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apan Report On Medical Equipment And Pharmaceuticals Market-Oriented, Sector-Selective (MOSS) Discussions (1986)

REPORT ON Medical Equipment and Pharmaceuticals

Market-Oriented, Sector-Selective (MOSS) Discussions

by the U. S. and apan MOSS Negotiating Teams

anuary 9, 1986

[Letter to]

Minister for Foreign Affairs Shintaro Abe

Ministry of Foreign Affairs

Tokyo

[and]

Secretary of State George P. Shultz

Department of State

Washington, D.C.

We are pleased to forward to you the attached official copy of the report by our negotiating teams on the market-oriented, sector-selective (MOSS) talks on medical equipment and pharmaceuticals. We believe that this report is responsive to the mandate entrusted to us. [letter signed by US and apanese Chairs]

Respectfully

Hitoshi Yoshimura

Vice Minister

Ministry of Health and Welfare

Tokyo

David C. Mulford

Assistant Secretary for International Affairs

Department of the Treasury

Washington, D.C.

[delegation lists]

U.S. AND APAN MOSS NEGOTIATING TEAMS

MEDICAL EQUIPMENT AND PHARMACEUTICALS MARKET-ORIENTED,

SECTOR-SELECTIVE (MOSS) DISCUSSIONS J

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T shi Min First Secret ry

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INTRODUCTION

A. OVERVIEW OF THE DISCUSSIONS

On Januar 2, 1985, Pr sid nt R agan and Prime nist r Nakas n met in L s Ang l s t dis uss, among th r issu s, bilat ral n mi issu s. Th S talks r sult d fr m that me ting.

On Januar 28 and 29, 1985, high-l v l ffi ials fr m Ja an and th Unit d Stat s met in T k t laun h th r ss agr d t b th Pr sid nt and th Prime nist r. Th Unit d Stat s r s nt d an a r a h that was mark t- ri nt d and s t r-s l tiv , with th a r n m S. Th mark t- ri nt d as t f this aM r a h meant f using n r moving barri rs that limit mark t a ss. Th s t r-s l tiv as t meant und rtaking this barri r-r moval within s ifi industrial s t rs -- t l mmuni ati ns, medi al qui ment and harma uti als, l tr ni s, and f r st r du ts -dis uss d b th Pr sid nt and th Prime nist r. Th Ja an s sid indi at d that it was willing t f ll w this S a r a h.

Th S dis ussi ns in th medi al qui ment and harma uti als s t r b tw e n th g v rnments f th Unit d Stat s and Ja an n ntrat d n furth r ning th Ja an s h alth ar mark t b addr ssing h trad ff ts f Ja an's r gulat r s st m f r r t ting ubli h alth and saf t and its insuran s st m f r r imbursing h alth ar x ns s. Th S dis ussi ns v r d th full s trum f r du t mark ting, in luding manufa turing r imp rt a r vals (sh nin), li nsing f r manufa tur r imp rt (k ka), and ri ing.

Th U.S. sid rais d th mark t- ning issu s fr m th vi w p int f r moving barri rs t trad and/ r t th ndu t f busin ss in Ja an b f r ign firms. Th U.S. sid n t d that in man as s th issu s r fl t d in ffi i n i s and infl xibiliti s in th r gulat r s st m whi h had th ff t f imp ding th ntran int th mark t f n w r du rs and n w r du ts, and f influ n ing busin ss d isi ns v n wh n h alth and saf t qu sti ns w r n t at stak . At th same time, th U.S. sid did n t qu sti n th basi mandat f th nistr f H alth and Welfar ( ) und r th Pharma uti al Affairs Law (PAL) t r gulat in fav r f th h alth and saf t f th Ja an s l and th v rall bj tiv f t r du Ja an s h alth ar x ns s.

Th Ja an s sid r s nd d that th Ja an Ms r gulat r s st m n ith r v rtl n r v rtl dis riminat d against f r ign firms in fav r f d mesti n s, r viding b th with qual rtuniti s t nt r th h alth ar mark t. It r gniz d, h w v r, th imp rtan f simplif ing administrativ r dur s, liminating administrativ d la s, and in r asing trans ar n , f r furth r fa ilitating M ss t Ja an's mark t and str ngth ning th fr trad s st m. Th Ja an s sid agr d t dis uss and s k s luti ns t th issu s as r s nt d in this wa .

Th int rag n d l gati ns f b th sid s met six times in 1985 t dis uss and d v l mark t- ning measur s, and w rk d int nsiv l t r aliz th int nt f th S initiativ . As a r sult, imp rtant r gr ss has b n mad thr ugh th s dis ussi ns and impr v ments in a ss t Ja an's mark t hav b n and will b r aliz d.

This r rt d s rib s th r bl ms addr ss d in th talks and th arti ular issu s f mark t a ss whi h th inv lv d. It x lains th s luti ns t th issu s t whi h b th sid s agr d. It s ifi s futur w rk lans f b th sid s in this s t r. M

The measu es a ee by he Uni e S a es an Japan sh ul elimina e D he a ve se a e effec s f he e ula y sys em while c n inuin safe ua he heal h an safe y f he Japanese pe ple. T fu he hese bjec ives, b h si es have a ee c n inue mee n a e ula basis eview implemen a i n f he a ee s lu i ns an es lve any c mplica i ns ha may a ise.

The U.S. sD e was le by Assis an Sec e a y f he T easu y f In e na i nal Affai s vi C. Mulf . The Japanese si e was le by Vice Minis e f MHW Hi shi Y shimu a. a

B. SUMMARY OF THE AGREE SOLUTIONS

II.Issues Res lve

Chap e II f his ep p vi es mo e e aile esc ip i ns f he issues an he a eemen s ha es lve hem. This sec i n is a summa y, esc ibe in he c n ex f he elevan pe a i nal fea u es f he Japanese heal h ca e e ula y sys em, f he specific measu es c mmi men s a ee up n by he MOSS ne ia s.

1. Main Fea u es f he Japanese Heal h Ca e Re ula y Sys em

The elemen s f he e ula y sys em mos elevan he iscussi ns an n which he ne ia s c ncen a e inv lve he p cesses f b ainin elevan app vals an licenses an he lis in f eimbu semen p ices un e he c mp ehensive Japanese me ical insu ance sys em. T b in a p uc ma ke , he ini ial s ep f f ei n an mes ic p uce s alike is b ain manufac u in imp app vals f he pha maceu ical me ical evice p uc s hemselves. Such app vals a e calle sh nin, an b ainin hem epen s essen ially up n cumen a i n, inclu in he esul s f clinical es in , which can sa isfy MHW ha safe y an efficacy equi emen s a e me . In i s ecisi n-makin p cess, MHW c nsul s wi h an a vis y b y, he Cen al Pha maceu ical Affai s C uncil (CPAC), which inves i a es f m a scien ific p in f view whe he i is app p ia e app ve manufac u in imp f new pha maceu ical me ical evice p uc s.

T p uce imp a u me ical evice, a license manufac u e imp , calle a ky ka, mus als be b aine n he basis f cumen a i n which emons a es (1) ha p ucin imp in es ablishmen s mee app p ia e safe y an manufac u in s an a s, an (2) ha b a membe s f he manufac u e imp e a e le ally able se ve in ha capaci y.

The sh nin is an e each pe s n (ju i ical pe s n) in en in manufac u e imp u s evices. The ky ka is an e f each manufac u in plan imp e 's business ffice.

