

HEALTH

❖ **Bedaquiline, India's anti-tuberculosis fight, and a patent battle**

➤ **CONTEXT: Recently the Indian Patent Office rejected an application by pharmaceutical giant Johnson & Johnson (J&J) to extend its patent on the drug bedaquiline beyond July 2023.**

- Bedaquiline is a drug in tablet form used to treat drug-resistant tuberculosis (TB). The rejection opens the door for drug manufacturers to produce generic versions of bedaquiline, which are expected to be more affordable and to contribute to India's goal of eliminating TB by 2025.

➤ **What is drug-resistant TB?**

- As of 2017, India accounted for around one-fourth of the world's burden of multi-drug-resistant (MDR) TB and of extensively-drug-resistant (XDR) TB.
- MDR TB resists treatment by at least isoniazid and rifampicin, the two frontline drugs in TB treatment. XDR TB resists these two drugs as well as fluoroquinolones and any second-line injectable drug. XDR TB is rarer than MDR TB: there were 1,24,000 cases of the latter in India (2021) versus 2,650 cases of the former (2019).
- TB incidence in India has been on the decline, but MDR TB and XDR TB endanger initiatives to locally eradicate the disease. During the COVID-19 pandemic, there were indications that TB treatment was hit by disrupted supply chains, availability of healthcare workers for non-pandemic work, and access to drug-distribution centres.
- A peer-reviewed 2020 study reported that TB becomes isoniazid-resistant when a person doesn't fully adhere to the treatment regimen whereas rifampicin-resistance emerges due to other factors. It also found that the incidence of MDR TB (i.e. resistance to both drugs) was "strongly correlated with treatment failure and spread through contact, and not to treatment compliance".

➤ **How is drug-resistant TB treated?**

- TB is an infection of the bacterium *Mycobacterium tuberculosis* in the lungs, but often in other organs as well. It can be treated by strictly adhering to the doses and frequencies of drugs prescribed by a physician.
- Deviations from this schedule can lead the bacteria to become drug-resistant. Yet they happen because the drugs often have side effects that diminish the quality of life and/or because patients haven't been afforded access to the requisite drugs on time.
- Drug-resistant TB is harder to treat. One important option for those diagnosed with pulmonary MDR TB is bedaquiline.
- In 2018, the World Health Organization replaced two injectable drugs for MDR TB with an oral regimen that included bedaquiline.
- At this time, bedaquiline hadn't completed phase III trials. The recommendation was based on smaller trials, outcomes in TB elimination programmes worldwide, the difficulty of treating MDR TB, and close monitoring of patients receiving the drug.

➤ **How good is bedaquiline?**

- Typically, bedaquiline needs to be taken for six months: at a higher dose in the first two weeks followed by a lower dosage for 22 weeks. This period is shorter than other treatment routines for pulmonary MDR TB, which can last 9-24 months.
- One phase II clinical trial observed that culture conversion (turning a patient's sputum culture from positive to negative) "at 24 weeks was durable and associated with a high likelihood of response at 120 weeks", due to bedaquiline.
- Unlike second-line treatment options that are injected and can have severe side effects, like permanent hearing loss, bedaquiline is available as tablets and is less harmful, although it has potential side effects of its own. Studies until 2018 found that it may be toxic to the heart and the liver. This is part of why it is recommended only when other treatment options for MDR TB have failed.

- India's Health Ministry has guidelines for bedaquiline use as part of the Programmatic Management of MDR TB under the National TB Elimination Program.

- The WHO's decision revitalised a debate about the ethics of making a much-needed but insufficiently tested drug available quickly, on compassionate grounds, versus lowering the safety threshold for pharmaceutical companies producing drugs for desperate patients.

