

IVRT

IVPT

Detail Introduction :

???

5 ??????????????????????

6 ????????(?????????????)?

7 ??????(In Vitro Release Test????IVRT)

8 ??????(In Vitro Permeation Test????IVPT)

9 ?????????????????????????

10 ?????????????????????????

11 ?????????????????????????

12 ?????????????????????????

13 ?????????????????????????

14 ??????????????(????????????)

15 ??????????????)?IVRT ?IVPT ?????

16 ?????????????????????

17 ?????????????????????????

18 ?????????????????????????

19 ?????????????????????????

20 ???IVRT/IVPT ?????????????

21 ?????????????????IVRT ?IVPT ???

22 ??????????????????????1~6? ???

23 ??????(1)?????(2)?????(3)?????24 (4)?????????(5)?????????(6)???

25 ?????????

26 ?????????????????????

27 ?????????????????????

28 ?????????????????????

29 ?????????????????

30 ????????(IVRT)₃₁ (?) IVRT ?????

32 ?????????????????????IVRT ???

33 ?????????????????????(??

34 ??????) ?????????????????

35 ?????????????????IVRT ?????

36 ?????????????????₃₇ (?) IVRT ???

38 ?????????????????????

39 ?????????????????????

40 ?????????????????????

41 ?????????????₄₂ 1.??

43 ??????IVRT ??????????????
44 ??????????????????????????
45 ??????????????????????46 2.?
47 ?IVRT????????????????(??
48 ???????????/?????????/????) ?
49 ????(? 0.45?m ?)?????????????1?
50 IVRT????????????????????
51 ?????????????????????????
52 ???IVRT????????????????
53 ?????????????????????????
54 ??
55 3.????
56 ?????????????????????
57?????????IVRT ?????????pH ???
58 ??
59 ?IVRT????????????????
60 ?????????????????????
61????pH5 ~ 7 ???-????
62 ?????????????????????
63 IVRT????????????????
64 ?????????????????
65? (??) ?????? (r2?0.97)? ?????????
66 ?????IVRT ?????????
67 ?????
68 4.????
69 ??????????IVRT????????
70 ???/? ??????????(Steady-StateRelease
71 Kinetics)?1? ?????????
72 ??????5 ?????????
73 ?????(Steady-StateReleaseRates)????
74 ???4 ?????????
75 ?????????????????(??76 30 ??????)????????
77 ?????????????????????78 ±15 ??±2% (?????)2?
79 ?????????
80 ?????????(±5%)????
81 ?????????????????IVRT??
82????????????????83 (Pseudo-Infinite Dosing)?3? ?????
84 ?????
85 ?????????
86??????? (????? 600 rpm)?1?87 (?) IVRT ??????2?

88 ??IVRT????????????????
89 ?????????????????????
90 ?????????????????IVRT ??????
91?????
92 ??????IVRT ??????????
93????????????????94 1.???
95 ??????????????????
96?????????????????
97 ??????????????????(?98 32C±0.5C) ????? ??????????
99 ???????±10%?100 2.??
101 IVRT?????????????
102????(?? 32C±0.5C????6 ??)????
103 ??????????????
104 ??????????
105?????????????
106????????????????100%
107 ± 5%?
108 3.?????
109 ??????????????
110 ??????????????
111 ??????????????
112 ?????? (?? ??????????)
113 ??????????????)? 114 4.???
115 ??????????????
116 ?????????????????21C 117 ±2C????50%RH±20%RH??
118 5.????
119 ??????????????
120 ?????????(?????????)?
121 ?????????(r2 ?0.97)?????
122 ?????????IVRT ??????????
123 ?????????????124 6.?????
125 ?????????(??) ??????
126 ??????????????
127 ?????????(%CV)????????(%CV)
128 ??????15%????????/??/????/
129 ??????????????
130 ?????????
131 7.???? (Dose Depletion)
132 ??????????????
133 ??IVRT ??????????

