

NO EXCLUSIVITY FOR BRIDGING DATA UNDER ARTICLE 10(3) OF THE MEDICINES DIRECTIVE: R (Napp Pharmaceuticals v The Secretary of State for Health acting as The Licensing Authority) [2016] EWHC 1982

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The Administrative Court has rejected Napp’s claim that bridging data submitted to the MHRA for its analgesic skin patch benefits from a period of data exclusivity under the Article 10(3) hybrid-abridged procedure.

Facts

This is a case about the interpretation of Article 10(3) of the Medicines Directive 2001/83/EC which provides that:

In cases where the medicinal product does not fall within the definition of a generic medicinal product as provided in paragraph 2(b) or where the bioequivalence cannot be demonstrated through bioavailability studies or in case of changes in the active substance(s), therapeutic indications, strength, pharmaceutical form or route of administration, vis-à-vis the reference medicinal product, the results of the appropriate pre-clinical tests or clinical trials shall be provided.

The drug at issue is an opioid analgesic whose active pharmaceutical ingredient is buprenorphine. It was first registered in 1992 by Schering-Plough under the brand name Temgesic which takes the form of a tablet placed under the tongue. In 2003-2005, Napp was granted Marketing Authorisations (“MAs”) in Denmark, the UK and other Member States for its own version of the drug, in the form of a skin patch, under the brand name BuTrans. Napp relied on Temgesic as the Reference Medicinal Product (“RMP”) for the purposes of Article 10(3) of the Medicines Directive since BuTrans does not count as a generic version of Temgesic given its different “route of administration”. Napp therefore submitted ‘bridging data’ comprising “*the results of the appropriate pre-clinical tests or trials*” which demonstrated the clinical effectiveness of BuTrans and its bioequivalence to Temgesic. The bridging data in question was the fruit of considerable investment by Napp which had commissioned 26 clinical trials

over a 9 year period.

Over a decade later, Sandoz successfully applied for MAs in Germany and the UK for its own buprenorphine product, an analgesic skin patch called Reletrans, under the 'hybrid-abridged' procedure in Article 10(3), with Temgesic as the RMP. Sandoz relied on the bridging data which had been submitted by Napp in its prior Article 10(3) application, with the only new data submitted by Sandoz showing that Reletrans was bio-equivalent to Napp's drug BuTrans.

Napp launched a wholesale challenge in the Administrative Court to the MHRA's grant of an MA for Reletrans - along with parallel proceedings in the Courts of other Member States - on the basis that the Medicines Directive does not permit a generic applicant to rely on bridging data submitted under Article 10(3) to support a further authorisation under that same article. At the hearing, Napp argued that the fact that the Medicines Directive is silent as to any period of exclusivity for bridging data amounts to a lacuna in the regulatory scheme which cannot be filled in by the UK Court, but only by virtue of a reference to the Court of Justice of the EU. Napp pointed to the fact that, by contrast to the hybrid-abridged procedure, innovators of RMPs are entitled to protection, and in particular data exclusivity, under the 8+2+1 formula laid down in Article 10(1) of the Medicines Directive, according to which: (i) 8 years must elapse before any application for authorisation of a generic version of an RMP may be made (ii) 10 years must elapse before the generic drug can be placed on the market; and (iii) that period is extendable to 11 years where the innovator obtains an authorisation for one or more new therapeutic indications which bring significant clinical benefit in comparison with existing therapies.

Judgment of the High Court

The Court found the case against Napp to be "overwhelming": the Medicines Directive does not protect bridging data submitted under Article 10(3). In a judgment in categorical terms, Whipple J held that the language of the Medicines Directive; the scheme and purpose of the Medicines Directive; the European and domestic case law; and advisory sources, all gave the same unambiguous answer.

Addressing each in turn:

i) Language of the Medicines Directive

Article 10(3) requires the provision of the results of clinical tests or trials which are "appropriate". It does not lay down any requirements as to the identity of the party commissioning or producing those results or refer to any restrictions in that regard. The Judge held that this means that, as a matter of ordinary language, there is no such restriction.

ii) *Scheme and purpose of the Medicines Directive:*

There is no reason why bridging data for Product B should not be repeated to support a subsequent application by Product C provided that there is data which shows that Product C is equivalent in effect to Product B. This achieves two important objectives under the Medicines Directive: (i) the paramount goal of ensuring that the subject-matter of the Article 10(3) application, Product C, is safe and effective; and (ii) avoiding repeat tests on humans and animals so far as possible (see recital 10).

