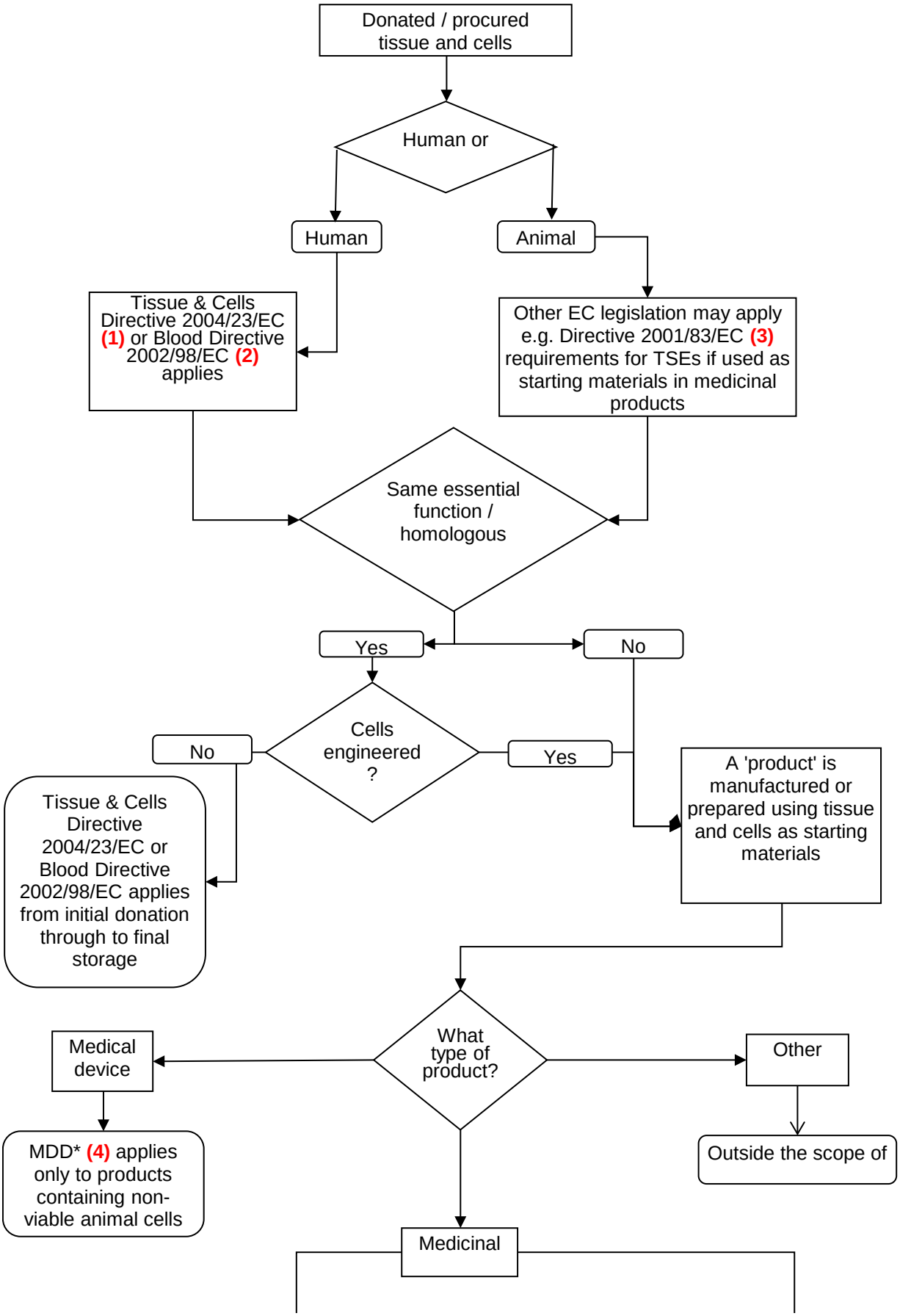
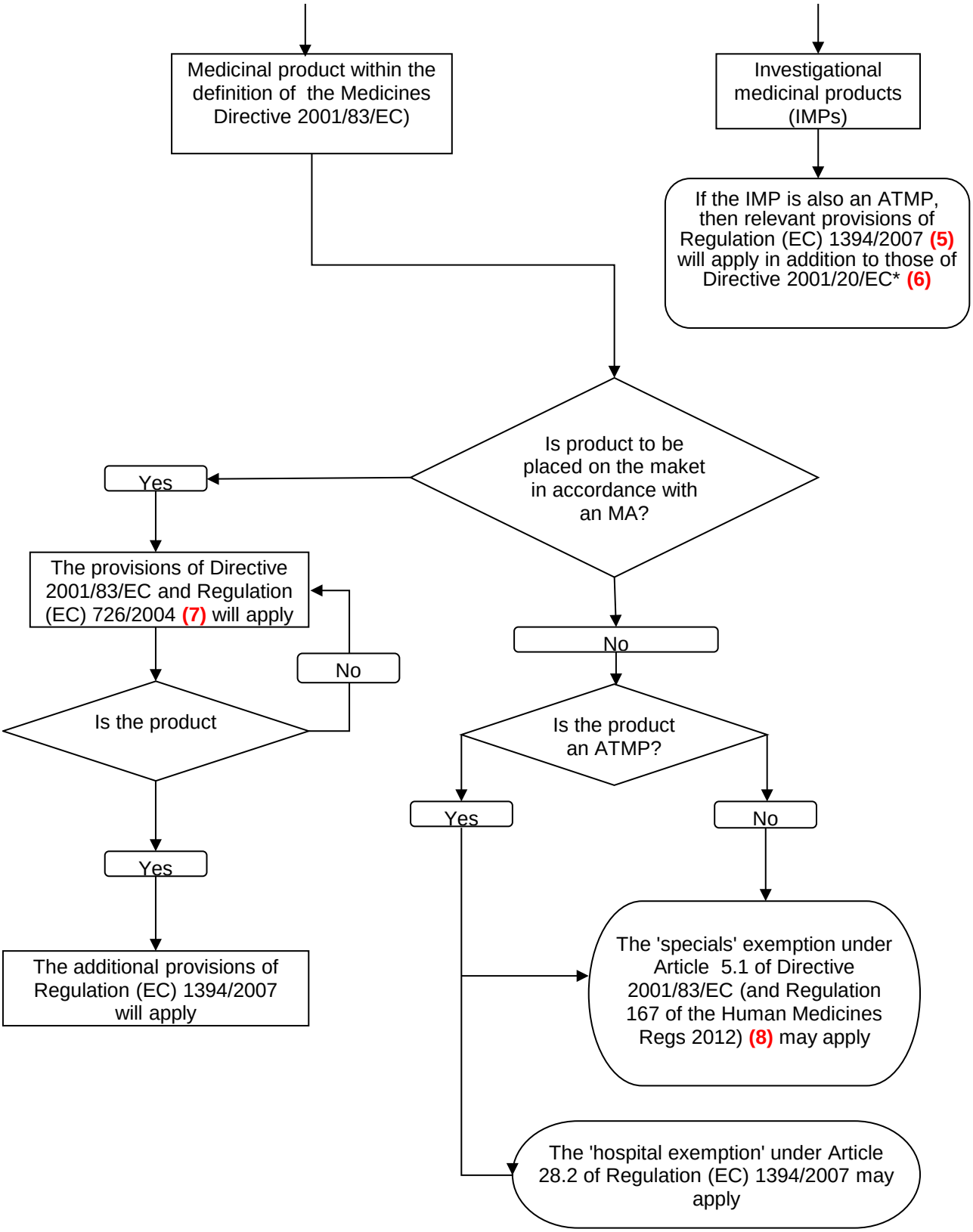
Flowchart for Determing the Regulatory Status of Tissue and Cell-Based Products (Version 5)





