

1 ***Agricultural wastewater reuse for a sustainable circular economy***

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34 **Sections**

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44 ***Abstract***

45 Facing climate change, effective management of water resources is crucial for global food
46 security, sustainable economic development, community well-being, and ecosystem services.
47 This review explores the potential benefits and challenges associated with treated wastewater
48 (TW) reuse for agricultural irrigation, offering strategic solutions to the escalating issues of
49 water demand and scarcity. By implementing adaptable centralized or decentralized reuse
50 schemes tailored to local conditions and supported by robust legal and regulatory frameworks,
51 we can fortify the production of safe agricultural products. Simultaneously, these initiatives
52 can free significant amounts of fresh water for other essential uses. Technological
53 advancements, particularly in treatment, recovery, monitoring, and overall management, can
54 facilitate the transformation of wastewater treatment plants into eco-friendly facilities. These
55 facilities can play a vital role in utilizing wastewater and biosolids to generate safe, fit-for-
56 purpose TW, energy, fertilizers, and valuable by-products within the circular economy
57 framework. To meet the potential, international organizations, governmental authorities,
58 academia, industry, stakeholders, and communities must collectively recognize the
59 transformative capacity of a circular TW management. Consequently, they should invest
60 substantial efforts and resources to facilitate the transition of this critical sector, aligning it with
61 sustainable practices that not only enhance ecological integrity but also effectively address
62 global water challenges.

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67 ***Key points***

- 68 • Treated wastewater (TW) reuse has the potential to alleviate water imbalances,
69 especially in water scarce regions, and boost/sustain food production by expanding
70 irrigated agriculture, thus promoting global food and water security.
- 71 • Best practices, including the establishment of TW-irrigated agricultural hotspots served
72 by either centralized, decentralized or hybrid TW reuse systems can promote
73 sustainable rural development that is sensitive to the climate-water-energy-food nexus.
- 74 • Comprehensive regulatory frameworks are essential to safeguard the smooth
75 functioning and sustainability of TW reuse systems, and vital to ensure environmental
76 and public health, and social acceptance of reuse schemes.
- 77 • Wastewater treatment plants (WWTPs) must operate as energy and carbon neutral
78 facilities, with water, nutrients and other materials recovered and reused, thus
79 promoting the circular economy and SDGs.
- 80 • Advanced wastewater treatment processes necessitate ongoing research and site-
81 specific evaluations for cost-effective and sustainable reuse practices.
- 82 • Modern advancements in wastewater treatment and recovery technologies, materials,
83 and Fourth Industrial Revolution (4IR) tools can transform wastewater treatment,
84 resulting in the production of high-quality fit-for-purpose TW.

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89 **Introduction**

90 Water scarcity is emerging as a critical concern for an increasing number of countries. Severe
91 water imbalances are anticipated to intensify spatially and temporarily under climate change
92 scenarios, causing catastrophic losses and substantial economic impacts¹. According to the UN
93 Environment programme, today, 2.4 billion people live in water-stressed countries, defined as
94 nations that withdraw 25 per cent or more of their renewable freshwater resources to meet water
95 demand. By 2025, 1.8 billion people are likely to face what the Food and Agriculture
96 Organization calls “absolute water scarcity” and two-thirds of the global population is expected
97 to be grappling with water stress. Extreme weather events, such as the recent extended
98 heatwaves in Europe, Western North America and Asia and floods in Pakistan, Bangladesh,
99 Australia, and Libya, are occurring at increased frequency and severity, causing further
100 disturbances to the hydrological cycle^{2, 3}, and exemplify that urgent actions need to be
101 undertaken^{4, 5}. The limited progress towards achieving the Sustainable Development Goal 6
102 (SDG 6) for universal access to safe water and sanitation by 2030 was confirmed at the latest
103 UN Water conference⁶. Due to the current inadequate rate of progress, it is estimated that by
104 2030, 1.6 billion people will not have access to safely managed drinking water and 2.8 billion
105 people will not have access to safely managed sanitation⁷.

106 In the context of this intensifying water crisis, the agricultural sector is facing the most
107 severe impacts as it is the major consumer of water globally (using 70% of abstracted water
108 worldwide), while also facing escalating competition from the other water use sectors due to
109 population growth, urbanization, improved standards of living and industrialization⁸. Water
110 imbalances in the agricultural sector will be further exacerbated by the inevitable need for
111 cultivation expansion to meet the demands of the growing population, and because of further
112 pressures on yield and irrigation needs posed by climate change^{8, 9}. Within this context, the
113 need to maintain food security by using non-conventional water resources of adequate quality
114 in the agricultural sector has never been more imperative. Adequately treated wastewater (TW)
115 (also referred to as reclaimed water) is an attractive alternative for the mitigation of irrigation
116 water scarcity, especially where conventional water resources are limited or absent. TW reuse
117 in agriculture is already a common practice in some countries worldwide, and can substantially
118 boost agricultural production and rural development, while promoting circular economy¹⁰.

119 The quantities of wastewater produced annually at the global level are substantial, as all
120 human activities that consume water inevitably produce wastewater. However, only a small
121 portion of the wastewater generated is currently treated (less than 20% globally, with rates

122 varying across different regions and countries according to their economic status)^{11, 12}. High-
123 income countries treat on average about 70% of the wastewater they generate. This ratio drops
124 to 38% in upper middle-income countries and to 28% in lower middle-income countries. In
125 low-income countries, only 8% of wastewater generated undergoes treatment of any kind¹².
126 Jones et al., (2021) estimate the global wastewater production at $359.4 \times 10^9 \text{ m}^3 \text{ yr}^{-1}$ of which
127 63 % ($225.6 \times 10^9 \text{ m}^3 \text{ yr}^{-1}$) is estimated to be collected and 52 % ($188.1 \times 10^9 \text{ m}^3 \text{ yr}^{-1}$) treated.
128 They also estimate that 48 % of global wastewater production is released to the environment
129 untreated, which is substantially lower than the previous figures^{13, 14}. The release of untreated
130 wastewater to various receiving environments, including agricultural land, surface water bodies
131 and marine environments, poses serious health, environmental and economic impacts¹². The
132 volumes of TW reused for agricultural irrigation are currently very low, as most TW is reused
133 for other purposes, or discharged to downstream environments, like rivers and lakes¹⁵. There
134 is thus vast untapped potential for productively reusing TW in agriculture. Increased adoption
135 of TW reuse in agriculture is currently constrained by challenges such as reuse application
136 governance, limited social awareness and acceptance, the presence of various microbiological
137 and chemical (micro) contaminants in treated effluents, and the will of governmental and
138 intergovernmental organizations to invest and subsidize this practice^{12, 16}. Hence, the
139 motivation of this review is to provide insights into how this practice can be made more
140 sustainable and expanded, while addressing the contemporary challenges posed by the climate
141 crisis.

142 In this review, we summarize the prospects of reusing TW in agriculture to safeguard
143 food security, enhance public health, and advance sustainable development at the global level.
144 We also highlight the challenges accompanying this practice, mainly evolving from insufficient
145 wastewater treatment and poor governance in some countries, and the presence (even at
146 extremely low concentrations) of problematic pollutants in TW. We show that evolving
147 technologies can promote circularity in the wastewater treatment sector by retrofitting
148 treatment facilities into resource recovery factories where energy, nutrients, and other valuable
149 by-products (in addition to water) can be recovered and reused. Finally, we propose actions
150 and future directions for promoting long-term, safe wastewater treatment and reuse in
151 agriculture, and present relevant future research directions and perspectives.

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156 **Droughts and global health**

157 This section seeks to examine the cumulative health effects resulting from droughts and other
158 climate-sensitive factors. Additionally, it aims to underscore the positive outcomes derived
159 from harnessing wastewater as a valuable resource amidst the changing climate. TW reuse in
160 agriculture is expected to be a key component in efforts seeking to promote global health.

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162 **Reuse benefits in a changing climate**

163 Climate change and variability¹⁷ influence the frequency, intensity, and seasonality of multiple
164 environmental exposures. The health impacts associated with climate-sensitive exposures are
165 becoming more broadly documented and include both direct and indirect mechanisms¹⁸.
166 Notably, extreme heat events are among the deadliest climate sensitive extreme weather events
167 globally with the highest impact in terms of attributable number of deaths. For example, over
168 60,000 heat-related deaths occurred in Europe during the summer of 2022¹⁹. In parallel,
169 precipitation anomalies have substantial direct and indirect impacts on human health. It has
170 been recently shown that, while anomalously wet conditions increase the risk of infectious
171 diseases among children in some humid, subtropical regions, these health risks were rather
172 exacerbated because of anomalously dry conditions in many other regions including tropical
173 savanna regions²⁰.

174 Drought can be decomposed into meteorological (negative precipitation anomaly),
175 hydrological (surface or groundwater water supplies), agricultural (when the amount of soil
176 moisture does not suffice for a particular crop) or socioeconomic (when water shortages begin
177 to affect people and economic activities) categories. The increasing patterns in droughts around
178 the globe are unambiguously related to anthropogenic climate change²¹. Droughts may impact
179 population health through various mechanisms including water-borne diseases, wildfires, dust
180 storms or vector borne diseases^{22, 23}. For example, in California (USA), droughts increase the
181 intensity and frequency of wildfires which are now becoming a central source of air pollution
182 in the Western US even eroding decades of air pollution abatement, but also have substantial
183 health impacts^{24, 25}. Droughts also exacerbate the occurrence of airborne mineral dust events
184 which can lead to Coccidioidomycosis (aka valley fever)²⁶.

185 Therefore, in parallel to mitigation efforts that aim at reducing the emissions and
186 concentrations of greenhouse gases which ultimately will reduce climate change and variability
187 in a few decades, it is timely to develop adaptation efforts, especially among most vulnerable
188 communities, to deal with the changes in precipitation regimes and the increasing incidence

189 and severity of droughts. In this context, the exploitation of wastewater for diverse usages
190 appears as a key strategy to minimize the public health burden associated with direct and
191 indirect impacts of droughts induced by anthropogenic climate change. It is thus imperative to,
192 not only advance epidemiological evidence in relation to emerging TW-related contaminants,
193 but also contrast such potential harmful impacts with potential health co-benefits regarding
194 water resources, quality, and cascading droughts.

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197 **Current status of wastewater reuse**

198 Wastewater has been reused for irrigation since ancient times, though the lack of specific
199 treatment posed several health and environmental risks²⁷. Rapid urbanization and increased
200 hygiene and food production needs, alongside scientific and technological progress,
201 subsequently enabled the development of the wastewater treatment and reuse sector.
202 Wastewater reuse for irrigation is currently regulated by various legal frameworks, and mostly
203 applied through comprehensive wastewater reuse systems.

204

205 **Urban wastewater**

206 Currently, nearly 400 km³ (359.410⁹ m³ yr⁻¹) of urban wastewater are generated each year
207 globally, with projections of 50% increase by 2050 due to population growth and
208 urbanization²⁸. These volumes of wastewater represent almost 10% of global fresh water use
209 (over 4000 km³), sufficient to meet nearly 15% of current irrigation water needs^{29, 30}. These
210 huge quantities of generated wastewater are a worldwide source of contamination that can
211 cause waterborne disease outbreaks and substantial environmental problems if discharged
212 untreated. At the same time, wastewater is a valuable source of water, energy, and nutrients.
213 Thus, wastewater collection, treatment and reuse offers multiple economic, social and
214 environmental benefits, and also contributes to meeting the global SDGs³¹. Advancements in
215 wastewater treatment technologies during the last century have been remarkable, enabling the
216 cost-effective production of high-quality TW that can be reused for multiple purposes.