➤ **Why was the patent application rejected?**

- J&J's patent application was for the production of a fumarate salt of a compound, with which to make bedaquiline tablets. Two groups opposed the patent: 1) 'Network of Maharashtra people living with HIV' and 2) Nandita Venkatesan and Phumeza Tisile, both TB survivors, supported by Médecins Sans Frontières.
- Both groups argued that J&J's method to produce a "solid pharmaceutical composition" of bedaquiline is "obvious, known in the art" and doesn't require an "inventive step". According to the Indian Patent Act 1970 Section 2(1)(ja), an 'inventive step' is an invention that is "not obvious to a person skilled in the art".
- They also objected that J&J's application didn't contain information about foreign patent applications, their specifications, and priority dates, among other details, required under Section 8.
- The latter also contended that the current application drew significantly from a previous patent, WO 2004/011436, which discussed a similar compound on which bedaquiline is based and whose priority date (2002) well preceded the new application.

- The Patent Office rejected the application on these and other grounds, including Sections 3d and 3e of the Act. These pertain to “mere discovery of a new form of a known substance which does not result in the enhancement of the known efficacy of that substance” and “a substance obtained by a mere admixture resulting only in the aggregation of the properties of the components thereof”, respectively, which are not patentable.
- **Why is the rejection notable?**
- India has the largest population of people living with drug-resistant TB. J&J’s patent on bedaquiline meant the drug cost \$400 (Rs 33,000) for the six-month schedule, in addition to the cost of other drugs (revised in 2020 to \$340). The rejection is expected to lower the cost of bedaquiline by up to 80%.
- So far, the Indian government has directly procured the drug and distributed it through state-level TB programmes. Since 2016, India has also availed bedaquiline donated at no cost by J&J and the U.S. Agency for International Development.
- The argument based on WO 2004/011436 is also relevant to ‘evergreening’: a strategy whereby a patent-owner continuously extends their rights and/or applies multiple patents for the same entity. Indian law disallows ‘evergreening’.
- J&J’s current patent will expire in July 2023.

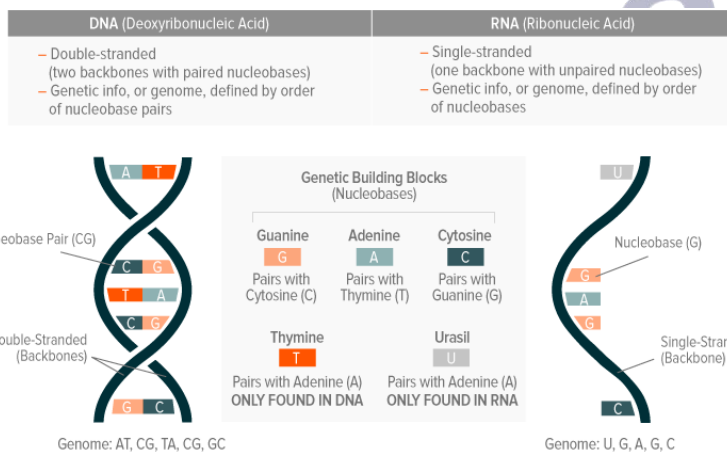
BIO-TECHNOLOGY

❖ **To err is viral: Why do most deadly viruses contain RNA?**

➤ **CONTEXT:** In March 1953, James Watson, the co-discoverer of the structure of DNA, received a note from Harriett Ephrussi-Taylor, a friend from the National Centre for Scientific Research in France. The note, titled “Top Secret”, contained news of a potential discovery that had enormous implications for molecular biology, virology, and immunology. The note read, “Burnet swears, from work in his lab, that flu virus has principally, possibly exclusively, RNA. Suspects same for Polioviruses.”

➤ **Why is DNA preferred over RNA?**

- Most organisms prefer DNA over RNA, its chemical cousin, to store genetic information. As life evolved from single-celled organisms to increasingly complex forms, the amount of genetic data that had to be transferred to subsequent generations became correspondingly higher. So organisms needed to make sure that the mechanism for copying the genetic material was that much more robust.