Wi h sh nin an ky ka in han , a fi m is echnically qualifie b in a p uc ma ke . Neve heless, sales f he p uc , in ene al, epen heavily up n eimbu semen un e he Na i nal Heal h Insu ance scheme, because i c ve s p ac ically 100 pe cen f he Japanese p pula i n. The ef e, he manufac u e imp e mus seek an app p ia e p ice lis in un e he sys em. The insu ance p ice lis in p cess is sepa a e f m he app vals p cesses which ene a e sh nin an ky ka. P ices a e se by MHW base n ene al ules f mula e by he S cial Insu ance Me ical Affai s C uncil (Chuiky), which is he an f ec ncilia i n f he in e es s f paye s an payees f insu ance eimbu semen .

2. The Issues an Thei Res lu i ns

The specific issues iscusse by he ne ia s can be upe un e he f ll win hea in s, each f which c esp n s an aspec f he app val an eimbu semen p ice-se in p cesses: (a) es in an es a a; (b) app val an licensin p cesses hemselves; (c) linka es be ween he app val an p icin mechanisms; ( ) he Na i nal Heal h Insu ance eimbu semen sys em; an (e) anspa ency. Gene ally, he ne ia s s u h s lu i ns which w ul p ec he in e i y f MHW's man a e un e he PAL p ec he heal h an safe y f he Japanese pe ple; elimina e elays in ma ke in new p uc s; elimina e s u ces f unnecessa ily hi he c s s f in business in Japan; an imp ve he c mme cial business ecisi n-makin envi nmen in Japan.

a. Tes in an Tes a

a

Re ula y au h i ies in b h Japan an he Uni e S a es equi e fi ms submi e aile ep s n p e-clinical an clinical u an evice ials in supp f app val applica i ns. A he ne ia i ns, he U.S. ele a i n D

pointed o t t t p ne e clinic l te ting req irement in effect for t e onin c ed problems for foreign firms in terms of co tly del y in pprov l nd ig er co t of doing b ine . T e U.S. ide noted t t MHW req ired ll clinic l te ting to be done in p n on re ident p ne e citizen . T i req ired co tly d plic tion of te ting performed el e ere in t e rld, even en difference mong te t bject may not ve d ny be ring on t e re lt . It introd ced del y ic co ld prevent ne prod ct from entering t e p ne e market q ickly. Dome tic firms did not be r e e d plic tive te ting co t . Problems of d plic tive te ting req irement r i ed by t e U.S. ide extended to p rmace tic l , medic l device , nd in-vitro di gno tic .

T e p ne e ide noted t t it w re of problems in t e te ting field. Prior to t e MOSS t lk , it d e t bli ed gro p of cientific expert to t dy t e i e of ccept nce of foreign clinic l te t d t T e negoti tor l o noted cert in ot er te ting i e ic concerned p n' in pection req irement for blood nd ot er biologic l , ll t bility nd terility te ting t nd rd .

T e negoti tor re c ed t e follo ng greement on t e te ting nd te t d t i e :

(1) Accept nce of Foreign Clinic ¦ D at

-- Wit reg rd to p rmace tic l , foreign clinic l te t d t ll no be ccepted for ll ex min tion nd te ting req irement except for t e follo ng t ree items ere t ere re immunologic l nd et nic difference bet en p ne e nd foreigner :

o Comp r tive clinic l tri l ;

o Do e finding te t ; nd

o Ab orption, di trib tion, met boli m, nd excretion te t .

-- For in-vitro di gno tic re gent , foreign clinic l te t d t ll no be ccepted except for t o e t ne p r meter (i.e., t o e ic me re n entirely ne b t nce di gno tic indic tor), nd t o e in ic imm nologic l re ction problems co ld occ r t t e mate i l to be te ted.

-- Foreign clinic l te t d t ll no be ccepted for medic l device , except impl nt ble nd t o e ffecting org nic d pt bility.

(2) Ot er Te ting I e

-- In erie of expert ' meeting , bot ide greed on ignific nt improvement in p n' te ting req irement for t bility nd terility te t nd for blood nd ot er biologic l prod ct .

b. Approv l nd Licen ing Proce e

T e MOSS t lk explored n mero b ine i e r i ed by t e U.S. ide ffecting foreign firms in rking t ro g t e proce e of obt ining onin nd kyok , nd in mending t e e doc ment b ine req irement nd rel tion ip c nced.

-- MHW d no t nd rd proce ing period for ne pprov l . T i often c ed co tly ncert intie nd del y nd it may ve cre ted perception in t e eye of foreign firms of rbitr rine in t e y tem.

-- No di tinctive y tem exi ted for pre-market revie of in-vitro di gno tic re gent . A re lt, firms enco ntered co tly del y in bringing prod ct to market, nd innov tive prod ct co ld not re c t e market q ickly.

-- T e reg l tory y tem did not provide for "tr n fer " of onin from one b ine entity to not er. T i diffic lt i e de lt t core principle of t e reg l tory y tem ic t e p ne e ide believed co ld not nd o ld not be c nged, b t t t e me time, t e U.S. deleg tion noted, it in ibited t e f ll exerci e of propriet ry rig t to prod ct .

T e y tem co ld not de l imply or e ily t niq e combin tion of dr g nd device (e.g., t e combin tion into ingle p ck ge of dr g nd it delivery y tem). S c p ck ge re incre ingly ed in rld market . T ey re tec nologic lly dv nced, medic lly perior, nd ble to offer gre t co t ving in medic l c re. w

Costly do tatio r q ir ts a d r g latory i[mp] di ts w e pla d o for ig fir[ms] wishi g to ha g th o try of [ma] fa t r of alr ady approv d prod ts;

o Mak [mi] or [mo]difi atio s a d i[mp]rov ts to alr ady approv d prod ts; or

o Cha g th addr ss s of i[mp]ort rs i Japa witho t disr pti g b si ss op ratio

I[mp]ort rs of dr gs a d d vi s o t r d ad[mi] istrativ d lays i i[mp]ort pro d r s b a s C sto[ms] a d MHW i ort l ara op ratio s w e ot i t grat d This probl [m] i r as d i[mp]ort rs' osts a d i[mp] d d ffi i t trad

Th gotiators r a h d t ally a ptabl sol tio s to a h of th s approval pro ss iss s, as follows:

Sta dard pro ssi g p riods hav b adopt d a d p blish d for approvals for phar[ma] ti als, diag osti s, a d d vi s If MHW a ot pro ss a appli atio withi th r l va t sta dard pro ssi g p riod, th appli a t will ow hav th right to b so i for d a d giv a xpla atio of th r aso s th r for

I -vitro diag osti r ag ts ow hav th ir ow n disti tiv , xp ditio s approval r vi w pro ss S h r ag ts ar xa[mi] d s parat ly fro[m] oth r phar[ma] ti als o th basis of si[mp]lifi d appli atio do ts

For tra sf rs of approvals: wh a o[mp]a y wish s to ha g o r ial arra g ts (for xa[mp]l , fro i orti g to li si g, fro o li s to a oth r, or fro[m] li si g to [ma] fa t ri g), a d th o a y's for r b si ss part r agr s to tra sf r [ma] fa t ri g or i[mp]orti g op ratio s a d all ssary data a d i for[ma]tio to th w part r or tity, th sho i will b tra sf rr d by otifi atio a o[mp]a i d by th vid of th ir agr t Kyoka will b iss d a d xisti g pri s will b list d withi thr ths aft r th dat of appli atio (prior appli atio for kyoka will b possibl) Wh th r is o s h agr t b tw e tra sf ror a d tra sf r , MHW will iss sho i a d kyoka withi thr [mo] ths of appli atio d r si[mp]lifi d pro d r s, if th appli a t s b[mi]ts data a d i for[ma]tio si[mi]lar to that for agr d tra sf rs, a d wh th for r b si ss part r as s to [ma] fa t r or i[mp]ort th prod t Th r i[mb] rs t pri o will b s t at th sa l v l as for th pr vio sly approv d

prod t withi thr [mo] ths aft r th w sho i is iss d Th U S a d Japa hav agr d to o sid r r sol tio of all typ s of tra sf r sit atio s o a as -by- as basis as th y aris withi th fra work of th follow- p pro ss d s rib d i Chapt r IV of th r port Both sid s ar o tt d to fi di g pra ti al sol tio s to l giti[ma]t b si ss probl [ms] that aris i this ar a

