Cell Therapy Regulatory Toolkit: an online regulatory resource

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Keywords: cell therapy • regulation • translation

Cell therapy has recently boomed with dramatic increases in investment, clinical efficacy, deals and partnerships, and government support. A requirement to focus on successful translation remains, with numerous groups dedicating research efforts toward novel business models, manufacturing solutions and regulatory strategies. With these latter considerations in mind, the Cell Therapy Regulatory Toolkit has been put together and is now available free of charge to use at www.lrmn.com/regs [1].

The Cell Therapy Regulatory Toolkit was devised by the London Regenerative Medicine Network (LRMN; London, UK), and developed with assistance from Lawford Davies Denoon (London, UK) and Carpenter Group Consulting, Inc. (WA, USA). The toolkit is designed to inform users about licensing, consent and banking requirements associated with different types of cellular products. It also provides details about applicable regulations, product classifications, manufacturing requirements, possible exemptions and available incentives. It is intended to be informative and educational, rather than providing tailored regulatory guidance, and was developed as an online capability in the first instance to ensure ease of access.

Due to the challenges of creating a globally relevant ‘generic’ tool, there are two different sections to the toolkit: one pertaining to the UK and EU regions, and the other covering the USA. Each section can be accessed from the other, or from the LRMN holding page.

The UK and EU site contains information in five main sections: banking, con-

sent, licensing, therapy and incentives. The fourth section, therapy, incorporates a comprehensive plan for informing those developing cells as therapeutic products, covering the relevant directives, regulations and classifications – all of which is easily navigated to from the home page (Figure 1). Users are taken through a series of questions designed to guide them to useful information relevant to their product, including a number of options to ‘see more’, where further background and supporting information relating to any complexities of the question asked is provided. In some cases, further clarification is also attained by viewing the ‘unsure?’ option provided with a question or answer. There is additional guidance on manufacturing requirements for specific product classes, potential exemptions that might be available for certain medicines in accordance with their particular manufacture and use and the process of EMA approval of a marketing authorisation for a product. A sixth section entitled resources contains further supporting information, such as the composition and tasks of the EMA’s Committee for Advanced Therapies (CAT), other tools that are available for users (see below) and links to the main statutes and regulations relevant to these medicinal products, along with the applicable UK and EU regulatory authorities.

The USA site is built around a standard clinical trial pathway from the research stage through to commercialization. Information is then set out in three sections: Steps to Product, Manufacturing and Expe-

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Figure 1. The UK Cell Therapy Regulatory Toolkit homepage, from where information on banking, consent, licensing, developing cells as therapeutic products, 'incentives', and resources can be accessed.
Data taken from [2].

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edited Programs, each of which is aligned with the clinical pathway displayed on the left hand side of the pages. This ensures clarity for the user on where the specific information included within each section is applicable in relation to product development. The first section covers the various meetings and applications required by US FDA, as well as the information and documents required for submissions, where relevant. The second section looks at the manufacturing requirements for each stage of product development, detailing information included within investigational new drug (IND) applications, as well as requirements on product potency assays and compliance with current good manufacturing practices (cGMP). The third section details the various expedited programs available to those developing cell therapies in the USA, which may be requested at various times during product development (Figure 2). These include fast track designation, breakthrough therapy designation, special protocol assessment, orphan status, humanitarian use device designation, accelerated approval and priority review designation. This section contains information on qualifying criteria, when to submit the request, the timelines for FDA response and the corresponding benefits for each program detailed.

Across all three sections, further supporting information is contained within the 'Find out more...' options displayed within the text, as well as 'links to other websites' options, which the user can click on to be directed toward useful FDA Guidance for Industry documents, website pages or publications. A fourth section, 'resources', briefly details the specific Code of Federal Regulations (CFR) that apply to the IND application process.

The toolkit was constructed using information available in 2014. It is inevitable that regulatory requirements will change over time, and looking ahead, users should therefore check whether there have been any subsequent changes introduced by the relevant regulatory bodies.

We would seek to encourage anyone interested in cell therapy translation to use the Cell Therapy Regulatory Toolkit. The information within the site should provide useful regulatory education about what to expect further down the line of development pipelines, as well as informing users of classification differences or consenting requirements, which would be helpful if you are at an earlier stage of development. Currently, the content is appropriate for those looking at the UK/EU and USA regions for product development; in due course, additional capability exploring other regulatory environ-

ments for cell therapies may be incorporated into the toolkit, including Canada, Japan and India.

Alternative toolkits are indeed available to other UK users seeking regulatory information for cell therapies. Consulting on Advanced Biologicals (UK) have previously published a set of tools covering product development, characterization, comparability, reference materials and agency advice [4]. In addition, the UK Stem Cell Tool Kit was initially developed around 2009 by the UK's Department of Health in order to inform individuals conducting human stem cell research in the UK about the regulatory requirements [5]. A related initiative is the NIHR's Clinical Trials Toolkit, which was initially developed in 2004 by the Medical Research Council and the Department of Health, and provides information about the legal and regulatory requirements in setting up and managing a clinical trial of an Investigational Medicinal Product (IMP) in the UK [6]. These are complementary to the Cell Therapy Regulatory Toolkit, and indeed all the resources work together to inform users seeking to understand locally relevant regulatory pathways.

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Figure 2. The 'Expedited Programs' section within the USA Cell Therapy Regulatory Toolkit, which details the various alternative regulatory pathways available to those developing cell therapies in the USA.

Data taken from [3].

Financial & competing interests disclosure

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