134 ?????????????????(??
135 ??????????????????)?
136 ?????????????????1g??????137 5%????????????50mg????????6
138 ???IVRT ?????????????????10mg?
139 ???50mg ???????10mg????????20%?
140 ??????????????(Average Percentage Dose
141 Depletion)?
142 ?????????????????30%??
143????30%????????????????
144 ?????????????????????
145????????????
146 8.??— ?????????? (Discrimination-147 Selectivity, SensitivityandSpecificity)
148 ?????????????IVRT ???
149 ???????????2? ??????
150 IVRT ?????????IVRT ?????????
151 ?????????????????????
152 ?????????????????????
153 ?????????????????????
154 ??????
155IVRT ?????????IVRT ?????????156 ?????????????????????157
????????????????????158 ?????????????????????159 ?????????????????
160????????IVRT ??????
161 IVRT ?????????IVRT ?????????162 ?????????????????????163????????????
IVRT ??????(164 ?) ?????????????????????????165 ?r2 ?????IVRT ?????IVRT????
????????????????IVRT????167 ? (??) ?????? r2 ??0.95????????168 ??169 9.??
????????IVRT????????171????????(??- 1°C ?+1°C ???32°C±0.5°C)?172
????????(????????+10%-10%)? ??173 ??????(? ???/?pH ??????)????174 ???(??
?????????)? 175 ???IVRT ?????????IVRT?????“176 ??????”????????
?????
177 IVRT????????????178 (?) ?????
179 ?????????????????
180 ?????????????3?
181 ?????????????
182 ?????????????(6 ~ 8 ?)
183 ???2? ???ICH M10 ?????????
184 ?????
185 (?) IVRT ??????1?
186 ?????????????IVRT?
187 ?????????
188 ?IVRT????????????

189 ??????????????????????
 190 ??????IVRT ??????????
 191 ???????6 ??????????IVRT
 192 ??????????????????????
 193 ????(ABABAB?BABABA)?????194 (?) ???????????1?
 195 ?????????????????????(t1?
 196 t2 ?)?????(??? $\mu\text{g}/\text{cm}^2$???)?????
 197 ?????????????????????t ?
 198 ??????????????????
 199 ??????????????????
 200 Mann-WhitneyU?????????????
 201 ???????(?) ??? 90%?????
 202 ??????????????????203 (R)?????????(T)???? R??
 204 ??????????????????????
 205 ????????????? (T)?????????
 206 ? (T) -?? (R) ?????????T/R ??????
 207 ?????????????TS ?????????RS ?
 208 ?????????T/R ??????
 209 ?1. ??????(TS)?????(RS)?

	RS1	RS2	RS3	RS4	RS5	RS6
TS1	TS1/RS1	TS1/RS2	TS1/RS3	TS1/RS4	TS1/RS5	TS1/RS6
TS2	TS2/RS1	TS2/RS2	TS2/RS3	TS2/RS4	TS2/RS5	TS2/RS6
TS3	TS3/RS1	TS3/RS2	TS3/RS3	TS3/RS4	TS3/RS5	TS3/RS6
TS4	TS4/RS1	TS4/RS2	TS4/RS3	TS4/RS4	TS4/RS5	TS4/RS6
TS5	TS5/RS1	TS5/RS2	TS5/RS3	TS5/RS4	TS5/RS5	TS5/RS6
TS6	TS6/RS1	TS6/RS2	TS6/RS3	TS6/RS4	TS6/RS5	TS6/RS6

210????T/R ??????36 ?T/R ??????
 211?????????8 ???29 ??????????
 212 ??(??? 100)????? 90%?????????
 213?????90%~111%?????????
 214 ???????????????4 ?(2 ??
 215 ??2 ??????6 ???) ??? ??????
 216?12 ?????????????18 ?T/R ??????
 217 ??????????324 ?T/R ?????????
 218 ???????110 ???215 ?????(?????)
 219 ???????90%?????????)? 90%~111%
 220 ??????????????
 221 ????????(IVPT)222 (?) IVPT ??????
 223 IVPT?????????????????
 224 ??????????????????????

225 ?????????????IVPT ????????

226 ?????????????????????????

227 IVPT????????????????????

228 ?????????????

229 IVPT????(FluxProfiles)?????????230 (Pharmacokinetic Profiles)???? IVPT

????????

231?????????????????(Cmax)???- ???

232 ????(AUC)???IVPT????????????

233 ??????????????????????“?”

234 ????? (Cutaneous Pharmacokinetics)”?????“?”

235 ?????????????????????” ?4?

236????????????????????????

237 ?????????????????????????

238 ?IVPT ?????

239 (?) IVPT ???

240 1.IVPT ??

241 ??????IVPT ?????????????

242 ?????????????????????????

243 ?????????

244 2.IVPT ??????1,3,4?

245 ??????????/? ?????????

