BRITISH PHARMACOPOEIA COMMISSION

Working Party ATMP: Advanced Therapy Medicinal Products 4th Meeting

SUMMARY MINUTES

A meeting of the working party was held at 10:00 via MS Teams teleconference on Wednesday 6th April 2022.

Present: Jacqueline Barry (Chair), Alison Niewiarowska, Clare Blue, David Caulfield, Franz Schnetzinger, Ian Anderson, Ilaria Santeramo, Jasbir Rattu, John Campbell, Josefina Nilsson, Juan Miguel Sánchez Nieto, Jenny McIntosh, Monica Pianella, Paul Getty, Rickard Nordstrom, Rita Rego, Ryan McCoy, Tishwant Kanwarjit, Vicky Smith, Victoria Vanhoutte, and Zara Hannoun.

In attendance: Gary Kemp, Ryan Smith, Elena Razzano, Janet Glassford, and Yuan Zhao.

Apologies from: Chris Burns, Kimberly Gilmour, Louise Bisset, Peng Wang, Stephen Vinter, and Huimin Tao.

1. **General Matters** **ATMP(22)01**

Ryan Smith reminded members that any Freedom of Information requests should be forwarded to the BP team. Members were also reminded of the confidential nature of the documents related to this work, and not to share anything marked as "Official Sensitive" outside of the group.

Members were asked to inform the BP team if their contact details had changed. A general list of Duties of members was attached to the meeting papers for reference.

A link to the 2020 annual report of the Human Medicine Regulations advisory bodies was included in the papers. The report was published in July 2021 and included the BP Commission Annual Report.

In the organisational update, members were made aware that the British Pharmacopoeia Commission was about to put an advert out via the Department of Health and Social Care for a new Chair. The current Chair, Professor Kevin Taylor, was stepping down after his term in the role had ended. The advert was expected to be published within the next week and would be shared with the group when it does. Members were asked to circulate within their networks.

The Chair updated the group to personnel changes related to WP ATMP; Alistair Gibb (former Editor-in-Chief of the British Pharmacopoeia) had left the Agency. Gary Kemp was now supporting the ATMP work. The secondment program between the British Pharmacopoeia and the Cell and Gene Therapy Catapult continued, Ryan McCoy continued to contribute, and Moira François had been replaced by Monica Pianella.

2. **ISO - Methods for the Assessment and Quantification of Viral Vector Functional Titre**

Ryan McCoy asked the group for any volunteers who wanted to contribute to the development of a new ISO standard - Methods for the Assessment and Quantification of Viral Vector Functional Titre. Any expressions of interest should be directed to Julian Braybrook from LGC

(Julian.Braybrook@lgcgroup.com). Experts should complete the ISO - Form 4: New work item proposal which was linked in the papers.

3. Progress Report ATMP(22)02

3.1 Flow cytometry - The first set of guidance provided information for the application of flow cytometry within the cell and gene therapy community. This guidance had been published on the BP website in November 2021. A planned marketing campaign included targeted emails, social media posts, news items, carousel banners and more.

3.2 Vector copy number (VCN) - The second set of guidance provided information related to the application of polymerase chain reaction techniques to vector copy number quantification, which had been split into two parts, one for Adeno-Associated Virus (AAV) and one for Lentivirus / Retrovirus (LV/RS). Since the last WP ATMP meeting this document had been through public consultation. There were eight responses received for the consultation, from a range of international organisations. These included small/medium and large pharmaceutical companies, suppliers, and cell and gene therapy groups. This diverse representation, as well as the expert familiarity of many of the respondents with vector copy number, indicated good feedback from the consultation. A consultation response document had been published on the BP website and members were made aware.

The vector copy number guidance had been published on the BP website in February 2022. A marketing campaign for would be arranged to focus on VCN.

3.3 Empty Capsids for AAV products – members were informed that the empty capsids for AAV products subgroup met for the first time on 23rd September 2021. The initial objectives for the group were outlined.

A scientific lead was appointed for the subgroup. The first task for the subgroup was to undergo a knowledge gap identification exercise which would allow a profile for experts to be created and expressions of interest sought. Membership appointment took place from 10th November 2021, with all newly appointed members being endorsed by the British Pharmacopoeia Commission.

The subgroup had met four times over six months and had scoped the contents of the guidance. Sections had been agreed within the group and delegated to an appropriate subject matter expert. The group had received input and endorsement from various MHRA experts regarding the methods covered. Agreement from the group around separating the guidance into three parts for “Methods for determining full/partial/empty capsid ratio”, “Encapsidated DNA characterisation”, and “Post translational modification” had been achieved

3.4 T and NK cell potency assay - The T and NK cell potency assay subgroup met for the first time on 22nd October 2021. A scientific lead was appointed for the subgroup. Membership appointment took place from 2nd December 2021, with all newly appointed members being endorsed by the British Pharmacopoeia Commission.

The subgroup had met three times over five months and had scoped the contents of the guidance. Sections had been agreed within the group and delegated to an appropriate subject matter expert.

During the most recent meeting of this subgroup a slight redirection in focus was discussed and the group agreed a more technical focus was required for the guidance. A "points for consideration" style had been adopted, relevant to potency assay development for cell based medicinal products, including genetically modified cells. The inclusion of probable Mechanisms of Action was agreed to be out of scope of this guidance. The group noted that mechanism of action is reflected in the potency assays selected and a certain level of rationale is expected to be given to support the assay claim. This would be made clear in the guidance with an explanatory statement.

4. **Empty Capsids for AAV products technical update Verbal**

A technical presentation describing what full and empty vectors capsids are, was given to the group. The safety and efficacy implications of the presence of empty capsids was detailed. The presentation continued into post translational modification describing how the viral protein can affect potency. Aggregates and multimers were also discussed but were agreed to be out of scope of the guidance. It was stated that only recently, understanding and concern had been associated with empty or partially full capsids. Although understanding was thought to be increasing it was important to realise that once the DNA is inside the capsid, it is protected from typical purification steps (e.g., endonuclease digest) and remains with the product – which potentially gave rise to safety issues. It was stated that the guidance was expected to cover the key variables that affect quality, safety and efficacy of the product. The presentation then reiterated the intention to split the guidance into three separate, but related parts which could be published as standalone pieces. When questioned on the reasoning for this it was made clear that this was to publish the guidance at the earliest convenience.

5. A table from the draft guidance was presented around the advantages and disadvantages of methods to be covered within the guidance. **T and NK cell potency assay technical update Verbal**

A technical presentation on T cell and NK cell characterisation assays was given to the group. The complex nature of creating guidance on this topic was outlined, it was explained that this topic was a natural progression from the flow cytometry guidance and that characterisation, potency determination, and validation would be the main focus. Mechanism of action was agreed to be important but would be explicitly out of the scope of this guidance.

It was explained to the group that defined guidelines for minimum cytotoxicity would be important to be included in the guidance and input from a Qualified Person on this topic would be necessary. A key question that would need to be answered was "what was the target minimum level of target-specific cytotoxicity for these products?".

6. **Closing remarks**

The Chair thanked everyone and informed them that the next meetings would be scheduled for November 2022 or April 2023.