217 Wastewater consists of up to 99% water with the rest being solids, dissolved and
218 particulate matter, and microorganisms, although the exact composition varies depending on
219 the source and the mixture of wastewater (for example, domestic, industrial, stormwater,
220 runoff) and the season^{11, 32}. A great variety of treatments, including physical, biological, and
221 chemical technologies, applied alone or in combination, can effectively remove

222 microbiological and chemical inorganic and organic pollutants from wastewater and produce
223 reclaimed water complying with acceptable quality standards for the intended use (often
224 referred to as ‘fit-for-purpose’ recycled water)³³. The most suitable treatment approach is
225 usually defined by local regulations and restrictions pertaining to recycled water quality
226 standards, system operation and maintenance costs, approved reuse purposes, the ecological
227 footprint, social acceptance of TW systems and other considerations³³.

228 With the objective to enhance comprehension and facilitate a more nuanced dialogue
229 regarding the diverse nature of contaminants and their implications for environmental and
230 public health, we would like to clarify the use of the two following terms in this review.
231 Micropollutants refer to substances present in the wastewater at very low concentrations,
232 posing potential risks to ecosystems and human health, some of which are already included in
233 policies and regulations. Contaminants of emerging concern constitute a broader category of
234 chemical contaminants in very low concentrations, and also antimicrobial resistant bacteria,
235 resistance genes and mobile genetic elements; not yet fully understood or regulated. In this
236 paper, the acronym "MCEC" is used as a concise shorthand to collectively refer to both
237 categories.

238

239 **TW agricultural reuse**

240 Despite the benefits and the technological progress in wastewater treatment and reuse, the
241 global TW implementation for agricultural irrigation still remains low^{11, 12}. Large quantities of
242 TW are either discharged to downstream aquatic environments or reused for other purposes.
243 These include landscape irrigation, recreation, environmental enhancements, groundwater
244 recharge, or in urban water systems (for example, toilet flushing, street cleaning, dust
245 suppression, and fire protection), and in industrial processes (for example, as process water in
246 the textile and paper industry, steelworks, or for heating and cooling, and in construction)³⁴. In
247 some areas with extreme water stress, municipal wastewater undergoes advanced treatment to
248 be used for potable purposes^{35, 36}.

249 TW reuse for crop irrigation and for the purposes mentioned above can free equal
250 volumes of high quality fresh water for the domestic and other sectors, while can also enhance
251 critical ecosystem services related with environmental flows^{12, 37}. To this effect, this review
252 paper aims at promoting TW reuse in agriculture mainly over discharge to aquatic
253 environments.

254 The long-term sustainable reuse of TW in agriculture requires complex systems,
255 managed all the way from collection to application. This requires infrastructures such as

256 sewage collection system, wastewater treatment plant (WWTP) facilities, hundreds or even
257 thousands of kilometers of pipes, reservoirs and distribution system³⁸. Major technical
258 components of a sustainable TW reuse system includes the urban WWTP and/or reclamation
259 facility (which might include further treatments such as disinfection), storage systems (for
260 example, reservoir), pumping stations and distribution pipeline network, treatment facilities
261 for irrigation purposes (for example, filters), and irrigation system components (for example,
262 irrigation hoses, drips, sprinklers), including components adjacent to the point of use (for
263 example, run-off canals and buffer strips)²⁸ (Fig. 1).

264 Assessing the global extent of TW use is challenging due to varying data and
265 interpretations of reuse across countries. For example, for some countries, the volumes of
266 reused TW submitted under regulatory reporting requirements are lower than those estimated
267 and reported in the literature^{14, 39}. Information on TW application in agriculture may account
268 both direct and indirect reuse, the latter indicating TW discharged into surface waters or
269 aquifers through artificial recharge, and subsequently withdrawn for irrigation. Direct use of
270 TW allows for better water quality control since rules and standards applies at the reclamation
271 facility outlet^{39, 40} (Fig. 1b). Irrigational water quality lacks similar control measures, unless
272 risks resulting from mixing TW with other sources are identified, hindering the systematic
273 promotion of direct reuse⁴¹. Further consideration should also be given to the TW-irrigated
274 soil and commodities produced from TW-irrigated crops (combining the application of specific
275 water quality of TW with irrigation systems and crop species at the right time and site), as these
276 are crucial factors for protecting environmental and human health²⁸ (Fig. 1 a).

277 Broad acceptance of TW reuse in agriculture as a standardized and safe practice requires
278 comprehensive evaluations of risks and continuous monitoring, including through
279 digitalization of as many components of TW reuse systems as possible, along with appropriate
280 and flexible regulatory and institutional frameworks^{28, 42}. According to the EU Water Reuse
281 Regulation 2020/741, a water reuse system risk management plan should be based on key
282 elements, including system description, identification of all parties involved with roles and
283 responsibilities, environmental and health risk assessment, preventive measures for controlling
284 exposure to hazards, quality control systems, environmental monitoring systems, incident and
285 emergency systems and coordination mechanisms^{28, 43}.

286 Apart from appropriate treatments to facilitate the generation of fit-for-purpose TW,
287 special attention should be given to storage and distribution systems, as suboptimal
288 management may allow for recontamination of treated effluent, either by algae growth in
289 reservoirs, formation of biofilm in pipes, and/or bacterial regrowth⁴⁴. The fate of

290 micropollutants (including disinfection by-products) during treatment, storage and
291 transportation deserves scrutiny in relation to their persistence and effects after their release
292 into the environment⁴⁵. The avoidance of pollution through input prevention and source
293 control, the application of realistic regulations and standards, and the promotion of green and
294 sustainable chemistry, on the base of the Precautionary Principle, are also crucial for enhancing
295 end-of-pipe TW quality and therefore reuse acceptance and promotion⁴⁶.

296 Countries that have historically suffered from water stress and shortages, such as the
297 Mediterranean countries, Middle East and Gulf countries, China, Australia, Mexico, and the
298 United States have a long history of reusing TW for irrigation (Box 1). This practice has been
299 most successful in urban and peri-urban areas, where TW is easily available and where there
300 is a nearby market for agricultural products⁴⁷. Box 2 presents the storyline and the important
301 success factors of Israel's journey into harnessing the wastewater potential for agricultural
302 growth.

303 In conclusion, as we confront the challenges of climate change, the systematic
304 establishment and implementation of wastewater reuse schemes are anticipated to gradually
305 expand into regions that were once water-rich but are now compelled to embrace sustainable
306 practices for the future⁴⁷.

307

308 **Current wastewater treatment for reuse**

309 The state of the art in the treatment of urban wastewater for reuse in agriculture changes
310 significantly according to the country or geographical area (Table 1) because of various factors,
311 including the existence of more or less stringent regulations, the availability of alternative water
312 resources, and the availability and cost of raw materials (including energy), land, and
313 technology. As a matter of fact, the war in Ukraine resulted in drastic increase in European gas
314 (115%) and electricity (237%) prices in 2023⁴⁸. Water utilities experienced a general
315 inflationary pressure (10.6% in October 2022) and, for the coming years, are likely to face
316 electricity costs of 100-300 EUR/MWh as opposed to past multi-year average values of 40-80
317 EUR/MWh⁴⁹. Therefore, the cost of energy is expected to influence current and future choices
318 of technologies to be implemented for wastewater treatment.

319 Typically, the state of the art of treatment of urban wastewater for reuse in medium-
320 large WWTPs includes a secondary biological process (activated sludge, membrane biological
321 reactor (MBR) etc.), conventional filtration on granular media (except in the case MBR is used
322 as secondary treatment), and disinfection with UVC lamps or with chemical agents (typically
323 chlorine or peracetic acid), as tertiary treatments³³. However, current challenges in wastewater

324 treatment such as the removal of MCEC, the control of antibiotic resistance spread and
325 microplastics, are expected to change the state of the art in the coming years.

326 The availability of alternative water resources and the corresponding costs are also
327 important factors. In California (USA), for example, the cost of urban wastewater reuse
328 projects (1.2 US \$/m³) was found to be higher than that of stormwater capture (0.5 US \$/m³),
329 but lower than seawater desalination (2.3 US \$/m³)⁵⁰. Reuse or irrigation is a widespread
330 practice in the southern USA, particularly in California, Florida, Texas, and Arizona. In several
331 African countries there have been important investments in recent years in wastewater
332 treatment and reuse facilities for the construction and upgrading of large WWTPs, such as in
333 Algeria (€14 million), Egypt (€132.6 million) and Morocco (€40.7 million). Urban wastewater
334 agricultural reuse in China and India is poor and not documented. The total municipal water
335 reuse in China reached 12.6 billion m³ in 2019, with \$88 billion invested in the development
336 of urban wastewater treatment and reuse facilities between 2016 and 2020^{51, 52}. In India, the
337 total installed capacity for domestic wastewater treatment from urban areas is 44% of total
338 produced wastewater (31.8 million m³/d vs. 72.4 million m³/d of generated wastewater) but the
339 actual treatment is only 28% (20.2 million m³/d). Wastewater reuse is 49% in Chennai, 19% in
340 Delhi and 6% in Hyderabad⁵³. The availability of large surface areas at relatively low costs
341 allows to opt for more energetically sustainable solutions, such as in the case of the Western
342 WWTP in Melbourne, where sequential anaerobic and aerobic lagoons have been successfully
343 implemented ([Table 1](#)).

344

345 **Assessment of secondary treatment processes**

346 Members of the international scientific network, i.e. NEREUS COST Action ES1403⁵⁴ titled
347 "New and emerging challenges and opportunities in wastewater reuse, chaired by the
348 corresponding author, undertook a thorough analysis of full-scale and pilot-scale secondary
349 biological technologies for a group of target MCEC relevant for wastewater reuse. 33 chemical
350 MCEC were selected according to their relevance for potential uptake by crops, public health
351 issues and/or environmental safety implications. Additionally, ARB and ARGs were included
352 because of their critical relevance to public health and, above all, their recognized persistence
353 and self-replication potential in environmental compartments. The analysis focused on the
354 performance of Conventional Activated Sludge (CAS), Membrane Bioreactors (MBR), and
355 Moving Bed Bioreactors (MBBR), and Constructed Wetlands (CW)^{54, 55}. This analysis, ([Table](#)
356 [2](#)), which is still valid today, showed the potential of four secondary biological treatment
357 technologies for the removal of selected MCEC and the need to reach effluent quality suitable

358 for irrigation purposes⁵⁵. This in turn, allowed defining the research needs for the analyzed
359 technologies in respect to the removal of MCEC.

360 The CAS process has been extensively studied for mitigating the presence of MCEC.
361 However, the traditional aerobic layout proves ineffective, and enhanced performance is
362 achievable with elevated solid retention times or sequential anoxic-aerobic phases for specific
363 MCEC. Therefore, it is imperative to focus research efforts on optimizing process performance
364 through the adjustment of operational parameters and exploring synergies with advanced
365 technologies for tertiary treatment⁵⁵. While MBR technology is well-researched for MCEC
366 removal, a comprehensive understanding of mechanisms, such as fouling layer interactions and
367 the role of membrane surface deposits, is still lacking. Additionally, the identification of
368 bacterial species or enzymes responsible for chemical MCEC removal, determination of
369 optimal operating conditions, and elucidation of (bio)transformation products during MBR
370 treatment are essential. Integrated MBR systems with cost-effective, synergistic effects warrant
371 further development, emphasizing system optimization, scalability, and full-scale validation⁵⁵.
372 CWs represent a novel research area for MCEC removal, yet current CWs exhibit limitations
373 in effectively eliminating MCEC. Further research is needed to assess the feasibility of full-
374 scale applications, with process efficiency contingent on operational mode, design, substrate
375 type, and the presence of specific plants. Considering the unique prerequisites of CWs,
376 including large area requirements and potential temperature dependencies, site-specific
377 application considerations are crucial⁵⁵. A limited number of studies have explored the fate of
378 MCEC in full-scale MBBR processes. Comprehensive research projects should delve into
379 MCEC removal pathways, including biofilm diffusion and hydrodynamic conditions, while
380 investigating the regulation of bacterial communities through biofilm thickness. While the
381 active biomass in MBBR biofilms holds potential for recalcitrant organic MCEC removal, the
382 thin biofilm often lacks sufficient biomass for realistic degradation in typical contact times.
383 Increasing available biomass in MBBR treatment trains is a crucial focus, and MBBR is a
384 noteworthy, advanced treatment technology for recalcitrant MCEC removal.

