

During the public hearing, Medicines Australia undertook to follow up on the below questions.

Question: *What type of processes are involved from the discovery of a new drug through to being approved – what types of delays are there in the clinical trial stages? What would limit achieving the 15 years effective patent term?*

Response

Research based pharmaceutical companies devote considerable effort in exploring potential new treatments. Companies initiate particular drug development programs after they have identified a disease or clinical condition where there are few or no effective treatments or for which there remains unmet medical need.

Broadly speaking, researchers begin by generating a hypothesis that the inhibition or activation of a particular protein or pathway will have a therapeutic effect in a particular disease or condition. This activity generally results in selection of a potential target which will require further research to validate in order to justify further drug discovery and development efforts. Extensive research is required to identify a potential small or large molecule for further development, also known as a development candidate.

Prior to testing in humans, the investigation compound or development candidate is considered to be in the preclinical testing phase versus the development phase. The focus of preclinical testing is to assess whether the drug development candidate is safe for human volunteers and whether it exhibits pharmacological activity to merit further investigation.¹

Question: *What is different about Australia's processes that would justify having the additional 5 year extension of term compared to other jurisdictions?*

Response

As outlined in our submission, the effective patent life of approximately half of all molecules is less than the intended 15 years. The Australian system requires both regulatory approval through the TGA as well as approval for reimbursement through the Pharmaceutical Benefits Advisory Committee (PBAC). Once the PBAC has recommended that a drug be listed on the PBS, there can still be a delay for ministerial approval.

Question: *For clinical trials, are there examples of the time frames and how a drug goes through the process?*

Response

¹ <http://www.phrma.org/sites/default/files/pdf/biopharmaceutical-industry-sponsored-clinical-trials-impact-on-state-economies.pdf>

The Clinical Trial process in Australia is complex and varied. As an indication of the broad timeframes associated with clinical trials²:

- Early phase research takes up to 6 years
- Pre-clinical toxicity and safety studies take approximately 1 year
- Clinical trials take on average 6.5 years through three phases:
 - Phase 1: Safety and tolerability in healthy volunteers
 - Phase 2: safety, efficacy and bioequivalence studies in small groups of patients
 - Phase 3: Large trials with diverse populations to prove efficacy, safety and quality
- Registration and manufacturing scale up takes up to 2 years
- Post market surveillance is then a continuous process.

Question: Does the decision to invest in R&D here in Australia take into account the PBAC and TGA timeframes? Are there any examples of this?

Response

Investment decisions are made in a global context where many factors influence the decision. As noted in our submission, there are multiple components in the development chain that will be influenced by expected processing times in the regulatory approval process. We also noted in our submission, a 15 year effective patent life is a key driver of investment.

Question: What is the impact of EoT on R&D investment – can Medicines Australia provide any return on equity figures that are just for Australia?

Response

Due to commercial sensitivity, figures for return on equity for the five year extension of term are currently unavailable for Australia. An indication of the broad costs of capital associated with clinical trial R&D may be found in the Tufts study on R&D costs³.

Question: How would the manufacture for export work within the provisions of the Australia/US Free trade agreement?

Response

The AUSFTA has a number of principles which may be violated if manufacture for export is allowed during the period a valid patent is applicable to a molecule. As outlined in Appendix 2-C:

“the importance of research and development in the pharmaceutical industry and of appropriate government support, including through intellectual property protection and other policies;

the need to recognize the value of innovative pharmaceuticals through the operation of competitive markets or by adopting or maintaining procedures that appropriately value the objectively demonstrated therapeutic significance of a pharmaceutical.”

There are a number of side letters to the agreement. Our understanding of these side letters is that manufacture for export is only permitted for the purposes of meeting marketing approval requirements in Australia.

² https://medicinesaustralia.com.au/wp-content/uploads/sites/52/2010/11/MAFactsBook4_update2015.pdf

³ http://csdd.tufts.edu/files/uploads/Tufts_CSDD_briefing_on_RD_cost_study_-_Nov_18,_2014..pdf

Question: *Are there examples of incremental innovation?*

Response

Incremental innovation advances medicines by:

1. Expanding therapeutic classes,
2. Increasing the number of available dosing options
3. Discovering new physiological interactions of known medicines, and
4. Improving other properties of existing medicines.

Some examples of the types of incremental innovation can include reformulating a medicine to encourage compliance with a patient group (e.g. children or older person), or increase the medicine's shelf life, method of administration or health stability.

In some circumstances, although a first-in-class medicine has debuted, researchers do not fully understand other possible therapeutic interactions. Research that leads to a subsequent addition to a class may shed light on the underlying mechanism of how the medicine works. For example, captopril was the first medicine to inhibit an enzyme, angiotensin converting enzyme or "ACE," that was found to be linked to congestive heart failure. It was later discovered that captopril was accompanied by unpleasant side effects such as itching and headaches. Subsequent R&D to address the limitations of captopril not only eliminated unwanted effects, but also yielded a completely new understanding of the enzyme involved.⁴

Question: *What are the barriers to transplanting the US FTC system here?*

Response

Before examining the barriers to introducing a FTC style system, the rationale for doing so should be considered. Australia's pharmaceutical competition landscape is significantly different from the US. There is an incentive for generic manufacturers in the US to prove that a patent is invalid with a period of market exclusivity being awarded on successful litigation. In Australia, there isn't a similar incentive, with the ACCC already having powers to investigate anti-competitive behaviour.

Question: *How the Multinational tax avoidance laws that have recently been implemented would provide additional information and scope for further examination of potential pay-for-delay arrangements.*

Response

The recently introduced multinational tax avoidance laws and country by country reporting will provide a range of new data to the ATO. It is suggested that the information reported to the ATO should be examined to determine if there is the possibility of detecting potential pay for delay arrangements.

⁴ Patchett AA, Harris E, Tristram EW et al. (1980) A new class of angiotensin-converting enzyme inhibitors. *Nature* 288 (5788): 280–3. doi:10.1038/288280a0. http://www.ifpma.org/wp-content/uploads/2016/01/IFPMA_Incremental_Innovation_Feb_2013_Low-Res.pdf