The Court therefore rejected Napp's argument that it was simply a matter of construction as: *"[T]o read the word "appropriate" as being limited to data derived from pre-clinical tests or clinical trials undertaken by or on behalf of the party making the application, would be to go far beyond any exercise of construction, even strict construction, of a derogating provision in EU law. Instead it would impose a significant limitation on the provision itself by reading in a separate and free-standing condition."*

On the contrary, the wording represents a clear policy choice – bridging data is not accorded a period of exclusivity (unless it comes within the limited scope of Article 10(5) for "new indications") because the Article 10(3) applicant, here Napp, was not the innovator and is not therefore entitled to benefit from a fresh period of protection.

iii) *Relevant Case Law*

There is a clear principle, established in the case law, that data provided by one company in support of its applications for MAs for its own products can be relied on by third parties to support their applications, subject only to the express protections contained in the Medicines Directive.

The Court cited with approval the principles distilled by Moses J in R (*Merck Sharp and Dohme Ltd*) v *The Licensing Authority (Acting by the Medicines and Healthcare Products Regulatory Agency)* [2005] EWHC 710 (Admin) including that:

"The identity of the applicant for authorisation is not a feature of the provisions of Article 10. It is irrelevant whether the applicant is an innovator which holds marketing authorisation for the original product or its development or a generic company which seeks authorisation."

iv) *Advisory sources*

The Court also drew support from the Commission's Notice to Applicants seeking an authorisation of medicinal products which provides that:

“... in those cases where a medicinal product authorised under Article 10(1) has been developed through an application submitted in accordance with Article 10(3) ...leading to a new indication, strength pharmaceutical form, a marketing authorisation application of a subsequent generic of this medicinal product can include the new indication, strength, pharmaceutical form, etc. **To this effect, it will also be possible to refer to the data submitted to support the development.**”

Napp's other arguments

The Judge dismissed, in short order, other arguments advanced by Napp that: (i) there can be no “generic of a generic” and (ii) that it was entitled to protection of its bridging data for all time. As to the former argument, Whipple J held that Article 10(3) deliberately leaves the assessment of the appropriateness of the evidence to the Member States’ competent authorities. Plainly, a second generation application is permitted, and will only be successful where the evidence submitted is appropriate. As to the latter argument, that would represent a distortion of the Medicines Directive which permits limited protections for some products and data in carefully defined circumstances for a limited time. Nor would Napp’s construction fairly reconcile the competing public and private interests since it would serve to promote only Napp’s commercial interests above all others.

The mutual recognition argument: a fight for another day - or not?

Perhaps the most interesting question raised in this case went unanswered. Relying on the Judgment of the CJEU in *Synthon* (Case C-452/06 R), the intervener, Sandoz, argued that the MHRA was obliged to recognise the Reletrans MA granted by the German authorities and therefore had no discretion to refuse to authorise Reletrans under the decentralised procedure. In particular, Sandoz relied on the CJEU’s statement, at §25 of *Synthon*, that:

“In accordance with the objective of abolishing all barriers to the free movement of medicinal products in the Community referred to in recitals 12 and 14 in the preamble to the directive, it is apparent from Article 28(4) that a marketing authorisation granted by a Member State must, in principle, be recognised by the competent authorities in other Member States within 90 days of receipt of the application and the assessment report from the reference Member State, and that that recognition is not dependant on the procedure followed by the reference Member State for granting that authorisation.”

The MHRA did not accept that it lacked the power to do anything other than recognise the German MA for Reletrans noting, in particular, that the Court in *Synthon* accepted that competition authorities may call into question, and

refuse to recognise, assessments conducted in other Member States where matters of risk to public health are concerned.

The Court left this question open given that, on the facts of this case, the MHRA did recognise the German MA. It noted however that *“it is a point of potential importance, going to the nature and scope of the MHRA’s powers to refuse recognition of a drug, acting as a competent authority within the harmonised procedure.”*

Perhaps the unspoken point of even greater importance is the very nature of the future inter-relationship between medicines regulation in the UK and the rest of the EU, and the future for the common marketing authorisation scheme, following the UK’s anticipated withdrawal from the EU. One area over which there may be a particular question mark is whether 8+2+1 data exclusivity will be retained within the UK. But that is a debate for another day ...

George Peretz QC acted for the MHRA

The Comment made in this case note are wholly personal and do not reflect the views of any other members of Monckton Chambers, its tenants or clients.