

American College of Rheumatology
Guideline for Vaccinations in Patients with Rheumatic and Musculoskeletal Diseases

Project Plan – April 2021

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1 **ORGANIZATIONAL LEADERSHIP AND SUPPORT**

2

3 This clinical practice guideline is being developed by the American College of Rheumatology
4 (ACR) with funding from the ACR.

5

6 **BACKGROUND**

7

8 Rheumatic and musculoskeletal diseases (RMDs) affect a large proportion of adults and children
9 in the United States [1]. These conditions are largely incurable and require prolonged use of
10 medications to suppress disease activity, slow damage accrual, improve physical function and
11 maximize health-related quality of life. Many of these RMDs (e.g., autoimmune rheumatic
12 diseases), as well as many of the immunosuppressive or immunomodulatory therapies used to
13 manage them, can place patients at higher risk of developing common or opportunistic
14 infections (including vaccine-preventable infections) and may also affect responses to vaccines.

15

16 Vaccines have been long used worldwide to reduce illness from common viral and bacterial
17 pathogens. Recommendations for standardized vaccine schedules for both children and adults have
18 been widely adopted, for healthy people as well as those with chronic medical conditions. [2, 3]

19

20 Individuals with RMD and those receiving immunomodulatory therapy may be more susceptible
21 to vaccine-preventable disease, or at higher risk of developing more serious complications of
22 the disease should they become infected, suggesting that vaccination is an important strategy
23 to reduce comorbid illness in affected patients. Therefore, individuals with RMD may benefit
24 from alterations in the standard vaccination schedule or temporary adjust immunomodulatory
25 medication schedules in order to maximize vaccine responsiveness and lower the likelihood and
26 severity of vaccine-preventable illness.

27

28 Because vaccines fundamentally work by generating an effective immune response against
29 pathogens, their effectiveness relies upon the function of an individual's immune system to
30 recognize the pathogenic antigen(s) introduced by the vaccine and to generate a neutralizing
31 immune response. Individuals with RMD and those on chronic immunosuppressive therapy
32 may have impaired responses to vaccines that may reduce protection against vaccine-
33 preventable illnesses.

34

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35 Some of these issues have been addressed in ACR practice guidelines for the management of
36 different diseases (e.g., RA, JIA), but because many issues regarding optimal vaccine use to
37 reduce the burden of vaccine-preventable illness apply across a wide range of RMDs and
38 immunosuppressive medications, the ACR created a dedicated group to review and compile
39 data related to vaccination among all RMDs, particularly autoimmune and inflammatory
40 rheumatic diseases (AIIRD) and the immunosuppressant and immunomodulating therapies
41 used to manage such diseases.

42
43 The ultimate goal of this guideline is to provide recommendations regarding vaccinations in
44 RMD populations, including if and when standardized vaccine schedules need to be altered due
45 to underlying disease or its therapies, or conversely, if temporary adjustments to the
46 immunosuppressive medication schedule should be made to optimize the efficacy and safety of
47 a vaccination. Unfortunately, there will be limited high-quality direct evidence to address these
48 issues comprehensively for every situation. Therefore, important questions have been included
49 that consolidate relative issues of vaccine safety and efficacy in different situations facing RMD
50 populations so that patients and providers may use the compiled background data to make
51 informed decisions about individual vaccines and current or planned therapeutic regimens.

52
53 **OBJECTIVES**

54
55 The objective of this project is to develop evidence-based recommendations for vaccination in
56 adults and children with RMDs including those on immunosuppressive or immunomodulating
57 medications. In many cases, data are not available comparing different vaccination strategies
58 to guide recommendations; therefore, indirect evidence of safety and efficacy (or
59 immunogenicity as a surrogate) will be compiled to inform individual decision-making.

- 60 • The recommendations will cover clinically relevant vaccines that are recommended for
61 use in the U.S. as well as select vaccines recommended for travelers or other sub-
62 populations.
- 63 • The recommendations will cover autoimmune and inflammatory RMDs in adults and
64 children that inherently affect the immune system or that often utilize
65 immunosuppressive or immunomodulatory medications for management.
- 66 • The recommendations will cover commonly used immunomodulatory medications
67 including glucocorticoids, conventional and targeted synthetic disease modifying
68 antirheumatic drugs (csDMARDs and tsDMARDs), traditional immunosuppressant
69 medications, and biologic therapies that are commercially available in the United States.