-- MHW has d vis d ad q at approval a d pri i g pro d r s for "kits" whi h o i dr gs a d th ir d liv ry syst[ms] S h kits a ow b bro ght to th Japa s [ma]rk t a d pri [m]appropriat ly d r th i s ra r i b rs t syst

-- Fir[ms] xporti g approv d dr gs or di al d vi s to Japa that wish to ha g th ir o try of [ma] fa t r d o ly otify MHW; approval difi atio s ar o lo g r r q ir d [b]

-- MHW has larifi d by offi ial oti th s op a d typ s of [mi] or prod t [mo]difi atio s whi h do ot r q ir approvals

-- I ort rs wishi g to ha g lo atio s of fa iliti s or pla s of b si ss [ma]y ow [ma]k adva appli atio for kyoka, bas d o wly si[mp]lifi d do tatio , so that b si ss op ratio s ar ot disr pt d

-- Th sto[ms] l ara pro ss for i[mp]ort d prod ts has b str a i d to provid for "o stop" s rvi If . i ort rs hav MHW approvals a d li s s d r th PAL, th ir goods a b l ar d by C sto offi ials d r or[p] al sto pro d r s

Li kag s B tw e Approval a d Pri i g M e ha is[ms]

[l]

B[p] a s th r g latory [ma] hi ry gov r i g approvals was s parat d fro[m] th pri i g [ma] hi [s]y of th Natio al H[e]alth I s ra[s] syst[m], a k y iss for th gotiators was th li[mi] atio of d lays b tw e th gra ti g of sho i a d th s tti g of r i[mb] rs t pri s S h d lays add d to th osts a d rtai ti s fa d by fir[ms] doi g b si ss i Japa .

The negot to g ee on gn f c nt nc e e n the f equency of p c ng ec on fo ug n me c l ev ce (ee cu on on t ming of e mbu ement p ce , below). The e ch nge w ll e ve to l nk pp ov l ec on much mo e clo ely w th p c ng ec on , thu gn f c ntly e uc ng the el y n unce t nt e th t to the co t of f ms.

. The N t on l He lth n u nce Re mbu ement Sy tem

Seve l majo ue e olve by the negot to ppl e to the e mbu ement p c ng y tem t elf. n the cu on the U.S. e not que t on the ove ll object ve of MHW to e uce J p ne e he lth c e co t . t eek, howeve , p c ng y tem wh ch woul ope te mo e egul ly n pee ly, un e cle ly ef ne c te .

-- At the out et of the negot t on , the U.S. e e te th t the l t ng of e mbu ement te w a too egul n gene lly nf equent. Th tu t on p o uce fo f ms not only unce t nty but co tly el y n ma ket ent y even fte the hu le of obt n ng hon n n kyok h been u mounte .

-- The U.S. te m l o ob e ve th t c te et by the Chu kyo n t el be t on n u e by MHW n ec ng how to et e mbu ement p ce well wh t p ce to et we e uncle . Th h n e e the b l ty of f ms to commun c te eff c ently the p ec e nfo mat on nee e to pee p c ng ec on n make them e pon ve to co t of o ng bu ne .

The negot to g ee th t fo ll new ug n many me c l ev ce (nclu ng many n-v t o gno t c), p ce l t ng w ll be p ov e qu te ly -- gn f c nt nc e e n f equency th t w ll e uce el y between pp ov l n p ce l t ng to no mo e th n 90 y ; n t on, MHW h committe t elf n p nc ple to el y of no mo e th n 60 y (n l mite c e , uch when few tems e e y fo l t ng n p c ng ue e not cont ove l, t might be po ble to ho ten the el y So bout 30 y). New, nnov t ve n-v t o gno t c (tho e n Cl , n the MHW cl f c t on) w ll be nt o uce nto the e mbu ement y tem w th n x month fte the pp ov l . The e ch nge w ll be mplemente u ng J p n' f c l ye (JFY) 1986.

A eg the c te et by the Chu kyo n t el be t on n u e by MHW, eve l ch nge we e g ee upon by the negot to . The fo mul u e fo c lcul t ng new ug p ce n fo ev ng ug t ff t n w ll be ma e publ c. When the e fo mul e to be ch nge , oppo tun t e w ll be p ov e fo fo e gn well ome t c n u t y ep e ent t ve to exp e the v ew s on gene l ue of e mbu ement pol cy. n t on, MHW, fte con ult t on w th the Chu kyo, w ll e t bl h n nnounce n JFY 1986 t gene l ule fo ett ng n ev ng p ce of me c l ev ce n n-v t o gno t c .

T n p ency

When the MOSS t lk beg n, the U.S. te m note th t fo e gn f ms h n uff c ent oppo tun ty to commun c te w th the egul to y utho t e on techn c l matte n o e to pee up n mp ove the egul to y p oce e fo me c l p o uct . A ple ge to nc e e t n p ency n ll egul to y bo e key element of J p n' ma ket-open ng effo t , t te cle ly by P me M n te N k one n July 1985. The U.S. e eque te th t t n p ency p nc ple be exten e to ll pect of the J p ne e egul to y p oce , nclu ng the Cent l Ph maceut c l Aff Counc l (CPAC), the Chu kyo n MHW t elf.

Du ng the cou e of the t lk , the U.S. eleg t on note w th pp ec t on th t MHW h te ly nc e e both the f equency n the openne of fo mal n nfo mal cu on on pp ov l n othe matte w th fo e gn f m n the ep e ent t ve g oup . U.S. cont ct w th ep e ent t ve of fo e gn f ms eve le h gh level of t f ct on on the p t of tho e bu ne e w th th p og e ve tt tu e of MHW off c l t ll level . MHW conf me th t t w ll cont nue th ucce ful pol cy.

The negot to g ee on eve l fo mal tep to nc e e the t n p ency of the egul to y y tem. The CPAC' "Common n t uct on " w ll be ma e publ c n meet ng w ll be hel to expl n them. Du ng CPAC el be t on , ppl c nt fo new ug pp ov l w ll ece ve oppo tun t e to he n t uct on f om CPAC membe , to k que t on , n to comment on the Counc l' n t uct on . A note bove, fo e gn well ome t c n u t y ep e ent t ve w ll be ble to p e ent the v ew s to the Chu kyo on gene l e mbu ement pol cy ue when the gene l ule of the t ff fo me c l fee o the ug t ff e to be e t bl he o I

changed. e consul a ion wi h he Chuikyo, MHW also will es ablish du ing JF 1 8 p ocedu es o closed hea ings a which individual company ep esen a ives (including p oduc o igina o s i hey wish o accompany applican i m ep esen a ives) may s a e o MHW hei opinions on p icing o hei pa icula p oduc s; hese hea ings will eceive es imony on e icacy, desi ed p ices, and o he a gumen s ega ding he p oduc p ices a issue; and MHW will p ovide adequa e p io public no ice when he hea ings a e o be held.