- In particular, organisms needed the ability to correct any inadvertent errors in the copying mechanism. The enzymes responsible for copying DNA, collectively known as **DNA polymerases**, possess this error-correction property, known in technical parlance as **‘proofreading’**. This proofreading ability allowed the total DNA of higher organisms, known as the genome, to be longer and more complex.

- On the other hand, the RNA counterparts to DNA polymerases, known as **RNA polymerases**, do not possess the ability to proofread. As a result, when RNA is the genetic material, the genomes typically tend to be shorter. Longer genomes would contain proportionately higher mistakes, and such genomes would be eliminated by natural selection.
- Coronaviruses beautifully illustrate this point since their genomes are typically three- or four-times the size of those of other RNA viruses. They can afford the longer genomes due to the presence of a unique protein, in addition to the RNA polymerase, that performs the proofreading function.
- RNA polymerases are also capable of recombination, a process that allows them to stitch together multiple pieces of different viral RNAs. This way, if one viral RNA contains a mutation at location X and another contains a mutation at location Y, recombination can create a virus containing both X and Y by sewing the two regions of the viral RNA containing those mutations. This is how, for example, the XBB variant of SARS-CoV-2 is the product of the BA.2.10.1.1 and BA.2.75.3.1.1.1 variants.

➤ **What is the advantage of RNA?**

- At the time Watson received the note from Ephrussi-Taylor, scientists widely held the view that DNA was the genetic material of all life forms. Frank Burnet’s discovery was groundbreaking because he showed, for the first time, that certain viruses existed that had RNA as their genetic material.
- The discovery was important because, if today we name any 10 viruses, most of them are likely to be RNA viruses. The most popular disease-causing viruses bear RNA, not DNA, including the causative agents of

COVID-19, AIDS, polio, influenza, dengue, chikungunya, Ebola, Zika, Hepatitis C, rabies, Marburg, yellow fever, and Japanese encephalitis.

- Except for HIV, which is responsible for AIDS, all of these viruses contain an error-prone RNA polymerase. HIV uses a slightly different mechanism to replicate, but the enzyme responsible shares the error-prone nature of its siblings.
- The better known DNA viruses included members of the pox family (smallpox and chickenpox) and Hepatitis B.
- At the heart of the domination of RNA viruses over human disease lies the error-prone nature of their polymerases. This singular property allows the virus to acquire multiple adaptations that serve as tools in the viral arsenal.
- Foremost, the RNA polymerase enables these viruses to exist in a form that scientists refer to as a quasi-species. This means that a given virus can exist in multiple variant forms simultaneously in each host. Such an existence directly results from these viruses' error-prone replication.
- **What are the consequences of RNA as genetic material?**
- Some of these viral variants will be non-infectious due to mistakes in the genome, and the host immune system will eliminate another significant fraction. However, such diversity also allows the creation of an odd variant that possesses a survival advantage against a vaccine or a drug. Such variants will undergo further natural selection, and the virus will continue to proliferate.
 - ✓ This is why multiple variants of SARS-CoV-2 continue to circulate to this day. It is also why developing highly effective vaccines against RNA viruses remains challenging.
- A second, indirect consequence of the low-fidelity replication process is the small size of the viral genome. This allows RNA viruses to have very short generation times. In a very short period after infection, the host's virus population becomes enormous.
 - ✓ This high viral output, together with the diversity, overwhelms the immune system.
- The third consequence of the nature of viral replication is that the viruses can 'jump' across species, a process termed zoonosis. This is because the high error rate and the short generation time enable the virus to adapt to newer conditions much faster, allowing the infection to spread easily among newer hosts.
 - ✓ This is why up to 89% of all human infectious RNA viruses are considered to be a result of zoonotic transmissions.
- **Why is viral surveillance important?**
- These remarkable properties have collectively made sure RNA viruses represent the largest group of pathogenic organisms that cause new diseases.
- Every year, two or three new RNA viruses that can infect humans are discovered. While this number is by itself enough cause for worry, it is also a worthless underestimate due to the lack of adequate surveillance in tropical and sub-tropical countries. Viral surveillance and monitoring must be stepped up in these regions to arrive at more accurate numbers.
- Viruses are primitive forms of life. Scientists have advanced multiple theories about how life may have originated on earth. They range from turbulent atmospheric conditions creating primitive forms of the cellular blocks to the idea that life evolved outside earth and was brought here on a meteorite.
- However, all those theories agree that once life begins, the ability to accurately transmit genetic information is absolutely necessary for it to continue.
- It is therefore incredible that RNA viruses thrive whilst making a mockery of something so vital to the existence of everything else.