70

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71 Specifically, we aim to:

- 72 1. Review the evidence for the risks of vaccine-preventable disease in individuals with
73 RMD compared to the general population.
- 74 2. Review the evidence for the immunogenicity and clinical efficacy and safety of vaccines
75 in RMD populations by underlying disease and immunomodulatory therapy.
- 76 3. Develop recommendations regarding the use of the high dose quadrivalent annual
77 influenza vaccine in RMD patients on different immunomodulatory therapies.
- 78 4. Develop recommendations regarding altering the Center for Disease Control Advisory
79 Committee on Immunization Practices (ACIP) [2] schedule of vaccines for RMD patients
80 on different immunomodulatory therapies, including:
 - 81 a. Deferring vaccinations in relation to disease activity and/or immunomodulatory
82 medication use
 - 83 b. Use of vaccines at age ranges outside of recommended guidelines in relation to
84 the underlying RMD and/or immunomodulatory therapy
- 85 5. Develop recommendations regarding temporary adjustments in immunomodulatory
86 medication dosing to maximize vaccine efficacy and responsiveness including:
 - 87 a. Timing vaccinations with respect to intermittently dosed medications
 - 88 b. Holding medications before or after vaccinations

89 **METHODS**

90 *Identification of Studies*

91
92 Literature search strategies, based upon PICO questions (Population/patients, Intervention,
93 Comparator, and Outcomes; *see Appendix A*), will be developed by a medical research librarian
94 in consultation with the Core Team. The search strategies will be peer reviewed by another
95 medical librarian using Peer Review of Electronic Search Strategies (PRESS) [4]. Searches will be
96 performed in OVID Medline (1946 +), Embase (1974 +), the Cochrane Library, and PubMed
97 (mid-1960s +).

98
99 The search strategies will be developed using the controlled vocabulary or thesauri language for
100 each database: Medical Subject Headings (MeSH) for OVID Medline, PubMed and Cochrane
101 Library; and Emtree terms for Embase. Text words will also be used in OVID Medline, PubMed,
102 and Embase, and keyword/title/abstract words in the Cochrane Library.

103

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104 *Search Limits*

105

106 Only English language articles will be retrieved.

107

108 *Grey Literature*

109

110 The websites of appropriate agencies, such as the Agency for Healthcare Research and Quality
111 (AHRQ), will be searched for peer-reviewed reports not indexed by electronic databases.

112

113 *Literature Search Update*

114

115 Literature searches will be updated just prior to the voting panel meeting to ensure
116 completeness.

117

118 *Inclusion/Exclusion Criteria*

119

120 See PICO questions (*see below*), which outline the defined patient population, interventions,
121 comparators, and outcomes. Case reports and case series with fewer than 10 patients will be
122 excluded.

123

124 *Management of Studies and Data*

125

126 References and abstracts will be imported into bibliographic management software (Reference
127 Manager) [5], duplicates removed, and exported to Distiller SR, a web-based systematic review
128 manager [6]. Screening forms will be created in Distiller SR. Search results will be divided
129 among reviewers, and two reviewers will screen each title/abstract, with disagreements at the
130 title/abstract screening stage defaulting to inclusion for full manuscript review. Following the
131 same dual review process, disagreements at the full manuscript screening stage will be
132 discussed and adjudicated by the literature review leadership, if necessary.

133

134 *Phases*

135

- 136 1. A search for randomized controlled trials and observational studies about interventions
137 will be performed to identify existing studies assessing the outcomes of interest.
138 Subsequently, we will conduct meta-analyses of identified studies using the RevMan

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- 139 software [7] and the rating of the certainty of evidence following the GRADE
140 methodology (and using the GRADEPro tool) [8].
- 141 2. Chosen studies will be assessed for risk of bias using modified versions of the Cochrane
142 Risk of Bias tool [9] and the Newcastle-Ottawa Scale [10].
 - 143 3. Additionally, recently published systematic reviews covering outcomes of interest will
144 also be sought and used for reference cross-checking.

145
146 *GRADE Methodology*

147
148 GRADE methodology [11] will be used in this project to rate the certainty of the available
149 evidence and facilitate the development of recommendations. The certainty of the evidence
150 (also known as ‘quality’ of evidence) will be rated as high, moderate, low or very low. This
151 rating is based upon the judgment of the GRADE criteria for downgrading (risk of bias,
152 inconsistency, indirectness, imprecision, and publication bias) or upgrading the certainty of
153 evidence (large magnitude of effect, dose-response gradient, and all plausible confounding that
154 would reduce a demonstrated effect). The strength of recommendations will be graded as
155 strong or conditional. The strength of recommendations will depend upon the balance of
156 benefits and harms, the certainty in the evidence, and patients’ preferences and values. A
157 series of articles that describe the GRADE methodology can be found on the GRADE working
158 group’s website: www.gradeworkinggroup.org.