II. ISSUES RESOLVED

. CCEPT NCE OF FOREIGN CLINIC L TEST D AT

1. Issue

In bo h he Uni ed S a es and Japan, manu ac u e s o medical devices and pha maceu icals mus submi new p oduc s o ex ensive ba e ies o p e-clinical and clinical ials in o de o demons a e adequa e sa e y and e icacy. The da a de ived om hese ials p ovide he ins umen al basis o egula o y decisions.

Japan's egula o y au ho i ies his o ically had no accep ed o eign-gene a ed clinical es da a. In o he wo ds, i espec ive o a p oduc 's es ing his o y ab oad, a o eign i m had o pe o m all o he clinical ials equi ed by he Japanese app oval p ocess, on Japanese subjec s in Japan.

The U.S. side explained ha hese es ing equi emen s had wo se ious ma ke e ec s. Fi s , he duplica ion o es ing, which is ex emely cos ly, placed upon o eign i ms a cos bu den which hei domes ic compe i o s in Japan did no have o ace. Second, duplica ive es ing in Japan b ough abou delays in p oduc ma ke ing.

The Japanese side no ed ha i was awa e o p oblems in his ega d, and ha i had es ablished a g oup o scien i ic expe s o s udy he p oblem o he accep ance o o eign clinical da a.

2. g eed pp oach

Expe s-level discussions ook place be ween he U.S. Food and D rug dminis a ion (FD A) and MHW in May 1 85 in Rockville, Ma yland, ega ding each na ion's policies o he accep ance o o eign clinical es da a in making egula o y app ovals. ha ime expe s discussed he possibili y o se ing, bila e ally o mul ila e al, common s anda ds o he accep ance o o eign clinical es da a. The FD A and MHW ag eed in p inciple ha i is desi able o wo k owa d a sys em o in e na ional ha moniza ion. Following hese expe discussions, he Uni ed S a es and Japan esolved a hei June 1 85 alks in Tokyo o p omo e he accep ance o o eign clinical es da a o egula o y pu poses in Japan.

Japan ag eed o accep o eign clinical es da a o egula o y app oval o pha maceu icals, medical devices, and in-vi o diagnos ic eagen s, as ollows:

(1) Wi h ega d o pha maceu icals, o eign clinical es da a will now be accep ed o all examina ion/ es ing equi emen s excep o he ollowing h ee i ems whe e he e a e immunological and e hnic di e ences be ween Japanese and o eigne s: compa a ive clinical ials; dose inding es s; and abso p ion, dis ibu ion, me abolism, and exc e ion es s.

(2) Fo eign clinical es da a will now be accep ed o in-vi o diagnos ic eagen s excep hose wi h new pa ame e s (i.e., hose which measu e an en i ely new subs ance as a diagnos ic indica o), and hose in which immunological eac ion p oblems could occu wi h he ma e ials o be es ed.

(3) Fo eign clinical es da a will now be accep ed o medical devices excep hose implan ed in he human body and hose a ec ing o ganic adap abili y.

The elevan egula o y ac ion aken by Japan is as ollows:

-- No i ica ion No. 660, "Handling o Fo eign Clinical Da a o Pha maceu icals, e c." (da ed: June 2 , 1 85; e ec ive: July 31, 1 85).

B. "TIME CLOCK" OR "ST ND ARD PROCESSING PERIOD" FOR NEW PPROV LS

1. Issue 9

The U.S. s e s ht the a pt n n Japan f a system f stan ar pr cess n per s anal s t that se n the Un te States. The U.S. s e sa that stan ar pr cess n per s w o l remove the p ss b l ty f r excess ve elays n l cens n wh ch s met mes cc rre n the Japanese system, an enerally el minate c stly ncerta nt es wh ch affecte b th Japanese an f re n f rms. It w o l c ntr b te t an hasten pr ress t war the lt mate al f sh rten n the appr val pr cesses.

2. ree ppr ach

s f Oct ber 1, 1985, MHW ntr ce stan ar pr cess n per s anal s t the FD 's "t me cl ck" pr ce res. These stan ar per s are n erst as ter l mits f r the appr val pr cess; where feas ble, as n the past, appl cat n pr cess n t mes can an w ll be sh rter. If an appl cat n cann t be pr cesse w th n these per s, the appl cant w ll be s nf rme an ven the reas n. MHW can "st p the cl ck" nly when t s necessary f r the appl cant t c rrect nc mplete appl cat ns, c n ct a A t nal tests, r answer nq r es fr m MHW. The stan ar pr cess n per s be n w th the s bmiss n f appl cat ns t prefect ral ff ces an en w th the ss ance f sh n n n T ky . (N te: The ky ka s n rmally ss e s multane sly w th the sh n n.) The appr val takes effect when ss e by MHW n T ky .

The stan ar pr cess n per s are as f ll ws:

New Dr s: E hteen M onths

"Me-T " Dr s: Tw o Years*

OTC Dr s: Ten M onths

In-V tr s: S x M onths

Q uas -Dr s: S x M onths A

Me cal Dev ces: One Year

"Me-T " Dev ces: F r M onths

C smet cs: Three M onths

The relevant re lat ry act n taken by Japan s as f ll ws:

-- N t f cat n N . 960, "Sett n f Stan ar Pr cess n Per s (ate : Oct ber 1, 1985; effect ve: Oct ber 1 A 1985).

*Pr v s nal.

C. REGUL TION OF IN-VITRO DI GNOSTIC RE GENTS

1. Iss e

The f el f n-v tr a n st c rea ents s a rap ly chan n , h hly nn vat ve, an c mplex market. Pr ct cycles can be very sh rt as pr ct a vances are ma e. Pr r t the MOSS ne t at ns, Japan ha n st nct ve system f r premarket rev ew t spee the ss ance f sh n n f r these pr cts. s a res lt, f re n f rms, the U.S. s e expla ne , s met mes face elay an ncerta nty wh ch can precl e market entry when pr ct cycles are sh rt an c nstant chan e n techn l y s pervas ve.

The sc ss ns centere n streaml n n the Japanese appr ach t re lat n n th s area s that the system c l (1) resp n q ckly an eff c ently t maj r r min r mo f cat ns n alrea y appr ve pr cts, an (2) reserve f r str n er re lat ry scr t ny nly th se cases where safety an eff cacy c ns erat ns req re t.

2. ree ppr ach

When experts f FD an MHW met n May 1985 n R ckv lle, Marylan , they sc sse each nat n's p l c es f r the re lat n f n-v tr a n st c pr cts as well as f r the acceptance f f re n cl n cal test ata. F ll w n these expert sc ss ns, Japan ann nce at the J ne 1985 talks the pr mul at n f a separate re lat ry A

channel f he a al f in- i diagn s ic duc s, and als he acce ance f f eign clinical es da a in a al a lica i ns as desc ibed e i usly. I was ag eed ha :

(1) A lica i ns f in- i diagn s ic a al will be ecei ed and exa mi ned se a a ely f m dina y ha ma ceu icals: and

(2) Th ee ca eg ies f in- i diagn s ic duc s will be se u : (a) new a a e ; (b) new h d; and (c) ld a a e . The a al equi e me n s f ca eg ies (b) and (c) will be si lified.

