# FRAGMENTATION OF EU GMP – NOT IN PATIENTS' BEST INTEREST?

by Peter H Gough

**The original structure of EU GMP made perfect sense; Chapters 1 to 9 of EudraLex Volume 4 contained the baseline GMP expectations required for all medicinal products and the annexes contained additional, detailed GMPs for different types of product. In the past year the European Commission has moved away from this logical model by issuing completely different GMP requirements for different product types. This fragmentation of GMP has not been supported by industry and is being moved forward against the advice that the Commission has received from regulatory authority experts within the EU and the Pharmaceutical Inspection Convention/ Cooperation Scheme (PIC/S).**

## ATMP GMP

In November 2017 the Commission issued GMP guidance for advanced therapy medicinal products (ATMPs) as a separate Part IV of EU GMP. This document duplicates many of the requirements in Chapters 1 to 8 of Part I and some of the annexes, but with some omissions; for instance, there is no mention of the need for self-inspections. The PIC/S had made strong recommendations to the Commission that this should be an additional annex to the existing GMP guideline and not a separate part.

## IMP GMP

Annex 13 on the manufacture of investigational medicinal products (IMPs) is due to be replaced with a new IMP GMP document when Regulation 536/2014 is eventually implemented. The new GMP document was published in December 2017 and is currently available from the EudraLex Volume 4 web page underneath the current Annex 13. However, the new IMP GMP document is not titled Annex 13 so it is not clear whether this revised version will become the new Annex 13 when it is implemented or whether it will become yet another separate part of EU GMP.


If the current Commission's logic is followed for other dosage forms, we would have a ridiculous multitude of different GMPs for the many dosage forms that are currently covered by annexes, e.g. radio pharmaceuticals, medical gases, metered dose inhalers, etc.

## APPLICABILITY OF ANNEXES?

It appears that, unless specifically referenced in the separate parts, the provisions of the existing annexes do not apply to these new parts of EU GMP. For example, does Annex 1 on sterile products manufacture, which itself is undergoing a significant revision, apply to the manufacture of ATMPs (many of which are required to be sterile) and, if the IMP GMP becomes Part V, will it apply to the manufacture of sterile IMPs?

## DRIVERS FOR FRAGMENTATION?

The original concept of having the basic GMP requirements in Chapters 1 to 9 and the detail for the diverse range of dosage forms in the annexes was sound. It is unclear what has driven the Commission to abandon this model. Is it due to legal pedants narrowly interpreting new regulations? Is it due to lobbying by interested parties to water down GMP for some sectors? Neither of these drivers are in patients' interests.

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Part of the problem could be that new expectations, from legislation such as the falsified medicines Directive 2011/62/EU, which legally only apply to marketed human medicinal products, have been added to the Chapters in Part 1. This makes them also applicable to IMPs and veterinary medicines where there has not been any corresponding legislative changes. However, rather than introducing a multiplicity of new GMP parts, a more scientific response to this issue would be to revisit the contents of Chapters 1 to 9 of Part I to ensure that they truly only contain the baseline expectations for all products and, if necessary, introduce a new annex to cover the specific additional requirements for marketed human products.

Looked at in isolation, these separate GMP standards may appear to make sense. However, the added complexity for any organization making conventional medicines, ATMPs and IMPs will prove challenging as it is always difficult to maintain different standards within the same organization.

This fragmentation of GMP for medicinal products is introducing unnecessary complexity and confusion for organizations trying to provide safe, effective medicines for their patients, which cannot be in patients' best interests.

## A WAY FORWARD – EU AND PIC/S TO DIVERGE?

The PIC/S GMP guidance has historically been virtually identical to that of the EU. Given their initial opposition to issuing the ATMP guidance as a separate part, it is hoped that PIC/S will continue to be more logical and issue its ATMP guidance as an annex to the current Part 1 and retain the IMP guidance as Annex 13. Post-Brexit, I would urge the UK MHRA to take a leadership role within PIC/S and champion the retention of the original GMP structure, rather than adopt the new fragmented EU structure. If the European Commission wishes to make GMP more complex, it will be advantageous for the UK to retain the logic and simplicity of the original concept.

## ABOUT THE AUTHOR

A chemist with a master's degree in analytical chemistry, Peter Gough has over 40 years' experience of pharmaceutical manufacture, control and quality management, culminating in the role of Senior Quality Consultant in Eli Lilly's Global Quality Systems division. He has broad experience, particularly with quality control laboratories and the manufacture of solid dosage forms and active pharmaceutical ingredients.

If you have a question on this article or need assistance, please don't hesitate to contact us at **pharmamail@nsf.org**.



Cite as: NSF International. January 2019. Fragmentation of EU GMP – Not in Patients' Best Interest? NSF: York, UK.

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