159
160 *Analysis and Synthesis*

161
162 The literature review team will analyze and synthesize data from included studies that address
163 the PICO questions using Review Manager (RevMan) [7]. A GRADE evidence profile and a
164 Summary of Findings table will be prepared for each PICO question using the GRADEprofiler
165 (GRADEpro) software (8). For each critical or important outcome, the GRADE Summary of
166 Findings table will contain the anticipated absolute effect, the relative effect (95% CI), the
167 number of participants/number of studies, and the certainty in the evidence (i.e., high,
168 moderate, low or very low).

169
170 For each critical or important outcome, the GRADE evidence profile will contain the same
171 information as in a Summary of Findings table, in addition to detailed judgments and
172 justifications for the GRADE criteria for downgrading or upgrading the certainty of evidence.

173

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174 If a meta-analysis is not possible (e.g., data are from non-comparative studies or not in a format
175 amendable to pooling) we will summarize the available evidence (or lack thereof) in a narrative
176 format instead.

177

178 *Development of Recommendation Statements*

179

180 PICO questions will be revised into drafted recommendation statements. Using the evidence
181 summaries developed by the literature review team, the voting panel will consider the drafted
182 recommendation statements in two stages. The first assessment will be done individually, and
183 the results will be anonymous; this vote will only be used to determine where consensus might
184 or might not already exist and develop the voting panel meeting agenda. During the voting
185 panel meeting, chaired by the principal investigator, the panelists will discuss the evidence in
186 the context of their clinical experience and expertise to arrive at consensus on the final
187 recommendations. The voting panel meeting discussions will be supported by the literature
188 review leader, the GRADE expert, and selected members of the literature review team, who will
189 attend the meeting to provide details about the evidence, as requested. Voting panel
190 discussions and decisions will be informed by a separately convened patient panel (which will
191 meet in the days before the voting panel meeting) to provide unique patient perspectives on
192 the drafted recommendations based upon their experiences and the available literature. Two
193 members of the separate patient panel will participate as full, voting members of the voting
194 panel that determines the final recommendations; their role at the voting panel meeting will be
195 to explicitly represent the patient panel's views to other voting panel members during
196 discussions and decision-making.

197

198 **PLANNED APPENDICES (AT MINIMUM)**

199

200 A. Final literature search strategies

201 B. Evidence summaries for each PICO question, including GRADE evidence profiles and
202 summary of findings tables, when available

203

204 **AUTHORSHIP**

205

206 Authorship of the guideline will include principal investigator, Dr. Eliza Chakravarty, as the lead
207 author and voting panel leader; Dr. Joann Fontanarosa, literature review leader; Dr. Elie A. Akl,
208 GRADE expert; Drs. Clifton Bingham, Leonard Calabrese, Laura Cappelli and Kevin Winthrop,

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209 content experts; and any other Core Team members added to the leadership. Members of the
210 literature review team and voting panel will also be authors. The PI will determine final
211 authorship, dependent upon the efforts made by individuals throughout the guideline
212 development process, using international authorship standards as guidance.

213

214 **DISCLOSURES/CONFLICTS OF INTEREST**

215

216 The ACR's disclosure and COI policies for guideline development will be followed for this
217 project. These can be found in the ACR Guideline Manual on [this page of the ACR web site](#),
218 under Policies & Procedures. *See Appendix E for participant disclosures.*

219

220 **REFERENCES**

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246

247 **APPENDIX A - PICO Questions (Population, Intervention, Comparator, Outcome)**

248 *See appendix B, C, D for lists of diseases, medications, and vaccines.*

249 **RISKS OF VACCINE-PREVENTABLE DISEASE (INCLUDING CERVICAL/ANAL CANCER FROM HPV)**

250 *Prognosis rather than intervention questions*

251

252 **1. Are patients with RMD disease X at increased risk to contract vaccine-preventable diseases**
253 **compared to the general population?**

254 P - RMD patients

255 C - General population

256 O - Contracting vaccine-preventable diseases

257

258 **2. Are patients with RMD disease X at increased risk for more severe outcomes from vaccine-**
259 **preventable diseases compared to the general population?**

260 P - RMD patients

261 C - General population

262 O - Outcomes (mortality/morbidity) from vaccine-preventable diseases (will include all markers
263 of severity, e.g., hospitalization, death)