385 Despite the technology employed, the removal of MCEC relies on treatment conditions
386 and physicochemical properties of individual compounds. The complex and variable factors
387 influencing their fate underscore the unique microbial ecosystems of each plant. As a result,
388 assessing the impact of MCEC on wastewater receiving environments and enhancing MCEC
389 removal necessitate ongoing research. This emphasizes the importance of biological processes
390 in maximizing MCEC removal while ensuring the effective removal of conventional
391 parameters for the safe reuse of reclaimed water.

392 **Assessment of advanced treatment processes**

393 The review paper by Rizzo et al.⁵⁶, again within the framework of the NEREUS COST
394 Action ES1403⁵⁴, critically examined well-established techniques such as ozonation, activated
395 carbon (AC), and membranes, along with emerging methods like Advanced Oxidation
396 Processes (AOPs). The evaluation focused on several key aspects: (i) the efficacy of these
397 methods in removing MCEC from wastewater, (ii) their respective advantages and limitations,
398 (iii) potential challenges hindering the widespread adoption of homogeneous AOPs, (iv)
399 technological constraints and future perspectives for heterogeneous processes in the mid to
400 long term, and (v) a thorough technical and economic comparison among diverse processes
401 and technologies. The review outlined the main gaps in the understanding and implementation
402 of advanced wastewater treatment, which persist still today (Table 3).

403 Advanced methods for urban wastewater treatment, including activated carbon (AC),
404 adsorption (utilizing both powdered AC and granular AC), ozonation, and nanofiltration or
405 reverse osmosis membrane filtration, demonstrate effectiveness in removing MCEC⁵⁶.
406 Notably, economically viable full-scale implementations of AC adsorption and ozonation have
407 recently been established in Germany and Switzerland. While filtration with tight membranes,
408 such as in nanofiltration or reverse osmosis, is found to be more cost-intensive, full-scale
409 applications of reverse osmosis membranes in potable reuse projects have been successful in
410 the United States, Singapore, and Australia, offering additional benefits in salinity and metal
411 reduction. However, the treatment of concentrated waste streams in membrane filtration
412 processes warrants further evaluation.

413 In regions with high annual solar irradiation (between latitude 40°N and 40°S), solar-
414 driven AOPs emerge as competitive alternatives for MCEC removal. However, these
415 technologies are currently at a lower technology readiness level, posing challenges for direct
416 comparisons. Similarly, many innovative processes and novel combinations of existing
417 processes, often studied only at small scale or under non-realistic source water conditions,
418 require further development and evaluation⁵⁶.

419 The removal of MCEC from wastewater through AOPs is influenced by operating
420 parameters, water matrix composition, and abatement mechanisms unique to each treatment
421 technology. Ozonation and AOPs may generate oxidation transformation products with
422 potential biological effects, necessitating eco-toxicological studies. Post-treatments such as
423 sand filters or biological activated carbon have proven effective in addressing this concern after
424 ozonation but come with increased treatment costs⁵⁶.

425 The significant local wastewater variability in MCEC and water matrix characteristics
426 underscores the need for optimization tailored to each application, encompassing choices in
427 adsorbents and/or flocculants, membrane selection, dosing procedures, system configurations,
428 mixing conditions, and more. Systematizing knowledge and developing tools for predicting
429 MCEC behavior in wastewater treatment is crucial.

430 The lack of comparative investigations between established methods (AC adsorption
431 and ozonation) and emerging processes (novel AOPs) complicates the conclusive evaluation
432 of the most suitable and cost-effective solutions for advanced urban wastewater treatment. Site-
433 specific limitations, such as space availability and solar energy accessibility, may lead to
434 different conclusions for different locations. Importantly, these comparative investigations
435 should consider various relevant endpoints for safe effluent discharge or reuse, including
436 MCEC removal, effluent toxicity, bacteria inactivation, by-products minimization or removal,
437 antibiotic resistance control, and treatment cost.

438

439 **Decentralized wastewater treatment**

440 Rural domestic sewage, especially in developing countries and low density population areas is
441 one of the foremost obstacles to achieving several global SDGs⁵⁷. Globally, less than 60% of
442 people are connected to sewage collection systems, however sewage treatment stands at a much
443 lower percentage, with the lowest proportion being reported in the Global South^{12, 58}.
444 Centralized wastewater treatment systems are a common choice in urban areas and megacities,
445 but typically infeasible and lacking in poor rural areas due to the significant construction,
446 operation and maintenance costs⁵⁹. To this effect, decentralized wastewater treatment systems
447 constitute a flexible, emerging approach for sustainable and economic water reuse at the point
448 of wastewater generation, in rural and suburban areas and scattered developments⁶⁰.

449 The application of decentralized wastewater treatment systems is not exclusively
450 independent from the traditional centralized system, as the integration of the two systems may
451 be preferable depending on the local conditions⁶¹. Several technologies have been reported in
452 decentralized systems, including among others constructed wetlands, anaerobic and biofilm
453 reactors, and membrane bioreactors (MBR),^{62,63} which might be applied individually or jointly.
454 However, more research is needed into the capacity of decentralized wastewater treatment
455 facilities to efficiently remove MCEC from wastewater intended for reuse, as limited research
456 so far exists regarding the type of decentralized technologies in relation to their efficacy to
457 remove a wide range of pathogens and MCEC⁶⁴.

458 Centralized urban wastewater treatment and reuse schemes are capable of supporting
459 intensive, mechanized agriculture practiced at the large scale, whereas decentralized ones can
460 support localized, less intensive and more traditional farming by full-time or part-time farmers
461 seeking additional income⁶⁵ (Fig. 2).

462

463 **TW-irrigated agricultural hotspots**

464 The climate-water-energy-food nexus, along with health benefits, can thrive in TW-irrigated
465 hotspots of agricultural production in urban and peri-urban areas. This involves producing food
466 within environmentally safe systems, ensuring an adequate and healthy supply for consumption
467 in local markets, simultaneously, implementing and promoting relevant SDGs⁶⁶. In this
468 context, such agricultural hotspot areas could be developed near either centralized or
469 decentralized WWTPs. Such an approach could result in freshwater savings, reduced
470 greenhouse gas (GHG) emissions and energy consumption through alleviating water pumping
471 and water and food transportation needs, while promoting public health by limiting irrigation
472 with untreated wastewater⁶⁷.

473 The example of the North-Western Sahara Aquifer System covering large parts of
474 Algeria, Tunisia, and Libya (one of the water-scarcest regions in the world) highlights the
475 importance of TW reuse for agricultural irrigation. TW reuse-based agricultural hotspots in this
476 region facilitated the alleviation of groundwater stress by halving the volume of water
477 abstracted from the deep aquifer, reducing the energy costs of pumping by about 15%, and
478 supporting sustainable food production in peri urban areas⁶⁸. In the rapidly developing city of
479 Hyderabad, India, TW reuse in agriculture resulted in food production with minimized
480 pathogen contamination compared to untreated wastewater irrigation, 33% reduction in GHG
481 emissions, and direct groundwater savings⁶⁹. The implementation of an integrated peri-urban
482 wastewater treatment and reuse system in Milan, Italy, is predicted to result in energy savings
483 of up to 7.1%, and a reduction of GHG emissions by up to 2.7%. The production of high quality
484 crops will generate more revenue and the recovery of nutrients will reduce input costs, as
485 well⁷⁰. In Jordan, a country facing increasing water scarcity, the decentralization of treatment
486 plants to rural and urban settlements and the reuse of TW for irrigation is considered as an
487 important component for the sustainable management of available water resources⁷¹.
488 Constructed wetlands provide decentralized wastewater treatment in rural communities in
489 India, thus allowing the production of TW-irrigated food in small agricultural hotspots with
490 reduced disease burden and decreased environmental pollution⁷².

491 In summary, reuse for irrigation has evolved with advancements in treatment
492 technologies, providing a valuable water source for agriculture. Reclaimed water, treated to
493 meet quality standards, offers economic, social, and environmental benefits. However, despite
494 progress, the percentage of treated wastewater reused for agriculture remains low.
495 Comprehensive systems, from treatment plants to irrigation, are essential for sustainability.
496 Decentralized wastewater treatment can address rural challenges. TW-irrigated agricultural
497 hotspots, exemplified in water-scarce regions, showcase significant water savings, reduced
498 energy consumption, and improved food production sustainability.

499

500

501 **TW reuse for irrigation: pros and cons**

502 The use of TW for irrigation offers several benefits, but careful consideration of the reclaimed
503 water quality is required to mitigate associated drawbacks. In this section we aim to highlight
504 the agronomic advantages and drawbacks of reusing TW in agriculture, as well as the
505 challenges related to the presence of MCEC in TW applied for irrigation.

506

507 **Effects on the agroenvironment**

508 In water scarce regions, TW irrigation offers farms with year-around stable and low-cost water
509 source. However, the agronomic implication of TW for crop irrigation is far from been a simple
510 change in water resources. This practice offers a spectrum of advantages and disadvantages
511 that can impact the overall sustainability and productivity of agricultural systems.

512 Implication of TW for crop irrigation can offer nutrient enrichment of the agro
513 environment which stands out as a significant agronomic advantage. TW carries essential
514 macro nutrients such as nitrogen, potassium, and phosphorus, functioning the water as a
515 fertilizer for crops. By integrating TW into irrigation practice, farmers can reduce their reliance
516 on commercial fertilizers, thereby cutting costs and minimizing the environmental footprint
517 associated with fertilizer application. This practice must therefore be associated with routine
518 monitoring and appropriate training of the farmers. Otherwise, access of nutrients will be
519 provided causing pollution rather than environmental and agronomical benefits. A potentially
520 notable disadvantage of TW as a sole irrigation source is related to the potential for soil salinity.
521 TW often contains elevated levels of salts, which can accumulate in the receiving soils and
522 more importantly impede crop growth crops⁷³. Furthermore, TW irrigation can contaminate
523 groundwater situated below irrigation sites⁷⁴. To reduce the potential risk, routine monitoring

524 of TW as well as region/state-level water management must be implemented to reduce salt
525 input into the sewage system. In various occasions, TW can be characterized by high sodium
526 adsorption ratio. This can deteriorate soil structure by clay swelling and dispersion leading to
527 unfavourable soil physical and hydraulic properties⁷⁵. Long-term TW irrigation can therefore
528 reduce water and oxygen availability to plants, ultimately harming crop performance.

529 The addition of dissolved and particulate organic matter originating from TW to soils
530 can change their physicochemical properties. One of the physical effects resulting from TW
531 application is water repellence. In a water-repellent soil, soil wettability is lower promoting
532 flow instabilities that lead to the formation of preferential flow paths⁷⁶. Also, careful attention
533 should be placed to boron (B) which is abounded in detergents and known to induce plant
534 toxicity at low concentration. Like sodium, boron level should be controlled at the source since
535 it is not removed during wastewater treatment. Furthermore, if TW is not adequately treated,
536 the water may carry pathogens that can harm farmers and infect crops and pose risks to human
537 health through the food chain. Thus, strict adherence to water quality standards and robust
538 monitoring systems are imperative to address this concern.

539 The agronomic advantages of using TW for crop irrigation come with challenges.
540 Balancing these factors is essential for realizing the potential benefits of TW in agriculture
541 while mitigating the associated risks.

542

543 **MCEC-related challenges**

544 Along with advantages, TW reuse in agriculture comes with limitations and considerations,
545 mainly driven by the inability of currently applied treatment technologies to completely remove
546 MCEC. Their environmental fate, as well as their potential impacts on living organisms pose
547 several challenges and therefore constitute an important research topic in the field of TW reuse
548 in agriculture.