The ele an egula y ac i ns aken by Ja an a e as f ll ws:

-- N ifica i n N . 662, "Handling f In-Vi Diagn s ic Reagen s" (da ed: June 29, 1985; effec i e: July 31, 1985) me

-- N ifica i n N . 5, "Handling f Sh nin A lica i n f In-Vi Diagn s ic Reagen s" (da ed: July 15, 1985; effec i e: July 31, 1985).-14-

D. TRANSFER OF APPROVAL

1. Issue

In dyna mi c, a idly changing indus ies, such as h se ma king me dical equi me n and ha ma ceu icals, ec n mi c efficiency and g d business ac ice f en equi e changes in c cial ela i nshi s by ma nufac u e s and/ i e s. This fac has s ecial significance in he Ja anese ma ke f d ugs and de ices because, his ically, f eign fi ha e en e ed he ke in s ages in l ing a i usly (1) i a i n and ke ing h ugh wh lesale s, (2) i a i n and di ec ke ing, (3) licensing f nufac u e Ja anese fi ms, and (4) es ablish me n f subsidia ies in Ja an ma nufac u e duc s ma ma y be ma ke ed ei he di ec ly h ugh wh lesale s. As f eign fi ms ass h ugh hese s ages and ada hei e a i ns he Ja anese ma ke , changes in a c cial ela i nshi s need be s hly acc da ed, subjec lega a ie a y igh s (e.g., a en igh s) and c n ac s, as well as MHW's egula y bliga i ns f he heal h and safe y f he Ja anese e le.

The U.S. and Ja anese delega i ns discussed Ja anese cedu es f s hly all wing he ansfe f a als (sh nin) e mi changes in c cial ela i nshi s in Ja an. The U.S. side s a ed ha he egula y sys e es ic ed he abili y f s f eign fi ke such changes. In de change he nufac u e f an a ed duc f ne en i y an he , MHW equi ed he la e sub da a and inf i n and b ain a new sh nin. When he f was unwilling c e a e, he change was ex e ly difficul . me mme

The U.S. side s a ed ha such difficul ies in changing a als c uld ccu e en in cases whe e c cial ela i nshi s, such as licensing ag ee s n s, had been legally e mi na ed. In he U.S. iew a he e a ea ed, he ef e, be a c n adic i n be ween he c n ac ual ela i nshi g e ning w o business fi a and he i lied ela i nshi g e ned by he egula y a als he ms el es, wi h he la e c ne ing and ec ing ma ke igh s n c n e la ed by he f me .

The U.S. side s a ed ha his issue had se e al s ecific, ac ical i lica i ns f f eign fi ms a e ing d business in Ja an as f ll ws:

-- Un il 1975, in es me n es ic i ns unde he F eign Exchange C n l Law, which was changed in ha yea , gene ally es ic ed f eign fi f m ma king di ec in es n s in Ja anese duc i n facili ies. Thus, he inci al me ans f en y he Ja anese ke ha was a ailable was license duc i n Ja anese fi ms. The U.S. side s a ed ha fi ms which in es ed in lan s in Ja an af e 1975 we e able, bu f und i ex e me ly difficul and i -c nsu mi ng, b ain ma nufac u ing a al because unde he basic f a w o k f he PAL he ma nufac u ing a al has n s ela i nshi wi h a en s and si mi la ie a y igh s held by fi ms.

-- In 1983, h ugh a e isi n f he PAL, Ja an ag eed all w ma nufac u e s in f eign c un ies h ld sh nin in hei wn na s when i e s in Ja an i ed hei duc s unde alid ky ka. The U.S. side s a ed ha f eign fi which e i usly had ei he licensed duc i n in Ja an ke ed in Ja an h ugh Ja anese fi ms h lding he sh nin c uld n effec i ely ake ad an age f his 1983 change f e i usly a ed m

products U S sid also stat d t at t 1983 c ang t us appli d only to n w products import d and introduc d to t Japan s mark t by for ign firms for t first time

Mor g n rally, t U S sid not d t at MHW ad no mac in ry for t transf r (or r vocation and r issuanc to n w applicants) of s onin in any of t many situations in w hic c anging busin ss and commercial r lations ips would mak suc transf rs advantag ous for for ign firms w h n t y ld cl ar and l gally d monstrabl propri tary rig ts (g , pat nts) und r Japan s busin ss law .

is broad issu was a difficult on for bot sid s U S t am saw it primarily as on d aling wit int ll ctual prop rty, namely, t rig t of for ign firms to old and b n fit from t ir propri tary innovations as t y c oos , subj ct only to MHW's undisput d mandat to prot ct t alt and saf ty of t Japan s p opl

Japan s sid ass rt d t at it is most appropriat to r quir t manufactur r or import r, w ho is wit in t Japan s jurisdiction, to b ar all t r sponsibiliti s for fficacy, saf ty, and quality of t product in ord r to prot ct t alt and saf ty of t Japan s p opl For t at purpos , t r gulatory syst m r quir s t manufactur r or import r to obtain s onin and kyoka individually for ac product In ot r words, und r t PAL, MHW as t grav r sponsibility to confirm t at t manufactur r or import r as full knowl dg and information on fficacy, saf ty, and quality control of t product and is abl to do its busin ss und r all obligations impos d by t law . In t at s ns , t Japan s sid not d, t pr s nt l gislativ framework is most ffici nt, r asonabl , and practical in ord r to prot ct alt and saf ty of t g n ral public

Furt rmor , t Japan s sid comment d t at t PAL, a public law for alt r gulation, as no conc rn wit privat busin ss r lations ips or propri tary rig ts gov rn d by privat laws and l av s privat disput s for t Pat nt Law, t Civil Law, tc r for , t s onin do s not int rf r wit pat nts or propri tary rig ts

On t ot r and, t Japan s sid agr d to consid r simplification of r l vant documents and sp d up of approval proc dur s for c anging manufactur rs to t xt nt t at t y ar consid r d to b abl to tak t ir own r sponsibiliti s for public alt and saf ty

2 Agr d Approac

a ransf rs Wh n Bot Parti s Agr

transf r of manufacturing approvals will now b nabl d so t at firms can r gist r in t ir own names all rig ts and titl s to t ir products wit out aving to r g n rat and r submit data upon t t rmination of t r l vant busin ss r lations ip wit t former approval or lic ns old r It was agr d t at t transf r of manufacturing approvals is p rmitt d:

(1) Upon submission of a transf r notification wit accompanying documentation t at s ows t at bot parti s av agr d to t transf r; and

(2) Provid d t at t transf r r c iv s from t transf ror all data on t fficacy, saf ty, and quality of t r l vant p armac utical or medical d vic

Aft r t transf r, t product's r imburs ment pric will b list d at t same l v l as t at appli d b for t transf r Issuanc of kyoka and pric listing will occur at t time of a s onin transf r if an application for kyoka and notification ar r c iv d at l ast t r mont s prior to t dat of transf r Ot rwis , t kyoka will b issu d and t pric will b list d wit in t r mont s aft r t dat of application

r l vant r gulatory action tak n by Japan is as follows:

Minist rial Ordinanc No 26 (dat d: Jun 29, 1985; ff ctiv : July 31, 1985)

Notification No 658, "Impl mentation of t Minist rial Ordinanc for Partial R vision of t Enforc ment R gulations, P armac utical Affairs Law" (dat d: Jun 29, 1985; ff ctiv : July 31, 1985); No 1 (1) "It ms Conc rning ransf r of Approvals

b ransf rs Wh n Bot Parti s Do Not Agr -

In the ca e that th a tie d n t ag ee t the t an fe f manufactu ing imp t a val, if the a licant u mit data and inf mati n f the a val imila t that equi ed in the ca e f t an fe when th a tie ag ee, and at the ame time the iginal a val h lde cea e t manufactu e imp t the duct afte the new a val i g anted f the a licant, implificati n f a licati n d cument , and accele ati n f the a val ce , will ccu , with the ame effect and within the ame time e i d a in ca e 2a a ve. The eim u ement ice will e et at the ame level a f the evi u ly a ved duct within th ee month afte the new h nin i i ued.

c. T an fe f Manufactu ing t Imp ting and Vice Ve a

In ca e f changing manufactu ing t imp ting and vice ve a, a licati n equi ement and implified cedu e identical t th e in ca e 2 a ve will a ly. A a e ult, the ame effect a in ca e 2a a ve will e achieved.

ficial n tice implementing the cedu e de c i ed in a ag a h 2 and 2c a ve will e i ued in Ma ch 1986, t take effect n A il 1, 1986.

d. F ll w-u

The United State and Ja an have ag eed t c n ide e luti n f all ty e f t an fe ituati n n a ca e- y- ca e a i a they a i e within the f amew o k f the f ll w-u ce de c i ed in Cha te IV f the e t. B th ide a e c mmitted t finding actical luti n t legitimate u ine lems that a i e in thi a ea.