PRELIMS

1. Depleted uranium

- **CONTEXT: Minister of State for Defence of the United Kingdom, said that some of the ammunition for the Challenger 2 battle tanks that Britain is giving to Ukraine includes armour-piercing rounds which contain depleted uranium.**
- **What is depleted uranium?**
- Depleted uranium is a byproduct of the process of creating enriched uranium, which is used in nuclear reactors and nuclear weapons.
- In comparison to enriched uranium, depleted uranium is much less radioactive and is incapable of generating a nuclear reaction. However, due to its high density (it's more dense than lead) depleted uranium is widely used in weapons as it can easily penetrate armour plating.
- According to nuclear expert, "It's so dense and it's got so much momentum that it just keeps going through the armour — and it heats it up so much that it catches on fire."
- The US began manufacturing armour-piercing rounds with depleted uranium in the 1970s and has since added it to composite tank armour to strengthen it.
- Depleted uranium to the munitions fired by the Air Force's A-10 close air support attack plane, known as the tank killer. The US military is still developing depleted uranium munitions, notably the M829A4 armour-piercing round for the M1A2 Abrams main battle tank.

➤ **Which countries have depleted uranium munitions?**

- Apart from the US, Britain, Russia, China, France and Pakistan produce uranium weapons, which are not classified as nuclear weapons, as per the International Coalition to Ban Uranium Weapons. Another 14 states are known to store them.

➤ **What are the risks of using such weapons?**

- Even though depleted uranium munitions aren't considered nuclear weapons, experts suggest that such weapons must be used with caution because they emit low levels of radiation and can cause severe diseases.
- Ingesting or inhaling quantities of uranium (even depleted uranium) is dangerous: it depresses renal function and raises the risk of developing a range of cancers."

• Moreover, according to the International Coalition to Ban Uranium Weapons, depleted uranium munitions which miss their target can poison groundwater and soil.

➤ **Where have depleted uranium munitions been used?**

- Depleted uranium munitions were used in the 1991 Gulf War to destroy T-72 tanks in Iraq. These weapons were again used in the 1999 NATO bombing of Yugoslavia and then during the 2003 invasion of Iraq.

- About 340 tons of depleted uranium were used in munitions during the 1991 Gulf War, and an estimated 11 tons in the Balkans in the late 1990s.

2. Pradhan Mantri Van Dhan Vikas Yojna

➤ **CONTEXT:** Under the Pradhan Mantri Van Dhan Vikas Yojna (PMJVM) Government is providing Rs 15 lakh per Van Dhan Vikas Kendra (VDVK) to encourage livelihood activities of tribal people across the country.

