative efficiency and consistency between the pharmaceutical regulatory framework and the SPC system.

Although the point is important, the outcome suggested by the Advocate General is not entirely surprising. In fact, in the previous case **Abraxis Bioscience LLC v Comptroller General of Patents** (C-443/17), where the Court considered a medicinal product consisting of paclitaxel, a known anti-cancer active ingredient, and albumin, which acted as a carrier in a nanoparticle formulation, the Court held that a carrier with no therapeutic effect of its own could not be regarded as an active ingredient within the meaning of Article 1(b), even if it allowed the active ingredient to exercise its therapeutic effect more effectively.

The Court therefore concluded that a new formulation of an old active ingredient, consisting of that active ingredient and a carrier with no therapeutic effect of its own, could not be treated as a product distinct from the active ingredient alone.

The Halozyme referral adds a further layer. The referring court asks, among other things, whether a substance expressly designated as an excipient in the MA can nonetheless be treated as an active ingredient for SPC purposes, particularly where it contributes to the overall therapeutic effect of the medicinal product.

In our view, it is highly likely that the CJEU will follow the Advocate General's Opinion. The reason is not merely formalistic. The classification of a substance as an active substance or as an excipient in an MA is not arbitrary: it is the result of a technical and scientific regulatory assessment in view of the definition of medicinal product provided in the Directive 2001/83/EC. Allowing that classification to be reviewed in SPC proceedings would risk creating parallel and potentially inconsistent evaluations by patent offices and courts, which are not necessarily the appropriate forum for reassessing the regulatory status of medicinal product components.

Anyway, the practical implications of this decision will be significant. Companies developing medicinal products involving complex formulations, delivery-enhancing technologies or biologically active excipients should pay close attention to the way each component is characterized in the regulatory file and, ultimately, in the MA. The SPC strategy cannot be separated from the regulatory strategy. If a component is expected to play a role in supporting future SPC protection, its regulatory classification may become decisive.

At the same time, the Advocate General's approach may reduce uncertainty in borderline cases. It suggests that SPC eligibility should not depend on an ex post scientific debate about the ancillary effects of a substance, but rather on the regulatory identity of the product as defined in the marketing authorization. This would make SPC prosecution more predictable, although potentially less flexible for innovative formulations where the boundary between "active ingredient" and "excipient" is scientifically complex.

The CJEU's forthcoming judgment will therefore be closely watched. If the Court follows the Advocate General, the decision will reinforce a narrow and MA-centered interpretation of "active ingredient" under the SPC Regulation.

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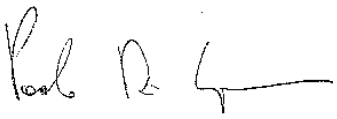

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