E. APPR AL AND REIMBURSEMENT F KITS

1. I ue V R

Among the many advance f mode n medicine and health ca e delive y ha een the eme gence n the w o ld ma ket f cedu e "kit " which c mbine medicine with thei delive y y tems in ingle ackage . Such kit gene ally ffe ima y advantage uch a h wn el w ve edece (n n-kit) delive y y tems:

(1) They mitigate infecti n i k ;

(2) They educe the i k f mi take in d age e a ati n ecau e d age a e eci ely e- ackaged:

(3) They e mit fa te eme gency t eatment;

(4) They gua antee imp ved t eatment quality;

(5) When u ed in clinic and h ital , they eliminate wa te and facilitate invent y c nt l, which lead t mate ial c t educti n; and

(6) They a e c nvenient, afe, and la - aving.

Du ing the MOSS di cu i n , the U.S. and Ja ane e delegati n a ce tained that Ja an did n t have fully c n lidated a licati n, a val, and icing cedu e f the kit , ecau e f thei di tinctive featu e a the unique c mbinati n f d ug and delive y y tems. A a e ult, the int ducti n f th e new techn l gy duct int the Ja ane e ma ket had een delayed. Yet uch cedu e needed t e w o ked ut in de f the kit t e a le t ente the Ja ane e ma ket mo thly.

The U.S. ide n ted that the f ll wing ecific difficultie needed t e lved.

C nce ning a val ,

(1) MHW had n time limit within which t decide whethe t a ve a kit.

(2) It equi ed manufactu e t g th ugh the enti e d ug a val ce f a kit even when the d ug ti n f the kit had al eady een g anted a val f imp tati n manufactu e. (the Ja ane e view n d ug a val, ee Secti n D, age 15.) O

n

(3) The s e it du manu cture, which is bec ming incre sing y c mmon s techn gy dv nces, w as ru ed ut.

C ncerning pricing,

(1) The he th insur nce reimbursement system c vered n y the drug p rti n it nd h d n mech nism r reimbursing the t t v ue the it s th t its se er c u d be de u te y c mpens ted.

(2) A me ns h d t be und r b sing reimbursement prices n the tru y inn v tive e ture it, n me y, the uni ue c mbin ti n drug nd de ivery system which gives the it its medic nd ec n mic dv nt ges.

2. Agreed Appr ch

. Appr v s

The G overnment J p n g ve the U.S. G overnment pr p s n the ppr v pr cedures r its. Acc rding t th t pr p s , MHW wi ccept pp ic ti ns r ppr v s r pr cedure its nd set reimbursement prices r its. Either the ma er the drug c mp nent the it r the ma er the device c mp nent the it may be the h der the ppr v s nd may be the manu cturer the c mp ete it.

MHW pr mised t c ri y the ppr v pr cedure r the it pr duct by issuing n ici n ti ic ti n. The c ntents wi be s ws:

(1) The it pr duct itse wi be tre ted s drug in the ppr v pr cess.

(2) When the manu cturer ph rmaceutic , wh h s re dy bt ined its ppr v , desires t manu cture it pr duct using the re dy ppr ved ph rmaceutic , he is re uired t see p rti modi ic ti n the ppr v the ph rmaceutic (the pr cessing peri d is within ne ye r).

(3) When manu cturer c nt iner nd s uti n (here ter re erred t s "device manu cturer") desires t m nu cture it, it sh pp y r n ppr v r the it nd rr nge r p rti modi ic ti n the drug ppr v , wing simp i ied MHW pr cedures. It is underst d th t ( ) the drug manu cturer is c nsidered the rm pp ic nt r the p rti modi ic ti n the drug ppr v , nd (b) the manu cturer pp ying r the it ppr v must supp y c pies the d t (deve ped by either p rty) supp rting the p rti drug ppr v nd the rigin sh nin he d by the drug manu cturer. B th ppr v s wi ccur t the s me time nd wi be pr vided by MHW within ne ye r.

The United St tes ccepted the pr p s with the wing greed c ri ic ti ns:

(1) Appr v re uirements re essenti y the s me r device nd drug manu cturers pp ying. F r pp ic ti ns r m device manu cturers, the tw o-p rt ppr v pr cedures wi be h nd ed simu t ne us y.

(2) Appr v s wi be gr nted in the s me peri d time irrespective whether n pp ic ti n is i ed by drug r device manu cturer, initi y n more th n ne ye r. MHW grees t ma e e rts t sh rten urther the pr cessing time nd intends t d s when e sib e.

(3) Either p rty, the device r drug manu cturer, may h d the manu cturing sh nin nd there re c n be the c nsign r.

(4) C mmerci rr ngements between the c nsign r nd the c nsignee wi n t be inter ered with by MHW. MHW wi regu te the re ti nship n y s reg rds the s ety nd e ic cy the it pr duct.

(5) C mmissi ned manu cturing is ccept b e r types its c vered by MHW's pr p s , which is intended t be gener s uti n r drug nd de ivery system c mbin ti ns. The neg ti ti ns h d cused n ur it types most c mmon y in use utside J p n nd the pr p s is b sed n these ex mp es. The neg ti t rs greed t ind in uture w-up t s pr ctic res uti n ny new pr b ems th t might emerge s it techn gy dv nces.

b. Pricing q

(1) The k duc self w ill be ea ed as a d ug n he e mbu semen sys em.

(2) C ns de ng he d s nc ve fea u e f he k duc , he e mbu semen ce w ill be se based n h ee c s elemen s 1) :he ce n he d ug a ff s anda d f he ha maceu cal c n a ned n he k ; 2) he ce n he d ug a ff s anda d f he s lu n c n a ned n he k ; and 3) he c s ce f he n n- ha maceu cal n wh ch sh ws he d s nc ve fea u e f he k duc . P c ng w ill be based n a f mula wh ch nc eases he sum f hese h ee elemen s by a f xed e cen age emium f he k duc demons a es ce a n f he med cal advan ages f m (1) (4) wh ch a e l s ed n he f s a ag a h f h s sec n. Th s emium, 3 e cen as a s anda d, can ange f m a min mum f l.5 e cen a max mum f 4.5 e cen de end ng n he s ze f he sum.

(3) When he d ug a ff s anda d s ev sed f ll w ing he nves ga n f ma ke ces f d ugs, he gene al calcula n ule f d ug ces w ill be a l ed f he k duc based n he ma ke ce f he k self, ega dless f he ce f ha maceu cals s lu n n he k .

c. Im lemen a n

Off c al n ces mplemen ng he ag eed a ach f handl ng a val f k s w ill be ssued n Ma ch 1986, ake effec n A l 1, 1986. When k s have been a ved acc d ng such cedu es, c ng w ill be execu ed n acc dance w i h he af emen ned ag eed a ach.