549 Although the reuse of TW for agricultural irrigation has gained acceptance as a viable
550 practice to service crop nutrient needs and water requirements, and major advances have been
551 made that support the production of TW that is safe for reuse, TW can still contain MCEC that
552 can induce negative environmental and health impacts^{77, 78}. MCEC can include biocides, flame
553 retardants, micro(nano)plastics, pesticides, personal care products, pharmaceuticals, synthetic
554 and natural hormones, and antimicrobial resistance (AR) determinants, such as antibiotic
555 resistant bacteria (ARB), resistance genes (ARGs) and relevant mobile genetic elements⁷⁹ (Fig.
556 3).

557 Biological treatment technologies such as conventional activated sludge (CAS) and
558 MBR, and combinations with membrane filtration methods (nanofiltration and reverse
559 osmosis), ozonation, advanced oxidation processes, and adsorption processes can achieve from
560 sufficient to very high removals of MCEC^{80, 81}. At the same time, these combinations of
561 technologies and widely used disinfection technologies including chemical oxidation agents
562 like chlorine and physical agents such as ultraviolet irradiation⁸², as well as emerging
563 disinfection processes using peracetic acid⁸³ and performic acid⁸⁴ bear limitations in addressing
564 holistically MCEC. Limitations include the fact that even though some technologies are
565 successful in removing parent compounds of micropollutants and chemical contaminants of
566 emerging concern, they do so while generating transformation products (often more harmful
567 than their parent compounds), toxicity, mutagenicity, and endocrine disruption effects for
568 example⁸⁵, the selection of potentially pathogenic bacteria (repair and/or regrowth) and
569 alteration of wastewater microbial community structures⁸⁶.

570 Furthermore, it is crucial to consider the impact of external contamination on treated
571 wastewater (TW) storage, particularly given that storage facilities are often uncovered.
572 Additionally, the influence of transportation piping, primarily attributed to biofilm formation,
573 (including also the pipes material and roughness) on the potential for post-treatment repair and
574 regrowth of harmful microorganisms, including pathogens and antimicrobial-resistant bacteria
575 (ARB), should be thoroughly examined in the context of reuse systems^{87, 88}. Currently, several
576 important questions concerning the presence of MCEC in TW reuse systems and their
577 subsequent release into the environment through TW irrigation remain, preventing potentially
578 a wider application of the practice of reuse^{89, 90}.

579

580 **Environmental fate of MCEC**

581 Advances in analytical techniques and instruments have enabled the acquisition of both
582 qualitative and quantitative information on organic pollutants in very low concentrations⁹¹.
583 Consequently, hundreds of micropollutants and chemical contaminants of emerging concern
584 are routinely detected and quantified in environmental matrices receiving TW downstream of
585 WWTPs, including TW-irrigated soils, surface and groundwater systems, parks, even drinking
586 water^{79, 89, 92}. Many of them are simultaneously released via treated effluents, forming cocktails
587 which vary in concentration and composition in receiving environments, both spatially and
588 temporally⁹³. Various micropollutants and chemical contaminants of emerging concern have
589 been shown to accumulate in TW-irrigated agricultural soils following transportation and
590 transformation (by both biotic and abiotic factors), to be taken up by wild and cultivated crop

591 plants and accumulated within their tissues^{89, 94}. Upon their entrance into the food web, a
592 number of them displaying favorable physicochemical properties can potentially
593 bioaccumulate in other organisms and in humans^{95, 96}, potentially provoking toxicity effects⁹⁷.

594 Studies performed under controlled conditions have uncovered mechanisms involved in
595 their uptake by plants, as well as their accumulation in different plant tissues, including edible
596 ones⁹⁸. In addition, it was shown that upon their uptake by plants, they can induce
597 transcriptomic and metabolomic rearrangements that impact normal plant physiology and
598 morphology, indicating stress responses^{99, 100}. Micropollutants and chemical contaminants of
599 emerging concern can be metabolized and detoxified in plant cells by a versatile system that
600 has strong similarities to those used by humans and animals, thus termed the ‘green liver’^{99, 101}.
601 Real-world field experiments (primarily on pharmaceutical compounds) and field surveys also
602 revealed their uptake and accumulation in the edible parts of crop plants under agricultural
603 conditions (the uptake potential is mostly affected by the plant species, the soil
604 physicochemical properties and environmental conditions governing evapotranspiration,
605 among others), as well as the potential associated human health risks¹⁰²⁻¹⁰⁴. Moreover, control
606 trials verified the presence of carbamazepine and its metabolites in the urine of people that
607 consumed vegetables collected from TW-irrigated fields for a prolonged period, compared with
608 control samples⁹⁵ (Fig. 3).

609 Accumulating evidence shows that WWTPs release significant quantities of
610 micro(nano)plastics into the environment as, despite the high removal efficiencies (up to 98%)
611 reported for currently applied secondary and tertiary treatment technologies, TW is
612 continuously released to the environment in huge volumes^{105, 106}. Due to their surface
613 properties, micro(nano)plastics can be colonized by wastewater microorganisms resulting in
614 the formation of dynamic biofilms, known as plastispheres¹⁰⁷, which interact with other co-
615 existing contaminants in WWTPs, including MCEC¹⁰⁸. Wastewater plastispheres can enhance
616 the persistence of AR elements and bacterial pathogens by favoring their microenvironment
617 and horizontal gene transfer^{108, 109} and limiting their inactivation by disinfection processes¹¹⁰,
618 thus accelerating their toxicological impacts in the downstream environments¹⁰⁹.

619 Micro(nano)plastics can accumulate in soil fauna, wildlife and plants and exert negative
620 impacts^{111, 112}. The uptake and accumulation of micro(nano)plastics in cultivated plants,
621 alongside other co-contaminants in TW and/or irrigated soil, can induce phytotoxic effects with
622 negative impacts on plant growth and development¹¹³. Moreover, the accumulation of
623 micro(nano)plastics in the edible parts of crop plants can further contribute to their
624 biomagnification in the food chain, with potential human health risks¹¹⁴. Thus, measures to

625 efficiently control and minimize the impact of micro(nano)plastics at the WWTP level should
626 be considered¹¹⁵.

627 Transformation products of micropollutants and chemical contaminants of emerging
628 concern often have similar molecular structure to their parent compound. They still contain the
629 toxicophore-like moiety, while some other derivatives incorporate almost the complete parent
630 compound structure and might thus show similar environmental behavior and bioactivity¹¹⁶.
631 Research has suggested that some TPs might pose a similar or greater risk than their active
632 parent compound exhibiting similar or higher ecotoxicological effects¹¹⁷. TPs along with their
633 parent compounds have been detected in the soil-crop continuum in TW-irrigated
634 agroecosystems^{118, 119}.

635 Regarding the current concerns about AR, the need to investigate the residual
636 antibacterial potential of antibiotic TPs is profound. While the relationship between the parent
637 antimicrobial compounds and AR is well documented, the impacts of their TPs on AR
638 development (through alternative or enhanced selective pressure on resistant bacteria) and on
639 TW-receiving environments are not well understood. Risk assessment studies on human and
640 environmental health should encompass not only parent compounds but also TPs as well as
641 other non-pharmaceutical selection pressures^{120, 121} (Fig. 3).

642

643 **AR determinants in TW-reuse schemes**

644 Irrigation with TW will entrain sub-minimum inhibitory concentrations of antibiotics, ARB,
645 ARGs and mobile genetic elements such as *intI1* into soil^{122, 123}. The enrichment of ARG
646 concentrations in TW-irrigated public park soil⁹², as well as the increase in the concentration
647 of antibiotic-resistant *E. coli* on the leaf surface of romaine lettuce following TW irrigation¹²⁴,
648 highlight the potential for human exposure to antibiotic resistant determinants as a result of
649 TW irrigation. However, no correlation of various investigated ARG concentrations between
650 TW and irrigated soils has been verified, despite the strong correlation of TW *intI1*
651 concentrations to those found in sandy soil fields, with a factor in this suggested to be
652 limitations of the quantification methods utilized¹²⁵.

653 Changes in the microbial community structure within soil-crop systems cannot be
654 ignored when considering potential AR determinant spread events in the agricultural
655 environment, as the abundance of putative antibiotic-resistant pathogens (often bearing
656 clinically relevant ARGs) might be impacted by TW irrigation, leading to selective pressures
657 acting on the resistome, especially in the presence of residual antibiotic concentrations^{126, 127}.
658 Advances in molecular and data analysis techniques, such as omics technologies and

659 bioinformatics methods, have offered increased resolution of genetic constituents of the
660 microbial community within various environmental matrices¹²⁸. The precise role of agricultural
661 practices on the dissemination of AR determinants in the agroecosystem and of their
662 subsequent entrance to the food web remains uncertain, largely due to very little data obtained
663 under real-world field scale conditions. The impacts on AR propagation posed by the climatic
664 conditions prevailing in a certain agricultural site, the applied soil amendment practices, the
665 type of irrigation system used, the cropping system and the type of crop cultivated, remain
666 largely unexplored^{123, 129, 130}.

667 A decreasing gradient of AR determinants has been observed in the soil-crop continuum,
668 as the ARG loads in soil and rhizosphere were found to be significantly higher ($\times 10^3$ - $\times 10^4$)
669 compared to those in the edible crop tissue¹³¹, with the ARGs *bla_{TEM}* and *sull* being of highest
670 abundance within the soil-crop system in the available studies¹³². On the other hand, the
671 prevalence of *intI1* and of *bla_{TEM}* and *sull*, was shown to be higher in *Lactuca sativa* compared
672 to *Lycopersicon esculentum* and *Vicia faba* L. crops, indicating the impact of crop species
673 selection on ARGs loads¹³¹. The prevalence gradient of AR determinant loads from TW-
674 irrigated soil to the above ground plant tissues showcases the impact that TW irrigation might
675 have on the soil microbiome, whereas AR determinants might in turn be taken up and/or
676 accumulate in crop tissue, though to a much lesser extent¹³¹.

677 Thus, plant rhizospheric and endophytic microbiome can be impacted by TW reuse
678 through the horizontal gene transfer of AR determinants in the soil and their transfer to
679 rhizospheric and plant bacteria, as stated previously^{133, 134}. In line with this, soil bacteria have
680 been shown to have the capacity to capture plasmids and mobile genetic elements from other
681 proximal bacteria and then migrate into the endophytic surface or internal tissue, thus spreading
682 these elements within the plant tissue microbiome along with nutrient plant uptake^{134, 135}.

683

684 **MCEC-mediated impacts on human health**

685 Limited research, together with technical risk assessment challenges currently hinder the
686 assessment of human health risks arising from exposure to AR determinants, sub-MIC
687 antibiotic concentrations and their associated TPs in TW and reuse environments^{121, 136}.
688 However, the associated potential risks driven by the environmental development and transfer
689 of AR to humans in the wastewater reuse settings should be evaluated having in mind the
690 international aspect of AR challenge, the Precautionary Principle, and the One Health concept
691 which recognizes the interconnectedness of humans, animals and the environment¹³⁷. To this
692 effect, AR hotspots and associated risks from reuse schemes should be counted and managed

693 alongside with risks derived from pharmaceutical manufacturing sites, food and animal
694 production (use of antibiotics in livestock, plant protection and aquaculture) and clinical
695 settings (hospitals)¹³⁸.

696 Currently, there are open discussions regarding the potential risks posed by the presence
697 of sub-lethal antibiotic levels (present in cocktails of parent compounds and TPs) and of
698 resistant endophytic bacteria in human gut as a result of the consumption of TW-irrigated
699 agricultural produce, and the potential of altering human microbiome and promoting adaptive
700 resistance selection¹³⁹⁻¹⁴¹. Risks assessment of AR should be grounded in the state of the
701 science and vetted by academic experts, and based on real-world research data on AR
702 determinants found in TW, soil and edible crops¹³⁹. The scientific community should address
703 relevant questions such as which are the relevant endpoints, risks thresholds and/or safe
704 exposure levels for ARGs when assessing AR risks. To enhance our understanding and to be
705 able to develop risk assessments for ARB and ARG in reclaimed water, it is imperative that
706 future data collection efforts adopt a standardized approach in reporting. While acknowledging
707 the importance of concentration data per unit volume, it's also worthwhile to consider that other
708 units may offer valuable insights in different scenarios¹⁴². It is also imperative to provide
709 sample metadata, encompassing a comprehensive explanation of the treatment technologies
710 employed and a delineation of the intended reuse purposes, methods for conveyance to the
711 point of use, and available physicochemical water quality data. Additional research is needed
712 aimed at identifying recommended ARB and ARG monitoring targets and for developing
713 approaches to incorporate metagenomic data into risk assessment^{136, 143}.

