Australian Government
Department of Health, Disability and Ageing
Therapeutic Goods Administration

Consultation on including a time-limited GMP exemption for manufacturing of personalised bacteriophages

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Purpose

This consultation paper seeks feedback on potential changes to the regulatory framework applying to bacteriophage therapy products (BTPs).

The TGA wants to ensure regulation of unapproved BTPs remains fit-for-purpose and considers patients' need to access (equity) as well as quality and safety of treatments administered.

Scope

The TGA is seeking your views on an interim provision for current domestic manufacturers of BTPs. Specifically, this consultation seeks feedback on the introduction of a time-limited GMP exemption for certain domestic manufacture of BTPs.

Submissions received in response to this consultation will help inform the drafting of the GMP exemption to be included in the *Therapeutic Goods Regulations 1990* (the Regulations).

The TGA will conduct further consultations to gauge views on industry standards and how to best develop an appropriate regulatory framework for these products at a later stage.

Background

Supply of therapeutic goods

Products that meet the legislative definition of a therapeutic good under the *Therapeutic Goods Act 1989* (the Act) are, in most instances, regulated by the Therapeutic Goods Administration (TGA) and generally need to seek pre-market approval and be included in the Australian Register of Therapeutic Goods (ARTG) before they can be imported, exported or supplied in Australia. To be entered on the ARTG, the TGA requires evidence of safety, quality, and efficacy as well as evidence of Good Manufacturing Practice (GMP) for the manufacturing facility that makes the goods.

Unapproved therapeutic goods that are not included on the ARTG can be accessed in limited circumstances, including through an approval or an authority issued by the TGA to a health practitioner in relation to a patient, or a specified class of patients, in their care. If a health practitioner decides an unapproved product is appropriate for their patient, they can apply to prescribe it via the Special Access Scheme (SAS) or Authorised Prescriber (AP) pathways for accessing unapproved therapeutic goods. A doctor can also advise if participation in a clinical trial for an unapproved product might be suitable for their patient. Unapproved therapeutic goods have not been evaluated by the TGA for safety, quality or efficacy.

Bacteriophage therapy

Bacteriophage therapy refers to the use of one or more bacteriophages (viruses) to target and kill a specific bacterial pathogen.

Bacteriophage therapies can be personalised therapies, utilised when the disease-causing bacteria has been identified. Alternatively, combining multiple phages with different host ranges allows a 'cocktail' of phages to target a wider variety of bacteria, which may be useful when the exact causative bacterial strain is not known. This approach ensures at least one phage in the mixture will be effective against the responsible pathogen. For example, a commercially available cocktail called Pyophage[1] targets multiple bacterial genera, including *Staphylococcus*, *Streptococcus*, and *Pseudomonas*, which are common in skin infections. This broad coverage makes the cocktail a good option for empirical

[1] The Pyophage cocktail is one of the main commercial products of the Georgian Eliava Institute of Bacteriophage, Microbiology and Virology and is used to cure skin infections. Registered under R-022600 in Georgia.

treatment, where therapy is initiated based on the most likely cause of an infection. The current medicines framework is not appropriate for approval of individualised bacteriophage therapy products as each bacteriophage or set combination of bacteriophages would be a distinct good that would need to be individually included on the ARTG.

There are currently no TGA-approved BTPs entered in the ARTG. BTPs have therefore not been subject to pre-market scrutiny, and most BTPs supplied in Australia are supplied as unapproved goods under the TGA's SAS or Clinical Trial Notification (CTN) scheme pathways.

This paper does not focus on these pathways, but rather on options to ensure the lawful *manufacture* of BTPs in Australia.

Increasing need for access to bacteriophages

Bacteriophage therapy is not a novel treatment and has been used for more than a century in many parts of the world. However, with the discovery of antibiotics, the use of bacteriophage therapy decreased in favour of these new therapeutics.

In the last 5-10 years, increasing anti-microbial resistance (AMR) and medical device-related infections have led to the resurgence in interest from researchers and clinicians seeking access to experimental therapy for their patients. As there are little to no options for patients with bacterial infections resistant or unresponsive to approved treatments, unapproved BTPs are increasingly being considered. BTPs are currently administered as an adjunct therapy to patients still being given standard care. Patients generally only receive BTP where a specialist confirms standard therapy is failing, making the benefit-risk high. Bacteriophage banks are currently being created across Australia and globally to enable identification of bacteriophage candidates with activity against the target bacterium to combat the increasing levels of antimicrobial resistance.