264

265 **QUESTIONS REGARDING VACCINE IMMUNOGENICITY/EFFICACY/SAFETY TO INFORM**

266 **GUIDELINE RECOMMENDATIONS**

267 *Prognosis rather than intervention questions*

268 **3. In patients with [RMD Disease X], what is the effect of [Drug Y/Drug Class] on**
269 **immunization responses to [Vaccine Z, Vaccine Type] in comparison with [General**
270 **population, or Drug Y']?**

271 P - RMD Disease X

272 I - Vaccine Z

273 C 1 - Patients receiving drug(s) Y

274 C 2 - Patients receiving drug(s) Y

275 C 3 - Healthy controls

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- 276 O - Immunogenicity (Geometric mean titer (GMT), fold increase in titer, seroconversion,
277 seroprotection, cell mediated immunity)
278
- 279 **4. In RMD patients, does the immunogenicity or efficacy of Vaccine Z differ in patients taking**
280 **high-dose steroids as compared to those using lower doses of steroids or those not using**
281 **steroids?**
- 282 P - RMD patients taking high dose steroids I - Vaccine Z
283 C 1- RMD patients taking low dose steroids
284 C 2 - RMD patients not taking steroids
285 O - Rates of infection, immunogenicity
286
- 287 **5. In RMD patients on drug Y, do immune responses to neo-antigens (not vaccines) differ**
288 **from responses seen in the general population?**
- 289 P - RMD patients receiving drug Y
290 I - Administration of neo-antigen
291 C 1 - Administration of neo-antigen to general population
292 C 2 - Administration of neo-antigen to RMD patients not receiving Drug Y
293 O – Immunogenicity
294
- 295 **6. In patients with [Disease X], is the duration of the immune response to [Vaccine Z]**
296 **diminished compared to [healthy controls]?**
- 297 P - Disease X
298 I - Vaccine Z
299 C 1 - Patients receiving drug(s)
300 C 2 - Healthy controls
301 O - Immunogenicity (see question #2), development of vaccine-preventable disease
302
- 303 **7. Do patients with [Disease X] have higher rates of adverse events following [Vaccine Z]**
304 **compared to [healthy controls]?**
- 305 P - Disease X
306 I - Vaccine Z
307 C 1 - Patients receiving drug(s) Y
308 C 2 - Healthy controls

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309 O - Reactogenicity (fever, vaccine site reactions, myalgia, arthralgia, headache, rhinitis, sore
310 throat)

311

312 **8. Do patients with [Disease X] experience flares of their underlying RMD after immunization**
313 **with [Vaccine Z]?**

314 P - RMD Disease X

315 I - Administer Vaccine Z

316 C - Do not administer vaccine Z

317 O - Increase in disease activity

318

319 **QUESTIONS ABOUT ANNUAL INFLUENZA VACCINE**

320

321 **9. In RMD patients age 65 and older, is high dose (Fluzone high dose) influenza vaccine more**
322 **effective than seasonal regular dose influenza vaccine?**

323 P - Patients with RMD age 65 and older

324 I - High dose (Fluzone) influenza vaccine

325 C - Regular dose influenza vaccine

326 O - Rates of influenza infection, immunogenicity reactogenicity

327

328 **10. In RMD patients age 65 and older, is adjuvanted influenza vaccine (FLUAD) more effective**
329 **than seasonal regular dose influenza vaccine?**

330 P - Patients with RMD age 65 and older

331 I - FLUAD influenza vaccine

332 C - Regular dose influenza vaccine

333 O - Rates of influenza infection, immunogenicity, reactogenicity

334

335 **11. In RMD patients *under* age 65 years, is high dose (Fluzone high dose) vaccine more effective**
336 **than seasonal regular dose influenza vaccine?**

337 P - Patients with RMD under age 65

338 I - Fluzone high dose influenza vaccine

339 C - Regular dose influenza vaccine

340 O - Rates of influenza infection, immunogenicity, reactogenicity

341

342 **12. In RMD patients *under* age 65 years, is adjuvanted influenza vaccine (FLUAD) more effective**

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343 **than seasonal regular dose influenza vaccine?**

344 P - Patients with RMD under age 65

345 I - FLUAD adjuvanted influenza vaccine

346 C - Regular dose influenza vaccine

347 O - Rates of influenza infection, immunogenicity, reactogenicity

348

349 **13. In RMD patients, does the immunogenicity or efficacy of influenza vaccine differ in patients**
350 **who have moderate to severely active underlying disease as compared to those in low-disease**
351 **activity or remission?**