714 In summary, the use of TW for crop irrigation has both advantages and challenges. On
715 the positive side, TW serves as a cost-effective and stable water source, enriching crops with
716 essential nutrients and reducing reliance on commercial fertilizers. However, challenges arise
717 from potential soil salinity, water repellence, and the presence of micropollutants, including
718 pharmaceuticals and antimicrobial resistance determinants. Current treatment technologies
719 have limitations in completely removing these contaminants, posing environmental and health
720 risks. Adequate monitoring, adherence to water quality standards, and further research on the
721 fate of contaminants are crucial for balancing the agronomic benefits and challenges of TW
722 irrigation.

723
724
725

726 **Wastewater reuse governance**

727 The global promotion of sustainable and safe reuse of TW in agricultural irrigation has led
728 international organizations and countries to develop regulatory frameworks and guidelines.
729 These policies ensure that TW meets quality standards to protect the environment and human
730 and animal health, while also promoting social acceptance and facilitating the international
731 trade of food. Comprehensive regulations often include a permit system for the production and
732 use of TW for various applications. This system is based on respecting a set of microbial and
733 chemical quality standards which depend on the technical specifications of wastewater
734 treatment, such as secondary, tertiary, or advanced treatment, nutrient reduction, and
735 disinfection. Regulations also detail the types of crops that can be irrigated with TW, the
736 components of the irrigation system, and rules on restricted entry and harvesting intervals after
737 irrigation. They may also establish physical barriers, such as buffer zones, and regulate the
738 proximity of TW application to sensitive or protected ecosystems^{28, 43}. In addition to
739 established criteria for water quality, some policies suggest or impose the use of a risk
740 management approach to identify and manage health and environmental risks in all
741 components of the TW reuse systems, under both regular conditions and emergencies²⁸. For
742 example, the Australian Guidelines for water recycling¹⁴⁴ and the US EPA Guidelines for
743 Water Reuse¹⁴⁵ require a risk management framework that could be voluntarily applied to water
744 reuse systems in their territories, allowing for the regional adaptation of rules. The International
745 Organization for Standardization (ISO) and the World Health Organization (WHO) also
746 developed risk management-based guidelines for the safe reuse of TW that could be applied
747 worldwide, particularly in less developed countries where local legal frameworks are
748 missing^{146, 147, 148}. In the EU, the Water Reuse (EU) Regulation 2020/741 aims at gaining
749 benefits of wastewater as a resource and alleviate the increasing water scarcity under the effects
750 of climate change⁴³. In addition to providing EU uniform minimum water quality and
751 monitoring criteria, this regulation requires a mandatory risk management plan (Fig. 4) applied
752 to water reuse schema in all the EU Member States (except those that have decided to make
753 use of a regulatory opt-out clause). To this effect, the Joint Research Centre (JRC) of the
754 European Commission developed an array of technical guidelines that can be applied for
755 assessing and managing health and environmental risks associated with water reuse systems²⁸.
756 Other countries in which TW reuse in agriculture is well-established have also developed their
757 own regulatory framework, including the Israeli water reuse law¹⁴⁹ and the Chinese water reuse
758 guidelines¹⁵⁰. As of January 2023, a national-level framework on the safe reuse of treated water

759 that provides guidelines on preparing reuse policies was launched in India¹⁵¹. Despite the
760 establishment of regulatory frameworks and guidelines, governance strategies for water reuse
761 need to address various challenges due to fragmented knowledge and expertise, diverse
762 institutions, a mix of stakeholders involved, and the willingness to implement policies. These
763 strategies should consider the interdisciplinary scientific evidence, acting on the science–
764 policy–practice interface for the coproduction of accepted governance solutions¹⁵². The main
765 regulatory frameworks currently applied around the world are described in [Box 3](#).

766

767 **Risk management frameworks**

768 The assessment and management of health and environmental risks associated with the reuse
769 of reclaimed water in agricultural irrigation, are addressed by several international guidelines,
770 and standards. Examples are the EU Water Reuse Regulation 2020/741⁴², the ISO 20426:2018
771 - Guidelines for Non-Potable Water Reuse¹⁴⁶, the ISO 16075:2020 - Use of Treated Wastewater
772 for Irrigation Projects¹⁴⁷, the WHO Guidelines for the Safe Use of Wastewater¹⁴⁸ and
773 Quantitative Microbial Risk Assessment¹⁵³, the WHO Sanitation Safety Planning Manual¹⁵⁴,
774 the Australian Guidelines for Water Recycling¹⁴⁴ and the US EPA Guidelines for Water
775 Reuse¹⁴⁵.

776 The WHO¹⁴⁸ and the Australian Guidelines¹⁴⁴, have influenced the structure of the risk
777 management plan ([Fig. 4](#)) proposed by the Technical Guidance on the Water Reuse Risk
778 Management for Agricultural Irrigation Schemes in Europe²⁸. Some of its technical
779 components, including identification of health hazards, health risk management framework,
780 environmental risk assessment on freshwater resources and the effects of reclaimed water on
781 soil and crops were developed based on relevant parts of the ISO 20426:2018¹⁴⁶, the ISO
782 16075:2020¹⁴⁷, and the Australian Guidelines¹⁴⁴. The risks to be addressed can be grouped into
783 2 categories: a) health risks to humans exposed to reclaimed water (workers, bystanders, and
784 residents in nearby communities), and b) risks to the local environment (surface waters and
785 groundwater, soil, and relevant ecosystems).

786 Considering that a water reuse system complies with the minimum requirements for
787 water quality of the Annex I of the Water Reuse European Regulation, the overall objective of
788 a risk management plan²⁸ is to guarantee that a water reuse system operates while ensuring the
789 protection of the health of workers, farmers, and consumers, and safeguarding the environment.
790 The risk management plan is considered as a tool of paramount importance to ensure the
791 integration of site-specific particularities and requirements into a larger regional, national, and
792 even European framework, usually defined by ordinances, laws and the EU Water Acquis. The

793 plan must be based on 11 key elements of the risk management plan (KRM) representing the
794 basis to ensure that the reclaimed water is used and managed safely to protect the human and
795 animal health and the environment²⁸ (Fig. 4, Box 4).

796

797

798 **Sustainability of wastewater reuse**

799 Wastewater treatment contributes significantly to anthropogenic GHG emissions and global
800 warming. However, technological innovations can mitigate energy consumption and enhance
801 circularity by recovering valuable resources, such as nutrients and other by-products. Below,
802 we discuss the current drawbacks in conventional treatment technologies and the potential
803 provided by technological advancements for energy and resource recovery.

804

805 **Major challenges and solutions**

806 Conventional wastewater treatment as currently applied in WWTPs is energy demanding and
807 a serious GHG emitter, thus contributing to global climate change¹⁵⁵. Modern wastewater
808 collection and treatment processes account for ~3% of global electricity consumption and total
809 GHG emissions, despite the substantial improvements achieved in the sector to date^{156, 157}. The
810 energy demands of CAS-based biological treatment and anaerobic sludge digestion can be as
811 high as 0.6 kWh m⁻³ of wastewater treated, depending on the process configuration and effluent
812 composition, with most of the energy consumed by biological aeration and mechanical
813 pumping^{158, 159}. Besides their high energy demand and large environmental footprint, WWTPs
814 are currently also characterized by low resource recovery and cost effectiveness, as they were
815 primarily designed to reduce effluent nutrients, suspended solids and pathogenic microbial
816 loads in order to protect downstream users and environments¹⁶⁰.

817 Climate change effects on water availability, energy and the resources crisis, all call for
818 a paradigm shift in the water-energy-sanitation-food-carbon nexus in a circular economy
819 framework, with sewage as the core backbone. Thus, the concept of ‘sewage collection,
820 treatment and disposal’ is redefined to ‘reuse, recycle, and energy and resource recovery’^{161,}
821 ¹⁶². Wastewater is a massive untapped resource of water, energy, nutrients and other products^{12,}
822 ^{155, 159}, which can potentially change WWTPs into energy and resource recovery facilities in
823 which wastewater and sludge will be used as raw material sources, promoting associated SDGs
824 and net-zero carbon schemes¹⁶³ (Fig. 5).

825 Although numerous technologies for the recovery of water, energy, fertilizer, and other
826 products from wastewater have been explored in the academic and industrial arenas, few of
827 them have ever been applied on a large scale. This is primarily due to technical immaturity
828 and/or non-technical bottlenecks such as costs, resource quantity and quality, operational
829 distractions, acceptance, and policy¹⁶⁰. Consequently, the implementation of full-scale circular
830 economy-oriented technologies in the wastewater sector is still very limited, with most
831 wastewater management utilities focusing on wastewater collection, treatment and disposal
832 rather than resource recovery^{164, 165}. However, the upgrade of technology readiness level,
833 economic performance and environmental benefits of these green technologies is expected to
834 promote their wider adoption in the coming years¹⁶³.

835

836 **Energy and carbon neutrality**

837 Although wastewater collection and treatment require substantial amount of energy, WWTPs
838 can be transformed to energy neutral or net positive facilities through the recovery of energy
839 contained in wastewater itself. Indicatively, the thermal energy released through the oxidation
840 of the organic compounds contained in wastewater is approximately 9-10 times greater than
841 the energy requirements of a typical WWTP (0.6 kWh m⁻³), thus recovering the chemical
842 energy contained in sewage is economically profitable^{166, 167}. The embedded thermal (~80%),
843 chemical (~20%) and hydraulic (<1%) energy contained in wastewater can be recovered in the
844 form of heating or cooling, biogas and electricity generation through either new or hybrid
845 technologies or by modifying the existing ones¹¹.

846 The anaerobic digestion process that has been applied for decades in WWTPs to stabilize
847 sludge produces biogas that can be utilized for combined heat and power, and can potentially
848 satisfy more than half of the energy needs of a typical conventional aerobic treatment plant^{159,}
849 ¹⁶⁸. The energy that can be recovered from the total volume of wastewater produced globally
850 through the conversion of biogas released by anaerobic digestion can be enough to provide
851 electricity to 158 million households or to up to 632 million people, with projections for steady
852 increase due to the increasing volumes of produced wastewater¹⁶⁹. Co-digestion of sewage
853 sludge with municipal waste can further result in improved biogas production rates in the
854 anaerobic digestion process leading to self-sufficient and energy positive WWTPs, while also
855 reducing the amount of sludge for incineration or landfill^{163, 170}.

856 Other anaerobic processes, such as anaerobic membrane bioreactor and upflow anaerobic
857 sludge blanket reactor are finding their way to the market, offering advantages such as
858 improved effluent quality, low sludge production, compact size and high biogas production,

859 which in turn promote their energy neutrality^{171, 172}. In this line, the anaerobic ammonium
860 oxidation process, either used as side stream or mainstream treatment for nitrogen removal (up
861 to 87%) can result in lower aeration demands and substantial energy savings (more than half
862 of influent COD can be converted to methane gas and at least 75% reduction in sludge can be
863 achieved)¹⁷³. However, the process still transforms ammonium to dinitrogen gas (N₂), as the
864 underlying principle of all biological nitrogen removal processes remains unchanged
865 (conversion of ammonium to nitrogen gas), failing to recover nitrogen¹⁷⁴.

866 Salinity gradient energy treatment processes, including pressure retarded osmosis,
867 reverse electrodialysis and single-pore osmotic generators can be characterized as mature
868 breakthrough technologies with power density comparable to intermittent solar and wind
869 energy¹⁶³. Moreover, bioelectrochemical systems, particularly microbial fuel cells,
870 photocatalytic fuel cells and microbial electrolysis cells display numerous benefits in
871 wastewater treatment and energy recovery when applied individually or in treatment trains,
872 although optimization of their architecture and durability, and lower installation costs are still
873 required^{175, 176}. The ability of microbial fuel cells to produce green hydrogen of very high purity
874 can potentially reduce the overall cost of this technology, while also promoting decarbonization
875 and the green energy transition¹⁷⁷ (Fig. 5).