246 ?????????????????????????

247 ??????????(? ?????????)

248 ??????) ??????(? ??????)

249 ??)?

250 ?????????????????????

251 ?????????????????????

252????????????????????

253 ?????????????????????

254 ??????????????????32 $\pm$ 0.5??

255 ?????????????????

256 ??????????IVPT????????

257 ?(Non-Dermatomed)??? ?????????/???

258 ????

259 3.IVPT ???????

260 ?????????????????

261 ?????????????????

262 ?????????????

263 ?IVPT ?????????

264 ?????????????????/?

265 ??????????????????????
266 ???₄?
267 ??????????????????????
268 ??????????????????????
269 ??????????????????????
270 ?????????₂₇₁ 4.IVPT ???₄?
272 ???????pH ??????????????
273 ??????????????????????
274 ??????????????????????
275 ??????????????????????
276 ?????IVPT ??????????????
277 ??????????????????????
278 ????????(??????)???????
279 ???????????(?? ??????????)?
280 ?????????????????????[???0. 1%₂₈₁ (w/v)? 0.2% (w/v)]????20 ??(?? Oleth-20
282 Volpo-20, ?Brij-20?CAS?9004-98-2) ????????
283 ??????????????????? (??????
284 ???????????)?????????????
285 ????
286 ?????????????????(?? ? 0. 1%?
287 ??????0.01%??????)?????????
288 ???????????/?????????????
289 ?????????????????₂₉₀ 5.IVPT ???₄?
291 ?????????IVPT ??????????
292 ??????????????????????
293 ?????????????????(??) ??????
294 ??????????????????????
295 ??????????????????????8
296 ???????
297 ??????????????????????
298 ?????????????(??) ????????
299 ??????????????????????
300 ??????????????????????
301 ??????????????????????
302 ??????????????????????
303 ?????????????????IVPT ??????
304 ????????????????? ????₃₀₅ ?????????????????????₃₀₆
????????????????????₃₀₇ ?(±5%)???????????? 2~15mg/cm² ??₃₀₈ ?₁?
309 ?????????????????₃₁₀ ??????(????? 600 rpm)?

311 ?????????????????(? 4~6 ?)312 ??IVPT ?????????????????4 ??313 (??
312 ?????4314IVPT ?????????????????315????????????IVPT ?????????316 ????????
313 1.????318 ????????????????????319 ????????????????????320????????
314 ????????????????(??321 32C±0.5C)????? ?????????????????322 ????????????±10%?323
315 ???????324 ????????????????????325 ????????????????????
316 326 ?????????
317 3.????????
318 ????????????????????
319 ????????????????????
320 ????????????????????
321 331 ?????? (?? ?????????????????
322 332?????????????????????)?333 4.????
323 334 ????????????????????
324 335 ????????????????????21C 336 ±2C?????50%RH±20%RH??
325 337 5.??????? (Permeation Profile and Range)
326 338????????????????
327 339 ??? (CumulativePermeation Profile)????????? 340 (?????????) ?????????????
328 341 ???
329 342 6.???????
330 343????????????????
331 344 ????????????????
332 345 ?????????????(%CV)??????????
333 346 ?????
334 347 ????????????????
335 348 ????????????????
336 349 ????????????????350 7.????
337 351 ????????????????
338 352 ??IVPT????????????
339 353 ????????????????(??
340 354 ?????????????????)?
341 355 ????????????????10mg????
342 356 ??5%????????500?g????
343 357 ?48 ???IVPT????????????35810?g????500?g ?????10?g???????359 2%
344 358 ????????????(????
345 359 ??)?
346 360 8.???—????
347 361 ????????IVPT ?????
348 362 ?????????4? ?????
349 363 ????IVPT????IVPT????????“?
350 364 ????????????????”????
351 365