➤ **About the scheme**

- The Van Dhan Vikas Program is an initiative of the Ministry of Tribal Affairs. It aims to give tribal people a means of livelihood by using the Van Dhan forest's resources.
- It largely falls under the purview of the Minimum Support Price (MSP) and the Creation of a Value Chain System for Selling Minor Forest Products (MFP).
- The programme makes an effort to modernise the traditional knowledge and skill sets of tribe members at each level and transform them into sustainable economic activity.
- In accordance with the Van Dhan Scheme, TRIFED will assist in the development of MFP-led multi-purpose Van Dhan Vikas Kendras in the tribal areas. These centres will have a collection of 10 SHGs that each house 30 indigenous MFP gatherers. Each Kendra would act as a central location for shared resources for buying and enhancing locally available MFPs and skill-based handicrafts. TRIFED provides technical support as well as instruction.
- The Van Dhan Vikas Program was created especially for tribal people. Each Van Dhan Vikas Kendra consists of 15 tribal Self Help Groups serving up to 300 beneficiaries.
- Minor Forest Produce (MFP)
- MFP, often called Non-Timber Forest Product (NTFP), is a significant source of income. This gives a lot of STs who live in and around the woods the sustenance, medical care, and monetary income they need.
- Providing MFP gatherers with a fair price for the MFPs they collect, through Minimum Support Price & Development of the Value Chain for the MFP Program aims to enhance their standard of living.
- The Ministry of Tribal Affairs will serve as the focal ministry for the administration and management of the programme. Technical guidance from TRIFED would be used by the Minister to select the Minimum Support Price.
- State-authorized agencies will be in charge of making MFP purchases through MSP.



ANSWER WRITTING

Q. There is a need for a review of defamation laws in India due to its misuse. In this context, explain the legal provisions regarding defamation and critically examine the need for defamation laws in India.

Defamation refers to communicating false statements about a person that injure that person's reputation. In India, defamation can both be a civil and criminal wrong. Defamation has been a misused offence in the hands of many, thereby causing a rise in debate on it with respect to the limitation on free speech. The recent misuse is visible in the disqualification of a senior opposition leader due to conviction under criminal defamation.

Legal provisions regarding defamation in India are mentioned in the Indian Penal Code:

- Section 499 of the IPC defines what is defamation and its exceptions: Defamation can occur through words, whether spoken or written and also by visible representations intended to harm the reputation of any person.
 - It also deals with defamation of a deceased person, a company, or an association of persons.
- Section 500 of the IPC deals with punishment for criminal defamation, which can be imprisonment for up to 2 years, with or without a fine.
- The IPC also punishes printing or engraving matter known to be defamatory or the sale of such printed or engraved substance containing defamatory matter about any person.

Arguments against defamation law in India:

- Against freedom of speech: The fundamental right under 19(1)(a) of the Indian Constitution is restricted by defamation laws in India. People worry about saying something that might cause upset or get them into trouble, whether they are speaking in private or in public.
- Learning from international experiences: Many countries, such as the United Kingdom and the United States, have scrapped criminal defamation. India's neighbour, Sri Lanka, too, has done away with it.
- Misuse against media and journalists: Freedom of speech and expression of media is very important for a vibrant democracy. However, the threat of prosecution under defamation leads to the suppression of truth. Influential people often misuse this provision in order to suppress any voices against them.
- Misused by the rich and powerful: Fighting a case in Indian courts is generally a tedious and expensive affair. The defamation law is exploited by individuals and corporations with deep pockets by threatening their critics with a protracted defamation suit.
- Exploited by the ruling party: In recent years, there have been countless cases where defamation law is misused to settle personal scores or to intimidate a weaker party.

Arguments in favour of defamation law in India:

- The supreme court in the Subramanian Swamy V. Union of India case agreed to uphold the constitutional validity of the criminal defamation laws.
- The court declared that Article 19(1)(a) right to free speech had to be balanced with Article 21 right to "reputation".
- Those who favour the law argue that defamation law has been part of statutory law for over 70 years and it has not abridged our free speech or has diluted Indian democracy.
- Misuse or abuse of the law should not be taken as a justification for declaring a provision unconstitutional. The lower judiciary should be made aware of the importance of preventing misuse.

Sections 499-500 of the IPC are vestiges of India's colonial past and are not appropriate for a modern democracy. Reforms to defamation can be best done through the enactment of a new statute. Such a law should decriminalise defamation and reform civil defamation to make it fairer and clearer in order to prevent its misuse.