BTPs have been supplied as an unapproved therapeutic good in Australia since at least 2007. Historically, supply was almost exclusively for patients with life-threatening clinical indications, so supply under the SAS-A scheme or in a clinical trial was seen as appropriate as the benefit-risk is high. However, more recently there has been supply for non-life-threatening indications (via SAS-B), where the benefit-risk is lower, and the application for approval to supply must be accompanied by clinical justification.

Between January 2023 and end of August 2025, the TGA received 41 SAS Category B applications and SAS Category A notifications for the use of bacteriophage therapies, as compared to only four (SAS A only) during 2022. There have been 14 SAS A notifications (no SAS B) in the first 8 months of 2025 alone. There are currently 3 bacteriophage clinical trials recruiting in Australia.[2]

Current bacteriophage manufacture

Currently, none of the BTP facilities in Australia hold a TGA GMP licence. The domestic sector is small, supply quantities are low, and facilities are still refining their manufacturing processes.

The manufacturing process of BTPs is multifaceted and complex. During the preparation and amplification of a lytic bacteriophage, the presence of bacterial and chemical contamination may introduce risks, such as through the production of endotoxins as the bacteria undergo lysis.[3] To ensure the safety of the final phage product, it is imperative to ensure that the product undergoes rigorous purification stages to keep bacterial and chemical contamination within established safety parameters.

In recent times there has been an increase in scope of products, and changes to the technology have altered the risk profile e.g., by the introduction of more infusions and inhalants as well as an increased use of cocktails targeting multiple bacterial strains or species simultaneously.

[2] ANZCTR (accessed 7 October 2025)

[3] https://www.mdpi.com/1424-8247/16/10/1347

In November 2021, a working group was established, comprised of representatives from the TGA, Office of the Gene Technology Regulator (OGTR), NSW Ministry of Health and Phage Australia. The role of this group was to explore improving access to bacteriophage therapies, creating a consistent approach to production via the implementation of regulatory standards, clarification of GMP requirements and development of an appropriate future regulatory pathway for high-precision bespoke bacteriophage products. The TGA fully supports this work and has been participating in this working group since its inception.

Domestic and international regulation of supply and quality of products

BTPs meet the definition of a therapeutic good and are currently regulated under the medicine framework in Australia, as the pharmacological and metabolic functions of phage meet the definition of a medicine.[4] This is consistent with live vaccines and similar therapeutics that also contain live viruses.

Regulatory and supply approaches differ between countries and are in various stages of development. The Food and Drug Administration (FDA) and European Medicines Agency (EMA) classify bacteriophage therapy as drugs and medicines, respectively. Like Australia, patient access in these jurisdictions is via pathways for unapproved goods

Bacteriophage therapy is used broadly in certain parts of the former Soviet Union and Eastern Europe. The Republic of Georgia is seen as the global centre for bacteriophage therapy usage where it is used by some physicians as a first-line therapy for a range of infections. Poland also has an established bacteriophage therapy sector.

Despite the long history of use of bacteriophage therapies overseas, there is limited agreement on quality and safety standards internationally. Outside of Slovakia, the Czech Republic, Georgia and Russia, no bacteriophage therapy has been approved as a medicine for supply, with the majority of access still on a compassionate basis as unapproved goods.

On 1 January 2025 the European Pharmacopeia (Ph.Eur.) introduced a *Phage therapy medicinal products* (5.31) 'general chapter'. This new general chapter provides a basic framework of requirements for the production and control of BTPs and allows a degree of flexibility commensurate with the complex approaches currently employed in this rapidly developing field. This 'general chapter' does not impose any requirements on Australian manufacturers and merely sets out information that they may or may not have regard to.

There is also a '*Phage active pharmaceutical ingredients*'[5] general monograph published by the Belgian Federal Agency for Medicines and Health Products, which outlines production, testing, storage, shelf life, labelling and surveillance requirements that are to be met for natural bacteriophages. Belgium uses a 'magistral preparation' approach, where bacteriophages are prepared by a pharmacist according to a doctor's prescription for a specific patient. This method allows for personalised treatment using phages as active pharmaceutical ingredients in compounded medications, circumventing the need for full marketing authorisation. However, this design is for use under a medicine compounding model for the finished product and it is not considered suitable for adoption in Australia.