876

877 **From wastewater to resource**

878 Besides potentially providing a safe alternative source of freshwater, wastewater could also
879 become a valued source of fertilizer nutrients and mitigate existing shortages in nutrients
880 supplies in agriculture^{178, 179}. Based on 53 wastewater quality datasets from across the world,
881 the average concentrations of major nutrients in wastewater were estimated to be 43.7, 7.8, and
882 16.5 mg L⁻¹ for nitrogen (N), phosphorus (P) as P₂O₅, and potassium (K) as K₂O respectively.
883 These nutrient concentrations are close to those reported in medium strength wastewater¹⁸⁰.
884 These nutrients concentrations and the global volumes of wastewater were used to estimate
885 that the nutrients potentially embedded in wastewater may contain up to 16.6, 3.0 and 6.3 Tg
886 (10⁹ kg) of N, P, and P, respectively, representing 14.4, 6.8 and 18.6 % of the respective global
887 fertilizer nutrient demands, or 13.6 billion \$ of potential total revenue¹⁶⁹. Nutrient recovery
888 from wastewater could thus constitute a major step towards circular economy, as it can promote
889 reuse and recycling, and effectively alleviate the need of applying energy-demanding and
890 environmental polluting processes for nutrient resource extraction and fertilizer
891 manufacturing¹⁶⁵.

892 Several nutrient recovery processes have been developed and applied either to the
893 mainstream wastewater treatment technologies or to the ‘side streams’ associated with sludge
894 handling. These processes include biological, electrochemical, ion exchange, crystallization or
895 membrane systems^{165, 181}. However, system combinations and plant-wide configurations are
896 necessary, as none of these methods alone can provide complete recovery of all major
897 nutrients^{165, 166}.

898 Struvite or vivianite crystallization is one of the most promising technologies for
899 recovering P (over 60%, depending on the physicochemical properties of wastewater) and to
900 lesser extent N (20-30%) and Mg in WWTPs. It can be used either for the main stream water
901 line or side streams (for example, anaerobic membrane bioreactor effluent or water from sludge
902 dewatering systems), and is currently at technology readiness level 7 or higher¹⁸². Integration
903 of membrane-based technologies such as osmotic MBR, electro dialysis and bioelectrochemical
904 systems can result in high N and/or P recovery even at the full-scale^{165, 183}. Moreover,
905 microalgae or autotrophic hydrogen oxidizing bacteria grown in photobioreactors or open
906 systems treating wastewater can display high nutrient recovery rates (50 to 70%) in the
907 produced biomass, which can subsequently be transformed into several end products, such as
908 fertilizers or animal feedstock rich in amino acids^{184, 185}.

909

910 **Sewer mining for valuable products**

911 The paradigm shift of changing WWTPs from wastewater treatment and disposal facilities to
912 resource recovery facilities can be further reinforced through the recovery of value-added by-
913 products. High monetary value by-products can be recovered in side streams, including sludge
914 handling, mainly by fermentation processes, bioelectrochemical systems and microalgae
915 treatment. Mining wastewater for hydrogen by microbial fuel cells to produce green energy
916 can provide important revenues which in turn lower treatment cost¹⁷⁷. Valuable trace elements
917 such as gold, silver, nickel, platinum and other can be also recovered through various
918 electrochemical extraction processes¹⁸⁶. Macroalgae-based integrated biorefinery, applied in
919 microbial fuel cells, photobioreactors or open systems can remediate wastewater with the
920 simultaneous production of bioelectricity and value-added products, as the harvested
921 microalgae biomass contains valuable biomolecules (for example, biopolymers, cellulose,
922 single-cell protein, polyhydroxyalkanoates, volatile fatty acids), which in turn can facilitate the
923 production of biofuels, bioplastics, biochemicals, nutrition supplements for animal feedstock,
924 antioxidants and nanoparticles^{187, 188}.

925 In summary, wastewater treatment can transition to a sustainable model through
926 technological innovations promoting energy and resource recovery. Shifting towards a circular
927 economy, where sewage is a resource, can transform wastewater facilities into energy-neutral
928 or positive entities. Technologies like anaerobic digestion, salinity gradient energy processes,
929 and microbial fuel cells offer promising avenues for energy recovery. Additionally, nutrient
930 recovery from wastewater can address global fertilizer demands, fostering a circular economy.
931 Sewer mining for valuable by-products further strengthens the paradigm shift towards resource
932 recovery in wastewater management.

933
934

935 **Future wastewater treatment systems**

936 Future technology development will underpin the sustainability and safety of TW reuse and
937 support expansion of this important sector. Further efforts by industry and academia are needed
938 to ensure that TW continues to meet the quality standards required under comprehensive
939 regulatory frameworks that are also in a state of development and essential for sustainable and
940 safe TW reuse.

941

942 **Upgrades in existing technologies**

943 Biological oxidation of organic and of nitrogenous compounds through CAS treatment
944 following the primary mechanical pre-treatment has been at the core of municipal wastewater
945 treatment since its introduction over a century ago. Large scale available advances to CAS
946 treatment include the MBR process and related modifications (which are still an integration of
947 CAS process and membrane filtration to separate treated water from biomass), as well as
948 granular sludge systems and anaerobic digestion^{189, 190}. However, the increasing complexity of
949 wastewater streams, stringent regulations on minimum discharge standards, and the myriad of
950 MCEC that can pose threats to environmental and human health are increasingly leading to the
951 introduction of advanced tertiary treatment technologies into treatment trains, post CAS or
952 MBR treatment.

953 Upgrades in WWTP treatment lines typically include unit processes such as ozonation,
954 activated carbon adsorption, chemical disinfection with chlorine or peracetic acid, ultraviolet
955 irradiation, advanced oxidation processes and membrane filtration and separation processes
956 such as ultra- or nano-filtration and reverse osmosis³³. Advanced treatment and disinfection
957 technologies in treatment trains should be selected to suit the intended water reuse, meet
958 discharge standards, mitigate health risks, service economic and environmental requirements

959 (limit energy use and GHG emissions), and based on life cycle assessment and decision support
960 tools¹⁹¹.

961

962 **Advancements applied at a large scale**

963 Bacterial and algal-bacterial aerobic granular sludge treatment has been implemented both at
964 the pilot and full scale levels with very good efficiency in terms of both effluent quality and
965 energy cost savings¹⁸⁹. The aerobic granular sludge systems commercialized worldwide under
966 the Nereda® technology tradename offer compact structure, lower energy requirement (35-
967 70%) and land footprint (40-50%), higher flexibility in emergency events (high loads),
968 excellent nutrient and organic pollutants removal, and also enable the recovery of valuable
969 products such as P, crude protein and biopolymers¹⁹². In addition, microbial electrochemical
970 technologies, specifically microbial fuel cells, electrolysis cells and recycling cells have been
971 successfully applied at the large scale for the treatment of industrial effluent, however several
972 challenges, mainly concerning high capital cost and low energy output, currently restrict their
973 scalability and hinder their full-scale application in municipal WWTPs¹⁹³.

974

975 **Innovations in wastewater treatment**

976 Nanotechnology and advanced materials are set to revolutionize the future of the wastewater
977 sector, as some materials offer unique benefits such as superior efficiency and selectivity, high
978 natural abundance, good recyclability, low production cost and sufficient stability to favor their
979 use in wastewater treatment¹⁹⁴. Nanomaterial-based membranes, including nanofibers-,
980 nanoparticles-, nanotubes-, nanocrystals-, nanowires- and nanosheet-based membranes can
981 substantially enhance MBR performance and reduce fouling, operation and maintenance
982 costs¹⁹⁵. Carbonaceous (for example, activated carbon, carbon nanotubes, carbon quantum
983 dots, graphene, or graphene oxide), or metal and metal oxide nanomaterials can be utilized as
984 nano- and micro-motors to enhance adsorption, mixing, photocatalysis and advanced oxidation
985 processes during wastewater treatment¹⁹⁶.

986 Technologies of the Fourth Industrial Revolution (4IR) constitute a technological catalyst
987 for all fields of human endeavor, and therefore could also be harnessed to support the climate-
988 water-energy-food nexus, facilitating the achievement of SDGs¹⁹⁷. For instance, computing,
989 digital transformation, digital twin, artificial intelligence, big data analytics and Internet of
990 Things (IoT) can facilitate online model-data optimization in wastewater treatment processes
991 and in reuse schemes (for example, smart farming), through sensors, high-resolution remote

992 sensing and communication technologies, and human-machine interaction for achieving
993 environmental and economic sustainability¹⁹⁸.

994 Artificial intelligence-driven data analytics can support WWTPs process design,
995 operation, and control. Its adoption can potentially reduce operating costs, improve system
996 reliability, predict maintenance requirements and conduct troubleshooting, thus increasing
997 water quality and process optimization¹⁹⁸. Artificial intelligence models have efficiently
998 managed biological¹⁹⁹ and MBR²⁰⁰ wastewater treatment processes in full scale WWTPs, by
999 predicting the performance, real-time problems and treated effluent quality. The reduction of
1000 costs and of management and maintenance challenges, as well as the elevated training of
1001 personnel will further facilitate the adoption of artificial intelligence in the wastewater
1002 treatment sector²⁰¹. Moreover, data-driven methods²⁰², as well as advancements in analytical
1003 chemistry tools, bioinformatics, and multi-omics data, can achieve fault detection, variable
1004 prediction and advanced control of WWTPs²⁰³ (Fig. 6).

1005 In summary, the future of wastewater treatment involves upgrading existing
1006 technologies, with advanced tertiary treatment technologies. Nanotechnology and advanced
1007 materials, particularly nanomaterial-based membranes, and the integration of 4IR technologies,
1008 are set to revolutionize wastewater treatment. These advancements promise improved
1009 efficiency, energy cost savings, and environmental sustainability, with artificial intelligence-
1010 driven data analytics playing a crucial role in optimizing processes and ensuring water quality.

1011

1012

1013 **Summary and future directions**

1014 Water management schemes around the world should be designed and implemented within a
1015 context of diminishing water availability posed by continuously growing demands and
1016 increasing stress to water resources driven by over-abstraction, pollution, and climate change.

1017 Within this setting, improved wastewater management stands as a major catalyst for sustainable
1018 development, simultaneously protecting human health and the environment, and promoting
1019 circular economy, rural development, and natural resource management. Applied wastewater
1020 treatment technologies can produce TW of sufficient quality to be fit-for-purpose for safe reuse
1021 in a variety of different applications. It is estimated that the total volume of TW produced
1022 globally can satisfy nearly 15% of all irrigation water needs, thus supporting the
1023 expansion/maintenance of irrigated agriculture and promoting food security, while also
1024 releasing equal quantities of freshwater for other uses. Decentralized and hybrid wastewater

1025 treatment approaches can provide flexible and resilient solutions fitted to local conditions,
1026 further facilitating the sustainable and safe production of food for local markets.

1027 The energy intensive linear approach currently applied in most wastewater treatment
1028 systems can potentially evolve to become fully resource efficient and circular, by shifting to
1029 the ‘reuse, recycle and resource recovery’ paradigm. Within this circular approach,
1030 technological opportunities can transform WWTPs into water, energy, and nutrient recovery
1031 facilities, achieving energy-carbon neutrality. To this end, effective management practices
1032 enforced by appropriate governance and regulatory frameworks and technological innovation
1033 can offer further opportunities towards transforming wastewater reuse at the global level,
1034 especially in developing countries. To progress efforts in this area, governmental and
1035 intergovernmental organizations should devote effort and resources to promote and fund
1036 wastewater treatment and reuse in agriculture in developing countries. This is especially
1037 important because over 80% of global wastewater is discharged untreated (over 95% in some
1038 of the least developed countries). This untreated wastewater can be used directly or indirectly
1039 for the production of potentially contaminated feed or food that can potentially be consumed
1040 anywhere in the world as a result of international trade²⁰⁴.