MCQs

1. In the context of the developments in Bioinformatics, the term 'transcriptome' sometimes seen in the news, refers to
 - a) a range of enzymes used in genome editing
 - b) the full range of mRNA molecules expressed by an organism**
 - c) the description of the mechanism of gene expression
 - d) a mechanism of genetic mutations taking place in cells
2. With reference to the recent developments in science, which one of the following statements is not correct?
 - a) Functional chromosomes can be created by joining segments of DNA taken from cells of different species.**
 - b) Pieces of artificial functional DNA can be created in laboratories.
 - c) A piece of DNA taken out from an animal cell can be made to replicate outside a living cell in a laboratory.
 - d) Cells taken out from plants and animals can be made to undergo cell division in laboratory petri dishes
3. Which of the following popular disease-causing viruses bear RNA, not DNA?
 1. COVID-19
 2. Dengue
 3. Zika
 4. Rabies
 5. Smallpox and chickenpox
 6. Hepatitis B
 7. Marburg

Choose the correct answer using the codes given below

- a) 1,3and 6 only
- b) 2,3,4 and 7 only
- c) 2,5,6 and 7 only
- d) 1,2,3,4 and 7 only**

4. Consider the following statements with respect to Tuberculosis (TB) :

- 1. Tuberculosis is caused by the bacteria Mycobacterium tuberculosis that most often affect the lungs.
- 2. People infected with TB bacteria have a very high risk of falling ill with TB.
- 3. Multidrug-resistant TB (MDR-TB) is TB that does not respond to at least isoniazid and rifampicin, the 2 most powerful anti-TB drugs.

Which of the statements given above are correct?

- a) 1 and 2 only
- b) 2 and 3 only
- c) 1 and 3 only**
- d) 1, 2 and 3

5. With reference to Depleted Uranium often mentioned in news consider the following

- 1. Depleted uranium a by-product of the uranium-enrichment process.
- 2. Because it is exceptionally dense, depleted uranium can be used in the production of tank armour or made into ammunition.
- 3. Unlike Uranium it is very cheap to dispose of because it has no radioactivity as a result arms manufacturers can obtain depleted uranium for minimal or even no cost.

Which of the above statement/s is/are correct?

- a) 1 and 2 only**
- b) 2 and 3 only
- c) 1 and 3 only
- d) 1,2 and 3

6. With reference to Pradhan Mantri Van Dhan Vikas Yojna (PMJVM) consider the following

- 1. It is an initiative targeting livelihood generation for tribals by harnessing the wealth of forest.
- 2. The nodal ministry for this scheme is Ministry of Environment Forest and Climate change.

Which of the above statement/s is/are not correct?

- a) 1 only
- b) 2 only**
- c) Both 1 and 2
- d) Neither 1 nor 2

7. Consider the following statements about "Sukanya Samriddhi Yojna":

- 1. It is a small saving scheme governed by Post Office Savings Account Rules, 1981.
- 2. A girl child is eligible for Sukanya Samriddhi Account (SSA) only if she is a resident Indian citizen at the time of opening of account
- 3. Partial withdrawal from a Sukanya Samriddhi account can be made after the account-holder attains the age of 18.

Which of the above statement/s is/are correct?

- a) 1 and 2 only
- b) 2 and 3 only
- c) 1 and 3 only
- d) 1,2 and 3**

8. Shyamala Gopinath Committee formula often mentioned in news is related to which of the following?

- a) Minimum Support Price
- b) Small Saving Schemes**
- c) Minor forest Produce
- d) National Pension Scheme

9. Bibhutibhusan Wildlife Sanctuary often mentioned in news is situated in which of the following state?

- a) Odisha
- b) Andhra Pradesh
- c) West Bengal**
- d) Assam

10. AMRUT 2.0 is a flagship scheme under which of the following Ministry?

- a) Ministry of Jalshakti
- b) Ministry of Education
- c) Ministry of Road transport and Highway
- d) Ministry of Housing and Urban Affairs**