352 P - Patients with moderate to severely active RMD

353 I - Influenza vaccination

354 C - Patients with quiescent/low disease activity RMD

355 O - Rates of influenza infection, immunogenicity

356

357 **14. In RMD patients, does the immunogenicity or efficacy of influenza vaccine differ in patients**
358 **taking high dose steroids as compared to those using lower doses of steroids or those not using**
359 **steroids?**

360 P - RMD patients taking high dose steroids

361 I - Influenza vaccination

362 C 1 - RMD patients taking low dose steroids

363 C 2 - RMD patients not taking steroids

364 O - Rates of influenza infection, immunogenicity

365

366 **15. In RMD patients, does the immunogenicity or efficacy of influenza vaccine differ in patients**
367 **taking Drug Y as compared to those not using drug Y at the time of vaccination?**

368 P - RMD patients taking Drug Y

369 I - Influenza vaccination

370 C - RMD patients not taking drug Y

371 O - Rates of influenza infection, immunogenicity

372

373 **QUESTIONS ABOUT TIMING OF VACCINE WITH RESPECT TO IMMUNOSUPPRESSIVE**
374 **MEDICATIONS OR DISEASE ACTIVITY**

375

376 **16. Should patients with RMD taking drug Y hold their drug for a period of time prior to or after**

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377 **receiving (not live-attenuated) vaccines?**

378 P - Patients with RMD on drug Y

379 I 1 - Hold drug Y prior to vaccine

380 I 2 - Hold drug Y after vaccine

381 C - Usual dosing of drug Y

382 O - Reactogenicity, disease flare, immunogenicity

383

384 **17. Should patients with RMD who are taking biologic medications with usual dosing schedules**
385 **of monthly or longer* schedule (not live-attenuated) vaccine administration relative to next**
386 **dose of medication?**

387 P - Patients with RMD on intermittent-dosing biologic medications

388 I 1 - Vaccination 1 month before next biologic medication dose

389 I 2 - Vaccination > 1 month before next biologic medication dose

390 C - No schedule adjustment of vaccine relative to medication dose

391 O - Reactogenicity, disease flare, immunogenicity

392

393 *Rituximab, ocrelizumab, belimumab, ustekinumab, tocilizumab (IV), TNF inhibitors (infliximab,
394 golimumab, certolizumab), IVIg, abatacept (IV), secukinumab, ixekizumab, guselkumab,
395 canakinumab, tildrakizumab, risankizumab

396

397 **18. Should moderately to severely ill RMD patients with disease X defer vaccination (for NOT**
398 **live-attenuated) until disease is better controlled?**

399 P - RMD patients with moderate to severe active disease

400 I - Delay vaccine until low disease activity or remission

401 C - Proceed with vaccinations without change in schedule

402 O - Reactogenicity, immunogenicity

403

404 **QUESTIONS RELATED TO VACCINATION OUTSIDE OF STANDARDIZED AGE RANGES**

405

406 **19. Should RMD patients be vaccinated against HPV at ages older than age 26?**

407 P - RMD patients older than 26 without complete HPV vaccination

408 I - Vaccinate for HPV

409 C - Do not vaccinate for HPV

410 O - Rates of HPV infection, incidence of HPV-related cancer (cervical, anal, head and neck cancer)

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- 411
412 **20. Should RMD patients with RMD receive vaccination against pneumococcus at ages less than**
413 **65 years?**
414 P - RMD patients under age 65 with RMD who have not received pneumococcal vaccine
415 I - Vaccinate against pneumococcus
416 C - No pneumococcal vaccination
417 O - Rates of pneumonia and associated complications, reactogenicity, immunogenicity
418
419 **21. Should RMD patients receive Shingrix vaccine (against varicella zoster virus [VZV]) at ages**
420 **younger than 50 years?**
421 P - RMD patients under 50 years who have not received Shingrix
422 I - Administer Shingrix vaccine
423 C - Do not administer Shingrix vaccine
424 O - Rates of herpes zoster (shingles) and shingles-related complications (post herpetic
425 neuralgia, disseminated herpes zoster infection), reactogenicity, immunogenicity
426
427 **22. Should RMD patients receive standardized regimens of vaccine combinations?**
428 P - RMD patients
429 I - Administer vaccines individually rather than in standardized combinations
430 C - Administer combination vaccines according to ACIP guidelines
431 O - Change in RMD disease activity
432
433 **QUESTIONS REGARDING USE OF LIVE-ATTENUATED VACCINES**
434
435 **23. Should RMD patients taking drug Y receive live-attenuated vaccines?**
436 P - RMD Patients taking drug Y
437 I - Receive live-attenuated vaccine
438 C - Do not receive live-attenuated vaccine
439 O - Development of vaccine-preventable infection
440
441 **24. Should RMD patients taking drug Y hold the drug for a period of time prior to or after**
442 **receiving live-attenuated vaccines?**
443 P - RMD patients taking drug Y