366 ?????????IVPT ??????????
367 ?????“????????”?????????
368 ?????????IVPT?????????
369 ?????????IVPT ??????????
370 ??????????????????????
371 ?????????????????(???)??
372 ????(Potency) ?????(??) ??????
373 ???/?IVPT ?????/??????????
374 ???IVPT ???IVPT ??????????
375 ??????????????????????
376?????(?????????????????)?
377 IVPT????????????????(?? ??
378 ???IVPT??)?? ??? IVPT ???????
379?????????????????????
380 ???₄????????IVPT ??????
381????IVPT ?????????????(??₃₈₂ 4 ~ 6 ?????)???????? 4 ???
383????₃₈₄ 9.??
385 ?????(?? ?????) ???
386 ??????????????????????
387 ??????????????????????
388 ??????????????????????
389????IVPT ?????????IVPT ?????₃₉₀ (?) ??????
391 ??????????????????????
392 ??????????????????????
393 ??????????????????????
394 ?????????????????????₃₉₅ (6 ~ 8 ?) ????????? ICH M10 ?????
396 ??????????????
397 (?) ????? (????) ?????₁?
398 ??????????????????????
399 ???
400????????????????₄₀₁ (????????????????) ?????
402 ??????
403 (?) IVPT ??????₄?
404 ?????????????????IVPT ?
405 ?????????????????₄₀₆ 1.???
407 ??????????????????
408 ?????????₄₀₉ 2.??
410 ??IVPT?????????????
411?????????????????
412 ??????????

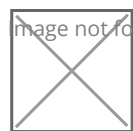
413 3.??
414 ?IVPT ?????????????????????415 (????) ?????????????????????
416????????????????????????????
417????
418a. ABABAB...
419 b. BABABA...
420 ????
421 ?IVPT ?????????????????????
422 ?????????????????????????
423 ?????????????????????????
424 ?????????????????????????
425 ?????????????IVPT ?????????????
426 ??IVPT ?????????????????????
427 ?????????????????????????
428????????????????????????
429 ?????????430 4.IVPT ??
431IVPT????????????????????
432 ?????????????????????????
433 ??(J)???????????? ?????????????
434 ?????????????
435 ??(?????) ???? Y-????????
436 X-??????Y-??“J”??????/??/? (??ng/
437cm²/h)????????????????????
438????????????????????????
439 ?????????????????????(????/?
440 ?ng/ cm²)???? Y-????????X-??
441 ?????????????????????
442 ?(?? 2.0 ng/mL)????????????(??443 6.0 mL)????????????(??444 1 c
)????????????????????
445 ????2 ?????????J ?????????
446 J = [(2.0 ng/mL) × (6.0 mL)]/ (1 cm²) / (2 h) = 447 6 ng/cm²/h
448 ?????????????????????
449 ?????????????????????
450????????2 ?????????????????451 0 ?2 ?????????(?? 1 ??)?
452 ?????????????????????(AMT)?
453 AMT ?????????(????????)?
454 ?????????????
455????????????????(Jmax????
456?????)? AMT????????
457????????Cmax ?AUC ?????????

496???????? (??)?(2021 ?3 ?)

497 ???IVPT?????4?
 498 ??????????(T)????(R)?
 499 ??????????n ?????T ??
 500 ?_{jth}(j= 1, ... , n) ??? r_{jT}?????
 501 ??R ??_{jth} (j = 1, ... , n) ??? r_{jR} ?????
 502 ?????(j)????(i)?????
 503 ?????
 504 T_{ij}= ?????_{jth}????_{ith}????
 505 IVPT ?? (Jmax ?AMT) ????? (i = 1, 2, ..., r_{jT}, j=506 1, 2, ... , n)
 507 R_{ij}= ???(????)? _{jth}????_{ith}?
 508 ?????IVPT ?? (Jmax ?AMT) ????? (i = 1,509 2, ..., r_{jR}, j= 1, 2, ... , n)
 510 r_{jT}= ?????_{jth}???????? (j=511 1, 2, ... , n)
 512 r_{jR}= ???(????)? _{jth}?????
 513 ??? (j= 1, 2, ... , n)
 514 r[?] = r₁(R)+ r₂(R)+ ... + r_{nR}= R?????
 515 n= ???
 516 ?????????T ??R??n????
 517 ??????????????????
 518 ??????????????
 519 ?????????T= T₁(T)= T₂(T)= ?520 = T_{nT} = T₁(R)= T₂(R)= ? = T_{nR}?
 521 ?????????(?????????
 522 ?????????) ??????(? ??????
 523 ?????????) ??????????
 524 ??????????????????
 525 ??????????????????
 526 ??????????????????
 527 ??????????
 528 ?????BE ??????????
 529 ?????????????(T?R)?
 530 ?????????3 ??????
 531 ??1
 532 ??IVPT??(Jmax ?AMT)?????
 533 ??S_{wR}?????
 534 S_{wR}= () 1/2
 535 ???  .j=  ?i(r)  1 R_{ij}?????j????T_{jR}
 536 ??????
 537 ??S_{wR}?0.294????2, 3.1 ?4.1?????