1041 Overcoming TW reuse governance challenges stands as a fundamental step for the
1042 expansion of reuse practices globally, simultaneously ensuring TW quality and public and
1043 environmental health. Suitable legal and regulatory frameworks, adapted and implemented
1044 either at the local or national level, should be empowered by sufficient implementation tools.
1045 This empowerment requires political, institutional, and financial support. Furthermore, these
1046 frameworks should be characterized by transparency and citizen involvement and engagement.
1047 In addition, regulations should incentivize wastewater management circularity by enabling
1048 recovered resources such as nutrient fertilizers and other by-products to enter the markets. The
1049 possibility of regulating the presence of MCEC in treated effluent should now be considered¹⁴³,
1050 given that this will be based on real-world research data concerning toxicological impacts to
1051 humans and the environment, the real magnitude of pollution burden in the end of the reuse
1052 systems, the impending cost, and the effectiveness of currently applied technologies.

1053 Upstream measures focusing on water pollution prevention at source through restrictions
1054 and development of greener alternatives should be also given priority over traditional end-of-
1055 pipe treatment measures¹². Moreover, the upgrade of treatment by incorporating advanced
1056 technologies, the implementation of control and preventing measures in the whole TW reuse
1057 systems and the adoption of best agricultural practices (advanced irrigation systems, use of
1058 sorbent materials, crops selection) can also contribute to the mitigation of TW reuse risks

1059 associated with MCEC introduction to the agroecosystems and the food web, including AR
1060 determinants and TPs⁷⁸.

1061 The diverse challenges faced by CAS, MBR, MBBR, and CW technologies, necessitate
1062 further research on operational adjustments and mechanistic understanding. The pivotal role of
1063 biological processes in achieving safe water reuse, urges continuous innovation and
1064 investigation for sustainable wastewater treatment practices. The efficacy of advanced
1065 wastewater treatment methods, including ozonation, activated carbon, and membranes, in
1066 removing MCEC is demonstrated through economically viable implementations in various
1067 countries. While solar-driven AOPs exhibit promise, yet they face technological readiness
1068 challenges. Considering site-specific factors and diverse endpoints for evaluating the most
1069 suitable and cost-effective solutions for advanced urban wastewater treatment is important. The
1070 need for ongoing research, system optimization, and eco-toxicological studies is emphasized
1071 to address gaps in understanding and implementation of such processes.

1072 Cost mitigation through decentralization, energy and nutrients recovery, and proper
1073 pricing of both freshwater and wastewater can efficiently promote wastewater reuse practices.
1074 Wastewater reuse systems should consider local data and information on wastewater volumes
1075 and quality, TW intended reuse applications and appropriate and affordable treatment
1076 technologies. Importantly, social acceptance through awareness raising and education aiming
1077 to overcome social, cultural and farmers and consumers barriers constitutes a prerequisite for
1078 a successful reuse scheme²⁰⁵.

1079 The role of science in solving the world's emerging water problems is well reviewed²⁰⁶.
1080 Academia and industry should cooperate in developing fit-for-purpose, science-based solutions
1081 through advancement in technology that will enable the affordable production of quality TW
1082 (minimization of MCEC in treated effluent) within a circular economy framework. Moreover,
1083 the incorporation of 4IR technologies in the entire TW reuse system is essential for advancing
1084 treatment, monitoring, and troubleshooting. Additionally, these technologies play a crucial role
1085 in promoting smart and precision agriculture through advanced irrigation and farming
1086 practices. This integration will further ensure the safe reuse of TW in agriculture (Fig. 6). The
1087 sustainability of reuse practices can be also enforced by the implementation of comprehensive
1088 risk management plans which will include among other toxicological endpoints regarding all
1089 involved environmental matrices (for example, water resources, soil, plants, wildlife, humans).

1090 Sustainable wastewater management incorporating TW reuse for irrigation can act as a
1091 major catalyst for circular economy and sustainable development. The social acceptance and
1092 adoption of this perspective by several international organizations and national authorities is

1093 the first step towards the capitalization of all derived opportunities arising from this practice.
1094 To progress this objective, the active involvement, and good services of all involved parties,
1095 including public authorities, relevant stakeholders, industry, academia, farmers, and the public
1096 (consumers), are necessary.

1097

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1103

1104 **Author Contributions**

1105 AC and DFK led the conceptualization and writing of the Review. VB, II, and PK contributed
1106 to data collection and analysis. VB, II, PK, CM, TB, BC, ED, YL, TTL, LL and ET discussed
1107 and amended the content of the Review. All authors reviewed and edited the manuscript before
1108 submission.

1109

1110 **Competing interests**

1111 The authors declare no competing interests.

1112

1113 Figure Captions

1114 **Fig. 1 a | TW reuse system.** Urban wastewater produced by anthropogenic activities is
1115 collected (from houses, offices, factories, etc.) within a settlement via a labyrinth-like piping
1116 system and conveyed to a WWTP through a final mainstream pipe. Applied treatment
1117 technologies in WWTPs can purify and decontaminate wastewater, finally achieving the
1118 production of reclaimed water of sufficient quality for reuse purposes. TW might undergo
1119 further treatment such as disinfection or filtration for the efficient removal of MCEC prior to
1120 its storage and further distribution for reuse practices, mainly agricultural irrigation. Based on
1121 its quality and the current reuse guidelines, reclaimed water can be reused for the irrigation of
1122 various crops (for example, fodder crops, vegetables, fruit trees), thus boosting the economy
1123 and ensuring food supply and security.

1124 **Fig. 1 b | Annual volume and percentage of TW used for direct irrigation.** Global direct
1125 reuse of TW (with no or little dilution with freshwater) for irrigation varies among continents.
1126 Direct application for irrigation is a prevalent practice in Middle Eastern and North African
1127 countries, Australia, the Mediterranean region, Mexico, China, and the USA, influenced by
1128 local water scarcity, availability of treatment infrastructure, presence and enforcement of
1129 regulatory measures, and economic motivations. Data source^{39, 40}.

1130

1131 **Fig. 2 | Centralized or decentralized wastewater treatment systems can facilitate the**
1132 **establishment of agricultural hotspots.** Wastewater treatment systems that are best suited to
1133 local conditions can effectively promote circular economy and SDGs. Wastewater treatment
1134 options can vary based on the volumes of wastewater to be treated and its quality, economic
1135 welfare, reuse purposes, available technologies, local regulatory frameworks, and social
1136 acceptance, among others. Centralized wastewater treatments can serve for the treatment of
1137 wastewater produced in big urban areas, generating large volumes of reclaimed water for reuse
1138 purposes. On the other hand, decentralized WWTPs can serve for the treatment of lower
1139 volumes of wastewater in small rural agglomerations, providing reclaimed water of sufficient
1140 quality and cost effectively, as substantial reduction in sewage collection and treatment and
1141 maintenance costs can be achieved. The reuse of reclaimed water for crop irrigation can
1142 promote the establishment of agricultural sites where intensive agricultural activities are
1143 practiced (for example, agricultural hotspots), with their size being in line with the reclaimed
1144 water produced (smaller and less intensive hotspots in decentralized systems). The production
1145 of food for the local communities can boost the local economy and promote the climate-water-
1146 energy-food nexus.

1147 **Fig. 3 | Challenges and limitations in TW reuse.** Applied treatment processes fail to
1148 completely remove MCEC from treated effluents, resulting in their continuous release to the
1149 environment through reuse applications. MCEC introduced into the agroecosystem can interact
1150 with other organisms with potentially negative impacts, promote the dissemination of AR
1151 determinants and their potential transfer to bacteria of clinical relevance, while entering the
1152 food web upon their uptake by crop plants. Micro(nano)plastics co-released with other
1153 contaminants may enhance AR dissemination and thus result in enhanced toxicological
1154 impacts. Associated challenges and risks posed to human and environmental health should be
1155 addressed taking into consideration that MCEC entering the agroecosystem and the food web
1156 are present in mixtures varying spatially and temporarily in composition, considering the
1157 Precautionary Principle. The upgrade of WWTPs to include advanced treatment steps and the
1158 implementation of risk management plans, covering the entire TW reuse system can effectively
1159 mitigate TW-reuse associated challenges.

1160

1161 **Fig. 4 | Key Risk Management Elements (KRMs, Box 4) and four modules for effective**
1162 **risk planning according to the Technical Guidance**
1163 **Water Reuse Risk Management for Agricultural Irrigation Schemes in Europe²⁸.** Module
1164 I consists of preparatory activities necessary to set up the risk management plan such as a
1165 detailed description of the entire water reuse system, with its extensions and limitations, and
1166 the identification of the roles and responsibilities of the involved actors. Module II entails the
1167 health and environmental risk assessments. Module III includes all the monitoring activities
1168 planned for the water reuse system: identification of procedures and protocols for the Quality
1169 Control of the system and for the Environmental Monitoring System (EMS). Operational and
1170 environmental monitoring programmes to provide assurances to workers, the public and
1171 authorities, of adequate system performance. Module IV includes management, emergencies
1172 and communication protocols and coordination.

1173

1174

1175 **Fig. 5 | Emerging technologies have the potential to retrofit the wastewater treatment**
1176 **sector in a circular global economy.** New technologies capable of retrofitting and upgrading
1177 all the functions of WWTPs towards a more circular model are in the pipeline for their
1178 commercialization in the forthcoming years (given that their technology readiness level is
1179 improved to an adequate level), while some of them are already applied at full scale. Future
1180 WWTPs are expected to display enhanced treatment efficiency through the incorporation of

1181 advanced technologies, thus acting as sentinel of public and environmental health. Moreover,
1182 the ‘reuse, recycle and resource recovery’ concept can turn WWTPs into energy and carbon
1183 neutral facilities, where nutrients and other added-value materials are recovered and reused. To
1184 this effect, the wastewater treatment sector can pave the pathway towards circular economy
1185 and SDGs in the forthcoming decades.

1186

1187 **Fig. 6 | Advancements in knowledge and technologies can transform the wastewater**
1188 **treatment sector, by enhancing efficiency and promoting circularity.** The incorporation of
1189 advanced materials and nanotechnology in wastewater treatment technologies can retrofit
1190 WWTPs, resulting in the production of high-quality reclaimed water within a circular economy
1191 model. Upgrades in advanced treatment and the use of nanomaterials in membrane filtration
1192 and separation processes, as well as the introduction of microbial electrochemical technologies
1193 (for example, microbial fuel cells, electrolysis cells) constitute important elements towards the
1194 operation of greener WWTPs. In addition, the incorporation of 4IR technologies (for example,
1195 artificial intelligence, autonomous systems, big data analytics, digital transformation, and
1196 internet of things), along with advancements in analytical chemical tools and the integration of
1197 omics and bioinformatics can improve wastewater systems through the optimization of
1198 operation and on-line monitoring and troubleshooting, thus improving their economic, energy
1199 and carbon footprint. The incorporation of 4IR technologies in TW-irrigated agroecosystems
1200 (smart farming) is expected to promote public health and environmental safety in TW reuse
1201 applications, while also can expand irrigated areas and therefore increase agricultural
1202 production.

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1216 BOXES

1217 **Box 1 | Long-standing adoption of TW reuse schemes for agricultural irrigation in various**
1218 **countries**

1219 **Israel**

1220 Israel can be classified as a pioneer in TW reuse for agricultural irrigation, a practice introduced
1221 due to the long-term severe water scarcity that the country has been experiencing. More than
1222 85% of the produced effluents are reused (direct reuse) in agriculture, providing more than half
1223 of the total irrigation needs of the agricultural sector. TW that is not reused during the winter
1224 months is stored in reservoirs. More than 160,000 ha of agricultural land (~45% of the
1225 cultivated land) are irrigated with TW, producing a considerable proportion of agricultural
1226 commodities in the country, while also allowing export of produce²⁰⁷.