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- 444 I 1 - Hold drug Y prior to vaccination
445 I 2 - Hold drug Y after vaccination
446 C - No alterations in drug dosing
447 O - Development of vaccine-preventable infection
448
449 **25. Should neonates/infants with second and third trimester antenatal exposure to TNF**
450 **inhibitors or Rituximab receive live-attenuated rotavirus vaccine in their first 6 months of**
451 **life?**
452 P - neonates/infants with 2nd or 3rd trimester exposure to TNF inhibitors or Rituximab
453 I - Administer rotavirus vaccine in first 6 months of life
454 C 1 - Do not administer rotavirus vaccine
455 C 2 - Delay live-attenuated rotavirus vaccine until after first 6 months of life
456 O - Rates of rotavirus infection
457
458 **26. Should family members of RMD patients receive live-attenuated vaccines?**
459 P - Family member of RMD patients
460 I - Administration of live-attenuated vaccines
461 C - Do not administer live-attenuated vaccines
462 O - Development of vaccine-preventable infection

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463 **Appendix B: Rheumatic and Musculoskeletal Diseases to be addressed (autoimmune and**
464 **inflammatory diseases) “Disease X”**

465

466

1. Inflammatory arthropathies

467

a. Rheumatoid arthritis

468

b. Psoriatic arthritis

469

c. Ankylosing spondylitis

470

d. Seronegative spondyloarthropathies

471

e. Entesitis-related arthritis

472

f. Inflammatory bowel disease-associated arthritis

473

g. Juvenile Idiopathic Arthritis

474

i. Oligoarticular

475

ii. Polyarticular

476

iii. Undifferentiated

477

2. Connective tissue diseases

478

a. Systemic lupus erythematosus

479

b. Sjogren’s syndrome

480

c. Systemic sclerosis/Scleroderma

481

d. Idiopathic Inflammatory myopathies

482

e. Mixed connective tissue disease

483

f. Undifferentiated connective tissue disease

484

g. Antiphospholipid antibody syndrome

485

h. Catastrophic anti-phospholipid syndrome

486

3. Vasculitides

487

a. ANCA-associated vasculitis

488

i. Granulomatosis with Polyangiitis (Wegener’s Granulomatosis)

489

ii. Microscopic polyangiitis

490

iii. Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss Syndrome)

491

b. Giant cell arteritis

492

c. Polyarteritis nodosa

493

d. Takayasu’s arteritis

494

e. Cryoglobulinemia

495

f. Relapsing polychondritis

496

g. Behcet’s disease

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- 497 h. Kawasaki's disease
498 i. Henoch Schonlein Purpura
499 j. Primary CNS vasculitis
500 k. Anti-GBM/Goodpasture's syndrome
501 l. Cogan's syndrome
502 m. Cutaneous small-vessel vasculitis
503 n. IgA vasculitis
504 o. Rheumatoid vasculitis
505 p. Urticarial vasculitis
506
507 4. Inflammatory disorders
508 a. Sarcoidosis
509 b. Adult-onset Still's disease (systemic onset juvenile idiopathic arthritis)
510 c. Systemic onset juvenile idiopathic arthritis
511 d. Polymyalgia rheumatica
512 e. Gout
513 f. Pseudogout
514 g. IgG4-related disease
515 h. Periodic fever syndromes
516 i. PFAPA (Periodic Fever, Aphthous Stomatitis, Pharyngitis, Adenitis)
517 ii. FMF (Familial Mediterranean Fever)
518 iii. HIDS (Hyper-IgD syndrome)
519 iv. TRAPS (Tumor necrosis factor receptor-associated periodic syndrome)
520 i. Autoinflammatory syndromes
521