There are 'default' pharmacopeial standards for therapeutic goods that already apply to manufactured BTPs, e.g., monographs that apply to all injectable or inhaled products, excipients, and endotoxin testing.

[4] *Defined in the* Act *as having a 'principal intended action by pharmacological, chemical, immunological or metabolic means in or on the body of a human'*

[5] Belgian General Monograph v1.0 – Phage active pharmaceutical ingredients

Importance of GMP and facility licensing

GMP in therapeutic goods manufacture is vital to ensure the quality and safety of manufactured drugs, via consistent manufacturing processes and rigorous quality control programs.

In practice, GMP describes a set of principles and procedures that, when followed, are designed to help ensure that therapeutic goods are manufactured consistently to a high quality and within the manufacturer's specifications. In practice, this includes training and validation of personnel, qualification and monitoring of manufacturing facilities and equipment, qualification and controls of raw material and consumables, validation of manufacturing process and Quality Control methods. These elements are complemented by oversight from relevant regulatory authorities to ensure compliance with application GMP standards.

Under the Act, licensing is required for all sites in Australia that manufacture therapeutic goods unless an exemption applies that relates either to the person undertaking the manufacturing, or the products being manufactured.

Existing exemptions from TGA GMP licensing

No domestic facility involved in BTP manufacture holds a TGA GMP licence currently. Exemptions from licensing in the Regulations that may apply to current domestic manufacturers of BTPs (based on our understanding of current governance arrangements) include in particular:

- the manufacture of therapeutic goods for initial experimental use in human volunteers, in accordance with Item 1 of Schedule 7 to the Regulations;
- the manufacture of therapeutic goods by a medical practitioner specifically for a patient under the practitioner's care, in accordance with Item 1 of Schedule 8 to the Regulations;
- the manufacture of therapeutic goods by a pharmacist where, most relevantly, the goods are manufactured in a pharmacy where the pharmacist practices and that is open to the public, or on the premises of a private hospital, for supply, other than by wholesale, on or from those premises, in accordance with item 2 of Schedule 8 to the Regulations; or
- the manufacture of therapeutic goods by a biomedical engineer, radiochemist or pharmacist in a public hospital when employed by a public hospital or public institution, for supply in hospitals or public institutions in the same State or Territory, in accordance with item 3 of Schedule 8.

In particular, item 1 of Schedule 8 to the Regulations provides that medical practitioners, dentists and other health care workers registered under a law of a State or Territory are exempt from the operation of Part 3-3 of the Act (which deals with manufacturing licence requirements) where the manufacture of the medicine is by 'a medical practitioner or a dentist specifically for a patient under their care'. This exemption (relevantly) applies where the following elements are met:

- The medical practitioner manufactures the good themselves (the exemption is unlikely to apply where the practitioner is only responsible for the oversight of the manufacture by staff under their direction); and
- The purpose of the manufacture by the medical practitioner is specifically for a patient under that medical practitioner's care.

However, BTPs are complex and time-consuming to manufacture, so it is not possible for health practitioners to prepare a BTP by themselves for a patient directly under their personal care. It would be similarly challenging for pharmacists and biomedical engineers, radiochemists and pharmacists in public hospitals, to manufacture such products in the circumstances in which the exemptions in items 1-3 of Schedule 8 set out.

Further, bacteriophage therapy has a long history of use and some BTP clinical trials are moving into Phase 2, with the effect that such trials are unlikely to be 'initial experimental use in human volunteers' (for the purposes of the exemption in item 1 of Schedule 7 to the Regulations).

Current oversight and governance of clinical practice in Australia

In Australia, clinical practice in hospitals is overseen by a combination of bodies, including the Australian Health Practitioner Regulation Agency (Ahpra), state and territory governments, and the hospitals themselves through their clinical governance structures. Ahpra, along with National Boards, regulates health practitioners to ensure they are qualified and safe to practice. States and territories are responsible for healthcare and hospitals. Hospitals also have their own systems of clinical governance to monitor and improve patient safety and quality of care.