538 ???????(SABE)????? IVPT ????BE

539 ??SwR ?0.294?????2, 3.2 ?4.2?????T



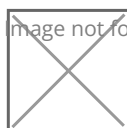
540 ??(TOST)?????????(ABE)????? IVPT

541 ????BE

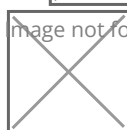
542 ??2

543 ??T ?R ?????????????(I?)?????(se⁵⁴⁴(I?)) ?????? (df?)?

545 ?????????????????I? ?se (I?) df??



546 $I? = I? = \text{?}_{j(n)=1} I_j \text{?} I_j = \text{?}_{i(r)=1} (T_{ij} \text{?} R_{ij})$



547 $Sl(2) = \text{?}_{j(n)=1} (I_j \text{?} I?)^2 \text{ (????????)}$

548 $se(I?) = ?Sl(2)/n$

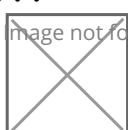
549 $df? = n? 1$

550 ???????????SAS?PROC MIXED(?

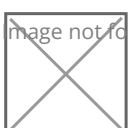
551 PROC GLM)?????I? ?se(I?) df??

552 ??3.1 SABE ?

553 ?SABE ??????????



554 $H_0 : \text{?} e$

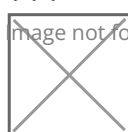
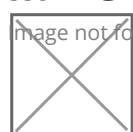


555 $H_a : \text{?} < e$

556 ???

557 $u_T \text{?} u_R = T \text{?} R \text{ ?????????}$

558 $G_{w(2)R} = R \text{ ?????????}$



559 $e = \text{?}_m = 1.2500 \text{ (BE ??) , and } G_{w0} = 0.25 \text{ } ^{560} \text{ (????)}$

561 ?????????????????????

562 ??Howe's Approximation (Howe, 1974) (? = 0.05)?
2

563 ?? ($u_T \text{?} u_R$) ? $eG_{w(2)R} \text{?} (1-\text{?}) * 100\% \text{ ???????}$

564 $X + Y + \text{sign}(V) \text{?} |V|^{1/2}$

565 ???

566 $X = I?_2 \text{?} se(I?)_2$

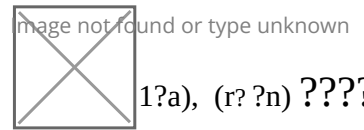
567 $Y = \text{?} eG_{w(2)R}$

568 $X? = (|I?| + t(1?a), df? \text{?} se(I?))$

569 $Y \text{?} = \text{?} e$



570 $\text{sign}(V) = 1 \text{ if } V > 0; 0 \text{ if } V = 0; -1 \text{ if } V < 0$



571 $t_{(1-\alpha), df} \text{ Student's } t_{(1-\alpha), df} \text{ } 100 \times X_{(1-\alpha), (r, n)}$

n) ??

573 $(1-\alpha) \times 100 \text{ } 3.2 \text{ ABE}$

574 3.2 ABE

575 ABE

576 $H_0: u_T = u_R \text{ } \ln(m) \text{ } u_T = u_R \text{ } \ln(m)$

577 $H_a: \ln(m) < u_T = u_R < \ln(m)$

578 ??

579 $u_T = u_R = T_{IVPT} \text{ } 580$

581 $m = 1.2500 \text{ (BE)}$

582 $\ln(m) \text{ BE}$

583 $“”$

584 $u_T = u_R \text{ } (1-\alpha) \times 100 \text{ } 585$

585 $I \pm t_{(1-\alpha), df} \text{ se}(I)$

586 $t_{(1-\alpha), df} \text{ } t_{(1-\alpha), df} \text{ } 100$

587 ???

588 $4.1 \text{ SABE (Scaled Average BE)}$

589 ??

590 $IVPT$

591 2

592 a. $(u_T = u_R) \text{ } e_{Gw(2)R} 95 \text{ } 593$

593 $0 \text{ } 594$

594 b. $T_{IVPT} \text{ } [1/m, m] \text{ } m = 1.2500 \text{ } 595$

596 $4.2 \text{ ABE (Regular Average BE)}$

597 ??

598 $IVPT \text{ } u_T = u_R \text{ } 90 \text{ } [0.8000, 1.2500]$