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- 522 **Appendix C: Immunosuppressive and Immunomodulating medications, “Drug Y”**
- 523 1. Glucocorticoids: prednisone, prednisolone, methylprednisolone, dexamethasone
- 524 2. Immunosuppressive/immunomodulating medications
- 525 a. Mycophenolate mofetil/mycophenolic acid
- 526 b. Azathioprine
- 527 c. Calcineurin inhibitors
- 528 i. Cyclosporine
- 529 ii. Tacrolimus
- 530 iii. Voclosporin
- 531 d. Apremilast
- 532 e. Intravenous immunoglobulin (IVIg)
- 533 f. Cyclophosphamide
- 534 g. Colchicine
- 535 h. NSAIDS
- 536 i. Acetaminophen
- 537 3. csDMARDs (conventional synthetic disease-modifying anti-rheumatic drugs)
- 538 a. Methotrexate
- 539 b. Leflunomide
- 540 c. Sulfasalazine
- 541 d. Hydroxychloroquine
- 542 4. bDMARDs (biologic DMARDs) including biosimilars
- 543 a. Tumor necrosis factor inhibitors (TNFi)
- 544 i. Etanercept
- 545 ii. Infliximab
- 546 iii. Adalimumab
- 547 iv. Golimumab
- 548 v. Certolizumab pegol
- 549 b. B-cell depleting agents
- 550 i. Rituximab
- 551 ii. Ocrelizumab
- 552 iii. Obinutuzumab
- 553 c. T-cell co-stimulation blockers
- 554 i. Abatacept

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- 555 d. IL-1 inhibitors
- 556 i. Anakinra
- 557 ii. Canakinumab
- 558 iii. Rilonacept
- 559 e. IL-6 inhibitors
- 560 i. Tocilizumab
- 561 ii. Sarilumab
- 562 f. IL-17 inhibitors
- 563 i. Secukinumab
- 564 ii. Ixekizumab
- 565 g. IL-12/IL-23 inhibitors
- 566 i. Ustekinumab
- 567 h. IL-23 inhibitors
- 568 i. Guselkumab
- 569 ii. Tildrakizumab
- 570 iii. Risankizumab
- 571 i. BLYS/Baff inhibitors
- 572 i. Belimumab
- 573 ii. Tabalumab
- 574 j. Interferon alpha blockers
- 575 i. Anifrolumab
- 576 k. RANKL inhibitors
- 577 i. Denosumab
- 578 5. tsDMARDs (targeted synthetic DMARDs)
- 579 a. JAK inhibitors
- 580 i. Tofacitinib
- 581 ii. Baricitinib
- 582 iii. Upadacitinib
- 583 iv. Filgotinib
- 584 v. Ruxolitinib
- 585

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586 **Appendix D: Vaccines of clinical interest (by mechanism of action) “Vaccine Z”**

587

588 1. Protein/Subunit/Recombinant/Inactivated organism

589 a. Seasonal influenza (inactivated or recombinant, injectable)

590 i. Standard dose

591 ii. High dose

592 iii. Adjuvanted

593 b. Tetanus toxoid/Td/Tdap

594 c. Hepatitis B

595 d. Human Papilloma Virus (HPV)

596 e. Hepatitis A

597 f. Herpes zoster (recombinant Shingrix)

598 g. Meningococcus B (recombinant MenB--Bexsero, Trumenba)

599 h. Inactivated polio (IPV)

600 i. COVID (when data available)

601 2. Polysaccharide

602 a. Pneumococcus (PPSV23, Pneumovax)

603 b. Typhoid (Vi-PS, injectable)

604 3. Conjugate

605 a. Pneumococcus (PCV13, Prevnar)

606 b. Meningococcus ACWY (conjugate—MenACWY, Menactra, Menveo)

607 c. H. influenza b (Hib)

608 4. mRNA and others

609 a. SARS-COV 2 (when peer reviewed published data are available) (Pfizer, Moderna,
610 Johnson & Johnson, and others, as they are available in the U.S.)

611 5. Live attenuated vaccines

612 a. MMR

613 b. Yellow fever

614 c. Zoster (live attenuated, Zostavax)

615 d. Rotavirus

616 e. Varicella

617 f. Influenza (live attenuated, nasal spray)

618 g. Typhoid (live attenuated, oral Ty21a)

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- 620 6. T-cell dependent Neo-antigens
- 621 a. Bacteriophage ϕ X174
- 622 b. Keyhole limpet haemocyanin (KLH)