* currently under revision

MHRA considerations:

Q1 - is the material a medicinal product?

For the purposes of this Directive [2001/83/EC], the following terms shall bear the following meanings:
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2.Medicinal product :
(a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or
(b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.

3.Substance :
Any matter irrespective of origin which may be:
— human, e.g. human blood and human blood products; [tissues and cells?]
— animal, e.g. micro-organisms, whole animals, parts of organs, animal secretions, toxins, extracts, blood products;
— vegetable, e.g. micro-organisms, plants, parts of plants, vegetable secretions, extracts;

Q2 - if a medicinal product, what type?

Article 2 of ATMP Reg:

(a) ‘Advanced therapy medicinal product’ means any of the following medicinal products for human use:
— a gene therapy medicinal product as defined in Part IV of Annex I to Directive 2001/83/EC,
— a somatic cell therapy medicinal product as defined in Part IV of Annex I to Directive 2001/83/EC,
— a tissue engineered product as defined in point (b).:

(b) ‘Tissue engineered product’ means a product that:
— contains or consists of engineered cells or tissues, and
— is presented as having properties for, or is used in or administered to human beings with a view to regenerating, repairing or replacing a human tissue.

A tissue engineered product may contain cells or tissues of human or animal origin, or both. The cells or tissues may be viable or non-viable. It may also contain additional substances, such as cellular products, bio-molecules, biomaterials, chemical substances, scaffolds or matrices.

Products containing or consisting exclusively of non-viable human or animal cells and/or tissues, which do not contain any viable cells or tissues and which do not act principally by pharmacological, immunological or metabolic action, shall be excluded from this definition.

(c~~) Cells or tissues shall~~ be considered ‘engineered’ if they fulfil at least one of the following conditions:
— the cells or tissues have been subject to substantial manipulation, so that biological characteristics, physiological functions or structural properties relevant for the intended regeneration, repair or replacement are achieved. The manipulations listed in Annex I, in particular, shall not be considered as substantial manipulations,
— the cells or tissues are not intended to be used for the same essential function or functions in the recipient as in the donor.

References:

(1) http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:102:0048:0058:EN:PDF
(2) http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2003:033:0030:0040:EN:PDF
(3) http://ec.europa.eu/health/files/eudralex/vol-1/dir_2001_83/2001_83_ec_en.pdf
(4) http://www.mhra.gov.uk/Howweregulate/Devices/MedicalDevicesDirective/index.htm
(5) http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:324:0121:0137:en:PDF
(6) http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/index.htm
(7) http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:136:0001:0033:EN:PDF
(8) http://www.legislation.gov.uk/uksi/2012/1916/contents/made