F. CHANGE OF COUNTRY OF MANUFACTURE

1. Issue

Lead ng ha maceu cal and med cal dev ce f ms f he w o ld e a e mul na nal manufac u ng e a ns and f equen ly sh f duc n l ca ns f m c un y c un y n es nse chang ng ma ke ng and he bus ness c nd ns. A he s a f he MOSS alks, MHW's egula y sys em equ ed he cedu e f mod f ca n f a val wheneve a f e gn f m w shed make such a change n manufac u ng s e f a ev usly a ved duc . The U.S. s de s a ed ha h s cedu e c ea ed an unnecessa y c s f d ng bus ness n he Ja anese ma ke , and eques ed ha MHW elax s a val mod f ca n equ emen s e mi f e gn f ms change c un y f manufac u e w i h s mple n f ca n MHW.

2. Ag eed A ach

F u ses f Ja anese egula n f f e gn med cal dev ce and ha maceu cal c mpan es, a change n he c un y f duc n f al eady a ved duc s w ill n w equ e s mple n f ca n MHW.

The elevan egula y ac ns aken by Ja an a e as f ll ws

-- M n s e al O rd nance N . 26 (da ed June 29, 1985; effec ve July 31, 19R55 :

-- N f ca n N . 658, "Implemen a n f he Min s e al O rd nance f Pa al Rev s n f he Enf cemen Regula ns, Pha maceu cal Affa s Law" (da ed June 29, 1985; effec ve July 31, 1985); N . 1 (2), "I ems Rela ed N f ca n f Changes n he S u ce C un y f Imp ng, e c., A vals."

G. MINOR PRODUCT MODIFICATIONS

1. Issue

Th s blem c nce ned MHW's handl ng f min duc mod f ca ns (e.g., c l changes n nfunc nal ex e nal des gn changes) ha d n affec safe y e f mance f med cal equ men , wh ch d d n equ e mod f ca ns f a val. MHW had n clea gu del nes f wh ch y es f duc changes equ ed mod f ca ns f a val. The c nsequence, n he v ew f he U.S. s de, was ha f e gn f ms faced en al unce a n es and d ff cul es a mp clea ance, and ha he n duc n n Ja an f duc s w i h min mod f ca n c uld be mpeded.

2. Ag eed A ach :

MHW has r irmed that mi r ha g s i medi al d vi s whi h d t a t sa ty a d i a y d t r quir kmodi i ati s appr val. T lari y guid li s, MHW has mad l ar by i ial ti xampl s mi r pr du t modi i ati s that d t r quir modi i ati s appr val. This i rmati has b suppli d t Cust ms auth riti s a d r lat d ag i s.

Th r l va t r gulat ry a ti ta by Japa is as ll ws: k

-- N ti i ati N . 155, "Ha dli g Appli ati s r Ma u a turi g r Imp rt Appr val Medi al D vi s" k (dat d: Ju 29, 1985).

H. CHANGE OF ADDRESS OF IMPORTER

l. Issu

Wh a imp rt r a appr v d medi al d vi r pharma uti al pr du t ha g s its addr ss i Japa , r purp s s th irmati that th stru tur a d quipme t its a ility ar mpatibl with th l gal sta dards as w ll as publi a u tability a d mai t a r l va t appr val r rds a d adv rs r a ti data, MHW r quir s th imp rt r t apply r a y a. Th U.S. sid stat d that MHW pr dur s i this ar a r quir d x ssiv d ume tati a d t aus d i t rrupti imp rt rs' busi ss p rati s.

2. Agr d Appr a h

Th U it d Stat s a d Japa agr d that (1) appli ati pr dur s r a ha g addr ss by imp rt rs as w ll as ma u a tur rs w ould b simpli i d by mitti g d ume ts that ar irr l va t t th ha g addr ss (su h as th s r lat d t it ms imp rt d, quali i ati t h i ia s, r physi ia 's rti i at), a d that (2) pri r appli ati r y a t ha g th addr ss was a ptabl i rd r t av id i t rrupti busi ss p rati s.

Th r l va t r gulat ry a ti s ta by Japa ar as ll ws:

-- Mi ist rial Ordi a N . 26 (dat d: Ju 29, 1985; tiv : July 31, 1985).

-- N ti i ati N . 658, "Impl me tati th Mi ist rial Ordi a r Partial R visi th E r me t R gulati s, Pharma uti al A airs Law" (dat d: Ju 29, 1985; tiv : July 31, 1985); N . 3, "Ha dli g Cas s Wh r Fa t ri s r Busi ss O fi s ar M ov d- -25

I. SIMPLIFICATION OF IMPORT CLEARANCE PROCEDURES

1. Issu

At th uts t th g tiati s, MHW r quir d imp rt rs t btai rti i at s r ust ms l ara thr ugh MHW i ials whi h sh w ed that th imp rt d pr du ts (a d th imp rt rs) mpli d with MHW r gulati s a d rmed with appli abl li s s (sh i , y a, t al.). Th U.S. sid said that th s pr dur s aus d stly d lays a d additi al admi istrativ w or r imp rt rs. With this i mi d, th U it d Stat s a d Japa dis uss d th simpli i ati imp rt l ara pr dur s r appr v d pr du ts thr ugh a si gl l ara by ust ms, as is d i th U it d Stat s.

2. Agr d Appr a h

It was agr d that:

-- Imp rts pharma uti als a d medi al d vi s will w b p rmitt d t pass thr ugh Japa s ust ms with ut MHW's i dividual rti i ati (as was rmerly r quir d) wh th imp rt r pr s ts a py th li s (sh i a d y a) r th ti i ati li i al trials pap r (as is r quir d u d r th Pharma uti al A airs Law).

Th r l va t r gulat ry a ti ta by Japa is as ll ws:

-- N ti i ati N . 667, "R qu st t Cust ms r C p rati Imp rt I sp ti Pharma uti als, t ." k (dat d: Ju 29, 1985; tiv : August 1, 1985).

J. HEALTH INSURANCE REIMBURSEMENT SYSTEM k

1. Issue

T e on l He l Insur nce sys em of J p n covers ne rly 100 percen of e J p nese popul on. T erefore, re mbursemen o p ys c ns, osp ls, nd cl n cs from e e l nsur nce sys em s domin n f c or n e marke en ry of p rmaceu c ls nd med c l dev ces.

T e U. . s de s ed fore gn manuf c urers of drugs nd dev ces ve d gre d ff cul y n unders nd ng ow MHW goes bou se ng re mbursemen r es nd del ys n se ng re mbursemen r es ve c used unnecess ry frus r on nd cos .

T e MO d scuss on n s re covered ree rel ed ssues: (1) e ming for se ng re mbursemen pr ces; (2) e cr er used n e off c l pr ce-se ng process; nd (3) e r nsp rency nd publ c v s b l y of e process, nclud ng ppropr e p r c p on n e process by ose w hose produc s re ul ma ely pr ced.

T e f rs ssue concerned bo e frequency of new pr c ng dec s ons nd e rel ed ques on of del ys be ween manuf c ur ng or mpor pprov ls nd e es bl s men of re mbursemen pr ces for pproved produc s.