As far as bacteriophage research and manufacturing of products for clinical trials occurring in a public institution or a university, this is overseen by a shared responsibility model involving various institutions and agencies. The Australian Research Council (ARC) and the NHMRC are key players, along with Human Research Ethics Committees (HRECs) and research institutions themselves. There is not one single Commonwealth agency solely responsible for research oversight.

Whilst there appears to be considerable oversight of clinical activities and research, none of these agencies oversee the standards and quality of therapeutic goods.

Current issues and concerns

Current medicines framework is not fit-for-purpose

Ideally, the TGA encourages the inclusion of all therapeutic goods on the ARTG where possible, as this ensures pre-market assessment, post-market monitoring of product safety, and the ability to ensure manufacturers meet appropriate GMP standards. However, the current medicines framework is too rigid to allow registration of personalised therapies or what might be considered ‘platform therapies’ such as many BTPs.

BTPs are often used for a broad range of indications not suitable to classical clinical trial design and this has made it difficult to collect safety and efficacy data to support a submission for ARTG registration. The TGA supports the development of innovative therapies, so is considering options intended to facilitate the sector to upgrade manufacturing facilities, develop standards and collect clinical data to support the safe use of these products for patients.

Manufacturing and quality standards are not sufficient

There are challenges in ensuring the safety, quality and efficacy of BTPs in circumstances in which they have not undergone a pre-market assessment by the TGA. Although these goods must comply with default standards that apply to all therapeutic goods, there are currently no such standards for bacteriophages. As such, there is a need to urgently consider the introduction of a specific standard to provide a minimum benchmark to ensure a level of product safety and quality.

Need to support patient access

Phages can be a potentially life-saving therapeutic option in the treatment of multidrug-resistant infections. It is therefore important that the TGA continues to support domestic manufacture and availability of bacteriophages and the collection of safety and efficacy data to inform future regulation. Inhibiting the supply of bacteriophage therapies may force medical providers to import bacteriophage therapy products from overseas which may significantly increase the timeframe for patients to receive treatment and would not necessarily ensure a higher quality product.

Regulatory option for manufacture of BTPs in Australia

Proposal: Introduce a time-limited GMP exemption for manufacturers of personalised BTPs

Features

The TGA proposes to introduce a temporary exemption from GMP requirements (i.e. from the operation of Part 3-3 of the Act and the requirement to hold a TGA manufacturing licence) for manufacturers of personalised and small batch BTPs. This is intended to ensure that continued access for patients via SAS, AP and clinical trial pathways is not impacted, and to provide time for such manufacturers to apply for and obtain a manufacturing licence under the Act. An exemption from GMP licensing would also allow the sector to continue to refine manufacture and collect supportive clinical data, similar to the exemption for products manufactured for early phase clinical trials.

The TGA proposes to introduce a 2-year exemption from the requirement for manufacturers to hold a licence issued by the TGA for:

Therapeutic goods that are:

(a) bacteriophage therapies where one or more bacteriophage(s) are used to treat an infection in a particular or small number of individuals;

(b) manufactured by a medical practitioner registered under a law of a State or Territory, or a suitably qualified person, when employed by a public or private hospital or a public or private institution, or a person under the professional supervision of such a medical practitioner; and

(c) for supply in a public or private hospital, or public or private institution, in Australia.

Considerations

a. Opening up the AP pathway

Under this proposal, the time-limited exemption would only apply in relation to GMP licensing of the manufacturing site. Supply of the products would separately need to continue to be under SAS or CTN provisions, where reporting of adverse events to TGA is still mandatory and advertising restrictions apply.

The proposed exemption would also open up the possibility of BTPs being supplied through the AP provisions, instead of SAS. To become an AP, a medical practitioner needs to be approved by the TGA and an HREC (or endorsement from a specialist college if applicable) to access and legally supply a specified ‘unapproved’ therapeutic good (or class of ‘unapproved’ therapeutic goods) to a class of patients with a particular medical condition. An AP is allowed to supply the product directly to patients in their immediate care without requiring separate approval for individual patients. APs are required to report patient numbers to the TGA every 6 months. It should be noted that the product must not be supplied to other practitioners who prescribe or administer the product. This model is similar to governance arrangements already utilised under the STAMP protocol[6], with the receiving

[6] The STAMP protocol (Standardised Treatment and Monitoring of Phage Therapy) is a clinical trial designed to standardise the treatment and monitoring of phage therapy for patients with bacterial infections. Standardised treatment and monitoring protocol to assess safety and tolerability of bacteriophage therapy for adult and paediatric patients (STAMP study): protocol for an open-label, single-arm trial. Khatami A., Foley DA., Warner MS, Barnes EH., Peleg AY., Li J., Stick S., Burke N., Lin RCY., Warning J., Snelling TL., Tong SYC., and Iredell J.