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APPENDIX E – Participant Disclosures - 2022 Vaccinations Guideline									
In order for the College to most effectively further its mission and to otherwise maintain its excellent reputation in the medical community and with the public, it is important that confidence in the College’s integrity be maintained. The cornerstone of the ACR’s Disclosure Policy is disclosure of actual and potential conflicts so that they can be evaluated by the College in order to avoid undue influence of potential conflicts. The purpose of the ACR’s Disclosure Policy is identification of relationships which may pose actual or potential conflicts. These actual or potential conflicts can then be evaluated by the College so that adjustments can be made that will avoid any undue influence. This policy is based on the principle that, in many cases, full disclosure of the actual or potentially conflicting relationship will of itself suffice to protect the integrity of the College and its interests.									
Participants	Role	Primary Employment	Sources of Personal Income	Intellectual Property	Research Grants/Contracts	Investments to include medical industry and nonmedical industry	Organizational Benefit	Activities with Other Organizations	Family or Other Relations
Eliza Chakravarty	Core Team/Principal Investigator	Oklahoma Medical Research Foundation		N/A	NIH/NIAMS	N/A	N/A	N/A	N/A
Elie Akl	Core Team/GRADE Expert	American University of Beirut	World Health Organization	N/A	N/A	World Health Organization; Robert Koch-Institut	N/A	N/A	N/A
Joann Fontanarosa	Core Team/Lit Review Team Lead	ECRI Institute	N/A	N/A	American Cancer Society; International Society for Thrombosis and Haematosi; Agency for Healthcare Research and Quality (AHRQ); Veteran's Administration/Department of Defense CPG program; Patient-Centered Outcomes Research Institute (PCORI); FDA report on PLGA material and a PCORI Covid19 Horizon Scanning Project	N/A	N/A	N/A	N/A
Clifford (Bing) O. Bingham	Core Team/Content Expert	Johns Hopkins University	Abbvie; Bristol Myers Squibb; Eli Lilly; Gilead; Janssen; Pfizer; Regeneron; Sanofi/Genzyme	N/A	Bristol Myers Squibb; NIH	N/A	Abbvie; Janssen; Gilead	OMERACT	N/A
Kevin Winthrop	Core Team/Content Expert	Oregon Health & Science University	Pfizer; AbbVie; Union Chimique Belge (UCB); Eli Lilly; Galapagos; GlaxoSmithKline (GSK); Roche; Gilead	N/A	BMS; Pfizer	N/A	N/A	N/A	N/A



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Len Calabrese	Core Team/Content Expert	Cleveland Clinic	Sanofi Regeneron; GSK; Roche Genentech; AbbVie; Amgen; Myriad; UCB; Gilead; Novartis; Lily; BMS; Horizon	N/A	N/A	N/A	N/A	Healio Rheumatology	Cassie Calabrese, daughter
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Cassie Calabrese	Lit Review Team	Cleveland Clinic	AbbVie; GSK; Sanofi-Regeneron	N/A	N/A	N/A	N/A	National Psoriasis Foundation	Leonard Calabrese, father
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Rebecca Sadun	Lit Review Team	Duke University	Lupus Foundation of America	N/A	Rheumatology Research Foundation; Arthritis Foundation; Lupus Foundation of America; CRDF Global; Human Vaccine Trial Network	N/A	N/A	N/A	N/A
Benjamin J. Smith	Voting Panel	Florida State University College of Medicine School of Physician Assistant Practice	N/A	N/A	Health Resources and Services Administration	N/A	N/A	ACR/ARP; National Commission on Certification of Physician Assistants; American Academy of Physician Assistants/Johns Hopkins	N/A



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Jeffrey Sparks	Voting Panel	Brigham and Women's Hospital	Pfizer; Gilead; Bristol-Myers Squibb; Optum	N/A	NIH/NIAMS; Rheumatology Research Foundation; NIH/NIAID	N/A	N/A	N/A	N/A
Jonathan TL Cheah	Voting Panel	UMass Memorial Medical Group; University of Massachusetts Medical School	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Lindsey Baden	Voting Panel	Brigham and Women's Hospital; New England Journal of Medicine	N/A	N/A	NIH; Wellcome Trust; Gates Foundation, IAVI	N/A	N/A	N/A	N/A
Reuben Arasaratnam	Voting Panel	UT Southwestern Medical Center	University of Kentucky; Methodist Hospital Dallas; Baylor University Medical Center; COVID-19 survey Techspert.io, Cambridge UK.	N/A	Alliance for Academic InterN/AI Medicine	N/A	N/A	N/A	N/A
Tiphannie Vogel	Voting Panel	Baylor College of Medicine	N/A	N/A	ANR Foundation; Thraser Research Fund; RRF; CHEST Foundation; Ligums Family	N/A	N/A	OPA Syndrome Foundation	N/A
Anne Bass	Voting Panel/ACR BOD Liaison	Hospital for Special Surgery	N/A	N/A	HSS complex joint reconstruction center; HSS rheumatology council	N/A	N/A	N/A	N/A
Ida Hakkarinen	Voting Panel/Patient Rep	National Oceanic and Atmospheric Administration	N/A	N/A	N/A	N/A	N/A	N/A	Sibling - William D. Hakkarinen, M.D., AAFP (past President of Maryland Academy of Family Physicians)