1227 **Cyprus**

1228 In the same line, Cyprus, a Mediterranean country with the highest water exploitation index in
1229 Europe (124% in 2019)²⁰⁸, reuses more than 70% of all tertiary treated effluent produced for
1230 agricultural irrigation, and considers TW as a substantial component of integrated water
1231 resources management plans²⁰⁹.

1232 **Other European Countries**

1233 TW irrigation is practiced in other European countries as well, though not in an extended level.
1234 The irrigation of rice and vegetables fields in Valencia, Barcelona and Murcia in Spain, and in
1235 Milan, Italy, are some examples²⁸.

1236 **United States**

1237 In the United States, TW reuse schemes in agriculture are based on comprehensive regulations
1238 and guidelines^{145, 210}. In Florida, most of the TW is reused for landscape irrigation even in areas
1239 with public access, while agricultural irrigation mostly refers to citrus orchards irrigation²¹¹. In
1240 the Monterey County in California, disinfected tertiary TW constitutes an important component
1241 of the ‘One Water’ management scheme²¹². TW is reused both for aquifer recharge aiming at
1242 managing seawater intrusion and supplying the indirect potable reuse system, and for the
1243 irrigation of thousands of hectares of high-value vegetables, including artichokes, broccoli,
1244 cauliflower, celery and lettuce²¹⁰.

1245 **China**

1246 In the south eastern suburb of Beijing, China, TW reuse for irrigation of hundreds of square
1247 kilometres of agricultural land has a long history in producing remarkable quantities of food
1248 for the city²¹³.

1249 **Australia**

1250 In Australia, TW reuse in agriculture is increasingly common as jurisdictions seek to secure
1251 ‘climate-independent’ supplies²¹⁴. Recycled water for multiple uses, including for agricultural
1252 irrigation, is now a key component of diverse water supply portfolios for many Australian water
1253 authorities²¹⁵. In 2019-20, Australian agriculture used about 6500 hm³ of water, of which 124
1254 hm³ (1.9%) was recycled water obtained from off-farm sources²¹⁶. Outcomes from the
1255 Australian experience to date indicate that TW recycled from capital city WWTPs adjacent to
1256 suitable vegetable growing land have been the most successful recycling schemes²¹⁶.

1257

1258

1259

1260 **Box 2 | Learning from the Past, Cultivating the Future: Israel's transformative journey**
1261 **in utilising wastewater for agricultural growth**

1262

1263 *The story*

1264 The initial use of TW in agricultural in Israel began in the early 1950s, and since then, its use
1265 has steadily increased. Initially, TW was utilized only for irrigation of non-edible crops, to
1266 expand cultivation in areas where fresh water sources were unavailable and/or could not be
1267 supplied constantly. Then, orchards and plantations were also added as areas where TW could
1268 have been incorporated. During the 1980s, water shortages became more frequent, and in the
1269 early 1990s, Israel faced a severe water crisis. In response, the government declared two main
1270 measures to overcome water scarcity: Increasing production of potable water by desalination
1271 and expanding the use of TW for irrigation. The TW use grew significantly, reaching currently
1272 45-50% of the total water use for agricultural irrigation.

1273

1274 *The facts*

1275 Recent data (2022) about sewage treatment and TW reuse referring to wastewater generation
1276 from a population of about 9 million, (i.e., 98.6% of Israel's population) indicate an estimated
1277 total amount of raw wastewater at 620.5 million m³, of which 616.4 million m³ is domestic and
1278 industrial wastewater and about 4.05 million m³ is cowshed wastewater. About 95.4% (about
1279 592 million m³) of total wastewater is treated in WWTPs. The wastewater to TW reclamation
1280 ratio is 84.7%²¹⁷.

1281

1282 *The success factors*

1283 The success in increasing the use of TW by the Israeli agricultural sector is attributed to several
1284 factors:

1285 (1) Centralized water system: Water is defined in Israel as a nationalized public good; all water
1286 is the property of the state, including fresh water (surface and groundwater), rainwater,
1287 wastewater, and runoff. Water planning, marketing and distribution are highly centralized.
1288 Centralized system like that enables fast transfer of water resources ensuring public and
1289 environmental safety.

1290 (2) Agricultural viability: Farmers were allocated with a specific water quota. This forced the
1291 farmers to shift from fresh water to TW, otherwise they would face underutilized production
1292 due to insufficient water.

1293 (3) Financial support: Allocation of funds (loans and grants) for construction the necessary
1294 infrastructure (WWTPs, pipelines, reservoirs, irrigation equipment, etc.).

1295 (4) Research: Funding for research to assess the impact of intensive utilization of TW on crops
1296 and soil, including the establishment of a comprehensive national survey that examined the
1297 effects over a ten-year period. The Israeli Ministries of Agriculture and Environmental
1298 protection took the lead to establish long-term national monitoring system including setup of
1299 specific experimental plots. This system enabled fast response to problems raised by farmers
1300 and a close feed-back between farmers, regulators, academia, and the water industry.

1301 (5) Regulations: Implementation of strict regulations regarding health and agronomic quality
1302 of TW. Understanding that TW is a key factor for agricultural and environmental health (soil
1303 and crop) led to massive upgrading of WWTPs to provide high-quality (tertiary) TW for
1304 unlimited irrigation use (TW that can be used to irrigate all types of crops using all type of
1305 irrigation techniques). Supplementary regulations were issued for the industry to minimize
1306 industrial impact on the quality of TW, including reducing pollutants at the source. A good
1307 example is related to banning the use of Boron-containing detergents to reduce the level of B
1308 in TW below 0.4 mg/L.

1309

1310 *Current challenges*

1311 Although the utilization of TW is high and expected to increase soon, the maximum capacity
1312 of TW utilization is still not maximal due to lack of infrastructure for transferring TW from
1313 surplus production areas (central region of Israel) to areas with high agricultural activities
1314 facing water shortage in the south and north parts of the country. After fully exploiting the
1315 current potential, future dependence on TW is expected to increase with population growth,
1316 leading to more water usage and higher demand for TW by both the agricultural as well as the

1317 urban sectors. Additionally, further upgrading of WWPTs is needed to address the concern
1318 regarding the presence of contaminants of emerging concern that have been shown to be
1319 introduced to the food chain and even monitored in biological samples of Israelis consuming
1320 produce irrigated with TW.

1321

1322

1323 **Box 3 | Legal and regulatory frameworks applied in different regions or countries to**
1324 **ensure public and environmental health during TW reuse for irrigation**

1325 **Frameworks by international organizations**

1326 The International Organization for Standardization (ISO) issued guidelines for the use of TW
1327 in agriculture. The ISO 16075:2020¹⁴⁷ covers guidelines for the use of TW in irrigation
1328 projects. It suggests standards for *E. coli*, BOD, TSS, turbidity for different water quality
1329 category depending on treatment levels. It also includes suggested levels for agronomic
1330 parameters (for example, nutrients, salinity, and heavy metals) for the protection of soil and
1331 crops irrigated with TW. The ISO 20426:2018¹⁴⁶ provides an approach for health risk
1332 assessment and management of TW used in non-potable applications. The WHO has also
1333 provided guidelines for the safe use of wastewater¹⁴⁸ which contains a methodology to ensure
1334 safe reuse of TW around the world.

1335 **European Union Water Reuse Regulation**

1336 The EU Regulation (EU) 2020/74⁴² sets out harmonized minimum water quality and
1337 monitoring requirements for *E. coli*, BOD₅, TSS, and turbidity for water quality classes A, B,
1338 C, D depending on crop types and irrigation methods. The regulation imposes the mandatory
1339 development of a risk management plan for water reuse systems, for which guidelines have
1340 been established²⁸. Additional requirements on water quality and monitoring, which may
1341 include non-regulated micropollutants, could be added based on the outcome of the risk
1342 assessment on the specific water reuse system. The competent authority designated at EU
1343 Member States level issues the permit(s) for the production and supply of TW by setting out
1344 any obligations and conditions for the permitted uses.

1345 **U.S. regulatory framework**

1346 In the U.S., standards for the use of TW in irrigation have not been established at federal level.
1347 The Twenty-eight states of the U.S. have own regulations for the reuse of TW for irrigation of
1348 food and non-food crops. Quality requirements varies greatly among the states depending on
1349 crop types, irrigation methods and wastewater treatment levels. For example, the Title 22 of
1350 California sets-out strict criteria on total coliform bacteria, turbidity, F-specific bacteriophages

1351 MS-2 or poliovirus for the irrigation of edible food-crops with the water quality class
1352 corresponding to disinfected and filtered TW (disinfected tertiary recycled water)²¹⁸.
1353 Additional to state-laws, the US EPA Guidelines for Water Reuse¹⁴⁵ provides a non-mandatory
1354 national guidance for planning and regulating water reuse across the states following a risk
1355 management framework approach.

1356 **Israel**

1357 The Israeli water reuse law¹⁴⁹ approved by the Ministry of Health (2010) regulates the
1358 unrestricted use of TW for agricultural irrigation. It established rules for granting permits for
1359 irrigation with TW ensuring the protection of public health and the environment.

1360 **The Australian Guidelines**

1361 The Australian Guidelines for water recycling¹⁴⁴ issued in 2006 aims at providing a guidance
1362 for safe use of TW. The document does not set out mandatory standards but provides
1363 indications on how to identify and set levels for the quality of water used in irrigation based on
1364 a health and environmental risk management approach.

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1369 **Box 4 | Key Elements of the Risk Management Plan of the European Regulation on Water** 1370 **Reuse²⁸**

1371 **System description (KRM1):** description of the entire water reuse system from the entry point
1372 to the urban wastewater treatment plant to the point of use.

1373 **Parties, roles, and responsibilities (KRM2):** identification of all the parties involved in the
1374 water reuse system along with their roles and responsibilities.

1375 **Hazards identification (KRM3):** identification of potential hazards (pathogens and
1376 pollutants) and hazardous events (e.g., treatment failures) associated to the water reuse system.

1377 **Populations and environments at risk and exposure routes (KRM4):** identification of
1378 populations and environments potentially exposed to each identified hazard.

1379 **Environmental and health risk assessment (KRM5):** identification of risks associated with
1380 each hazard for receptors (people, animals, crops, terrestrial biota, aquatic biota, soils, and the
1381 environment) across exposure routes. Use qualitative and semi-quantitative methods due to
1382 data constraints, adhering to regulatory and legislative obligations outlined in the specified
1383 Regulation and relevant national or local laws.

1384 **Additional requirements (KRM6):** the risk assessment may lead to the identification of
1385 heightened water quality and monitoring needs, potentially surpassing those outlined in the
1386 Regulation. Any additional parameters or limits should stem from the assessment outcomes
1387 and be substantiated by scientific evidence, ensuring their connection to the water reuse system
1388 rather than external sources. These added parameters may encompass heavy metals, pesticides,
1389 disinfection by-products, pharmaceuticals, micropollutants, microplastics and antimicrobial
1390 resistance determinants.

1391 **Preventive measures (KRM7):** identification of preventive measures or barriers, additional
1392 or already in place, to be applied to parts of the water reuse system, for example access control
1393 methods, additional water treatments or specific irrigation technologies or barriers to limit or
1394 mitigate any identified risk.

1395 **Quality control systems (KRM8):** determination of quality control measures, including
1396 protocols for monitoring the reclaimed water for the relevant parameters and maintenance
1397 programs for the equipment, to ensure the effectiveness of the treatment chain and of the
1398 preventive measures adopted.

1399 **Environmental monitoring system (KRM9):** set up of an environmental monitoring system
1400 to assess the release of the identified pollutants in the exposed environmental receptors (e.g.,
1401 freshwater, groundwater, soil).

1402 **Incidents and emergency systems (KRM10):** set up of protocols to manage incidents and
1403 emergencies.

1404 **Coordination mechanisms (KRM11):** definition of coordination and communication
1405 mechanisms amongst the different actors involved in the water reuse system.

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