HREC responsible for determining the suitability of supply and ensuring appropriate data collection. This model also goes some way to mirror governance of clinical trials in Australia for personalised BTPs.

b. Restricted to personalised therapies

This proposal would only involve an exemption for manufacturers of personalised bacteriophages, regularising most of the current domestic supply of such products in Australia.

The proposed restriction of the exemption to personalised BTPs is because supply of these products into classical clinical trials has so far been difficult. In contrast, for bulk manufacturing of BTP it is considered that the full medicines regulatory requirements should apply. Such products can be supplied under the clinical trial provisions, with the manufacturer exemption applying to BTPs for initial experimental use in human volunteers (Item 1, Schedule 7 of the Regulations) but not when used in later phase trials.

c. Persons who can manufacture expanded

Phage manufacturing is complex and multifaceted requiring personnel to have expertise in phage biology, molecular virology, microbial fermentation as well as downstream purification processes. It is unlikely that a single registered medical practitioner could manufacture these alone without a suitably qualified and trained team.

Therefore, allowing bacteriophage manufacture by medical practitioners as well as suitably qualified persons employed by a public or private hospital or a public institution is designed to ensure current manufacture does not cease and refinement of processes and collection of patient data can continue.

Importantly, the scope of the proposed exemption would cover where BTPs are be transferred between public or private hospitals, public institutions or private institutions, in Australia, for the purposes of treating patients of such hospitals or institutions, ensuring patient equity and would not limit treatment to patients of the same hospital or institution.

d. Remaining challenges

In the absence of GMP licensing or specific product standards, there is a risk that the quality of BTPs across different manufacturers may be inconsistent. This could result in patients not having sufficient confidence in the safety and quality of these products as used. However, this risk is currently considered low, as most of the supply of BTPs in Australia is approved by an HREC, and there is a strong historical safety record for the use of natural bacteriophages and generally a high benefit-risk profile.

The TGA intends to consult further with the sector next year on the need to introduce a specific product standard for BTPs in Australia.

Transition

It is proposed this exemption will be in place for 2 years. During this time, we intend to consult on further reforms to the way BTPs are regulated in Australia, and in this context the need for an extension to the exemption will be considered.

Your views are sought

1. Do you support the introduction of a time-limited exemption from GMP licensing for manufacturers of personalised BTPs?
2. If so, are the details of the proposed exemption appropriate? That is:
    a. Do you support the exemption being limited to manufacturers of personalised BTPs?
    b. Are the persons proposed to be covered by the exemption appropriate and adequately described?

   c. Would the 2-year limit provide enough time for the sector to achieve GMP or allow TGA to further consider an appropriate level of regulatory oversight of bacteriophage in Australia?

3. What would the impact of the proposed time-limited GMP exemption be on your facility, particularly for hospitals and practitioners currently using BTPs?

4. Do you consider that this option would appropriately address requirements for public health and safety? Please provide the reasons why it would or would not.

Consultation details

This consultation enables stakeholders to provide feedback on proposed changes to the regulation of bacteriophage manufacturing. Table 1 details the key dates for the consultation period.

Table 1: Key Consultation Dates

Action	Date
Consultation Paper Published and consultation commences	16 October 2025
Closing date for consultation period and submissions	13 November 2025

How to provide feedback

Feedback can be provided using the online submission form at TGA Consultation Hub (tga.gov.au).

Submissions are due by **11.59 pm on 13 November 2025.**

What happens next?

We will consider all your feedback before proposing any changes to the Regulations.

We will let you know the outcome and publish a summary of all the feedback and our decision.

If you have any questions about this proposal, please email TGA.Scientific@health.gov.au

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Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	SOMS, SEB, MRD	October 2025

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