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From The Registrar
Dr Andrew Goddard FRCP
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27 October 2016

Dear Sir or Madam

Re: Concept of 'similar medicinal product' in the context of the orphan legislation: adaptation to technical progress

The Royal College of Physicians (RCP) plays a leading role in the delivery of high quality patient care by setting standards of medical practice and promoting clinical excellence. We provide physicians in the United Kingdom and overseas with education, training and support throughout their careers. As an independent body representing over 33,000 Fellows and Members worldwide, we advise and work with government, the public, patients and other professions to improve health and healthcare.

The RCP is grateful for the opportunity to respond to the above consultation. We have liaised with our Joint Specialty Committee for Clinical Pharmacology and Therapeutics and would like to make the following comments.

30 The principal molecular structural features are the relevant structural components of an
31 active substance.

Our experts note that 'relevant' is only useful if the definition states to what. In particular, is the relevance to the action of the drug, or to some other property? For example, are drugs which bind to a given receptor site in the same way by virtue of their structure 'similar'?

36 active substance only with respect to minor changes in the molecular structure,
37 such as a structural analogue would be considered similar.
Our experts note that to a chemist 'Minor changes in the molecular structure' mean - for example - small changes in substituents. However, there is no consideration of pharmacological function. Since Alquist's work on adrenoceptors in the 1940s it has been clear that very small chemical changes have important pharmacological effects.
By contrast, the definition for synthetic poly nucleotides clearly does consider functional changes, since at lines 42-43 the definition stipulates 'not significantly affecting the kinetics of hybridisation'

48 – Biological Medicinal products
49 It is proposed to update the examples to take into account new technological
50 developments such as conjugation (conjugated coagulation factors), monoclonal

51 antibody technology, cell-based medicinal products and gene therapy medicinal
52 products.

Our experts support this proposal.

54 The principal molecular structural features are the structural components of an active
55 substance that are relevant for the functionality of that substance.

Our experts note the definition of 'Functionality' means 'function' [Cf. Chambers: functionality, the capacity to be functional or practical; purpose; a specific application of a computer program.]
The above makes this functional similarity explicit for biologics. Therefore the definition of chemical medicinal products is inadequate.

Our experts explain that with Paragraphs 66-86 there seems to be scope for uncertainty, since examples are provided, but the reasons for differentiating between similar and non-similar products are not clearly stated.

96 The same radiopharmaceutical active substance, or one differing from the original in
97 radionuclide, ligand, site of labelling or molecule-radionuclide coupling mechanism
98 linking the molecule and radionuclide provided that it acts via the same mechanism.

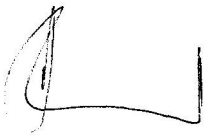
Our experts note that this paragraph omits the phrase 'would be considered similar substances.'

100 (aa) ATMPs
The abbreviation ATMP (advanced therapy medicinal product) is not explained

105 which have significant impact on the biological characteristics and/or activity
106 relevant for the intended therapeutic effect of the product.

Our experts believe that these lines appear ambiguous: 'biological characteristics relevant for the intended therapeutic effect of the product and/or activity relevant for the intended therapeutic effect of the product' or 'activity relevant for the intended therapeutic effect of the product and/or biological characteristics [whether or not relevant for the intended effect].

Yours faithfully



Dr Andrew Goddard
Registrar