In d scuss ng e second ssue, e U. . deleg on soug nforma on reg rd ng cr er n ev lu ng produc s for pr c ng dec s ons nd sked ese cr er be made publ c. T e U. . s de w as espec lly concerned bou one cr er on -- marke pene r on (.e., gener l ccep nce nd use of p r cul r produc by e J p nese med c l commun y). T s cr er on, e U. . s de dded, mpeded marke en ry bec use made pr c ng dec s ons d ff cul o ob n for nnov ve med c l ec nology no un formly v l ble roug ou J p n.

T e J p nese s de responded S s proper for MHW o judge w he er p r cul r med c l ec nology s ould be v l ble o e gener l publ c. T Se on l He l Insur nce sc eme covers ne rly 100 percen of e J p nese popul on nd, erefore, MHW mus be concerned w i equ y w hen judg ng ow bes o prov de n dequ e level of med c l c re for e people.

T e J p nese s de lso expl ned under new progr m n ed n Oc ober 1984, med c l dev ces ncorpor e g ly dv nced ec nolog es nd re n ended for use un vers y osp ls nd equ v len f c l es w il be rev ewed f er one ye r for re mbursemen by n exper s group of e C u kyo. If MHW concludes f er rece v ng s group's repor n em s ould be ncluded n e on l He l Insur nce sys em, re mbursemen pr ce w il be l s ed n e nex rev s on of e fees for med c l serv ces. T e re mbursemen sys em w il cover e nc ll ry cos s nvolved n us ng e dev ce dur ng e per od pr or o e C u kyo rev ew. Dur ng e course of e MO lks n 1985, 16 g ly dv nced med c l ec nolog es n 56 c ses 31 osp ls rece ved des gn on under s progr m.

D scuss on on e rd ssue revolved round s mil r reques -- no only dec s on cr er be made publ c bu lso ll n eres ed p r es be g ven oppor un y o prov de ppropr e nforma on nd rgumen on o respons ble u or es (nclud ng e C u kyo) n e pr ce-se ng process.

2. Agreed Appro c

T e Un ed es nd J p n greed on e ree ssues n e e l nsur nce re mbursemen re s follows:

(1) T e ming for se ng re mbursemen pr ces.

. ew drugs w il be regul rly l s ed four mes ye r n ccord nce w i e ming of manuf c ur ng or mpor pprov l for e purpose of e r f s er n roduc on n o e drug r ff f er e r pprov ls.

T ey w il be l s ed s soon s poss ble f er e r pprov ls, w i n 60 d ys n pr nc ple, nd no l er n 90 d ys.

T s pol cy w il be ppl ed for new drugs pproved n nd f er JFY 1986.

b. ew med c l dev ces nd n-v ro d gnos cs w il be ndled s follows, n ccord nce w i e med c l S ec nolog es for w h c ey ppl ed.

i. The highl ce me ic l tech olog is i iti ll i tro uce i to the s stem of "highl ce me ic l tre tme t" i which the b sic ch rges such s hospit liz tio fees re reimburse , fter MHW co sults with the expert group u er the huik o (the meeti g is to be hel o ce mo th). MHW will i tro uce the pro uct i to the ge er l reimburseme t s stem t the time of the re isio of the t riff for me ic l fees, if it recog izes the i tro uctio s ppropri te fter o e e r from esig tio s "highl ce me ic l tre tme t."

ii. Other ew me ic l tech ologies will be regul rl i tro uce i to the reimburseme t s stem four times e r.

Howe er, those for which ew poi ts shoul be pro i e u er the "fee-for-ser ice" reimburseme t s stem will be i tro uce i to the s stem t the time of re isio of the t riff for me ic l fees. New i o ti e i - itro i g ostics (l ss I IVDs) will be i tro uce i to the reimburseme t s stem withi six mo ths fter their ppro ls, with impleme t tio b MHW i JFY 1986.

(2) The criteri use i the offici l price-setti g process.

. Opportu ities for he ri g from foreig s well s omestic i ustr represe t ti es o ge er l issues of reimburseme t polic will be pro i e whe the formul for the re isio of the rug t riff st r or the c lcul tio formul for prices of ew rugs. e ch of which w as est blishe b the huik o i September 1982, re ch ge . The formul will be ma e public.

b. The ge er l rules for setti g re isi g prices of me ic l e ices i - itro i g ostics will be est blishe ou ce b MHW, fter co sult tio with the huik o, i JFY 1986.

(3) The tr sp re c of the process.

. The opi io s of foreig s well s omestic i ustr represe t ti es will be he r i the huik o, whe the ge er l rules of the t riff for me ic l fees or of the rug t riff re to be est blishe or ch ge .

b. Opportu ities to st te opi io s o their p rticul r pro ucts will be pro i e b MHW for i i i u l comp represe t ti es. The proce ures for he ri gs will be ma e public rules co cer i g the p rticip tio of the comp ies co cer e will be ma e.

i. At the he ri gs, testimo o the effic c , esire price, other spects reg r i g the pro uct bei g pplie for will be he r . The he ri gs will ot be ope to the public. If the origi tor so esires, he will be gi e the opportu it to tte with the pplic t comp to st te his opi io s.

ii. The te pl ce for the he ri gs will be ma e public t le st o e week or 10 s before the he ri gs t ke pl ce.

(4) The me sures liste i (2) (3) will be impleme te i JFY 1986 fter co sult tio with the huik o.

K. TRANSPAREN Y OF THE APPROVAL PRO ESS

(Note: The issue of tr sp re c i the price reimburseme t ecisio process is co ere i Sectio J o the he lth i sur ce reimburseme t s stem.)

1. Issue

The U ite St tes J p ffirme the import ce of tr sp re c i he lth c re regul tio , s emph size i the Jul 30, 1985 Actio Progr m.

At the st rt of the MOSS t lks, foreig firms felt th t the oper tio s of the PA MHW i the ppro l process were ot tr sp re t e ough th t the s stem ma e it u ecess ril ifficult to solicit timel rele t i formatio from them to tr smit publicl i formatio th t woul be of use to them. The U ite St tes J p iscusse w a s of i cre si g the tr sp re c of the regul tor process i J p for the be efit of J p ese foreig ma uf cturers of ph rmaceutic ls me ic l e ices.

Duri g the course of the t lks, the U.S. eleg tio ote with ppreci tio th t MHW h ste il i cre se both the freque c the ope ess of formal i formal iscussio o ppro ls other matters with foreig C

firms an ir r r s n a iv grou s. U.S. con ac s wi r r s n a iv s of for ign firms r v al a ig l v l of sa isfac ion on ar of os busin ss s wi is rogr ssiv a i u of MHW officials a all l v ls.

2. Agr A roac

Wi r gar o n w rug a roval roc ss, i was agr a :

T a lican will b giv n o or uni i s o ar ins ruc ions ir c ly from memb rs of CPAC, o ask qu s ions, an o mak commen s on Council's ins ruc ions.

T numb r of rsons an amoun of ime allo o ac a lican will b fix b for an .

T Council's "common ins ruc ions" will b ma ublic an me ings will b l o x lain m.

In a i ion, MHW will con inu i s succ ssful olicy of fr qu n , o n, informal xc ang s of informa ion an iscussion of r gula ory ma rs wi in us ry r r s n a iv s, bo in ivi ually an roug organiza ions suc as American C amb r of Commerc in Ja an (ACCJ) an conomic an commercial r r s n a iv s of U.S. Embassy. As no abov , is rogr ssiv a i u as on muc o romo armony an goo r la ions b w n in us ry r r s n a iv s an MHW officials a all l v ls.

T r l van r gula ory ac ion ak n by Ja an is as follows:

No ifica ion No. 664, ransmission of Ins ruc ions Conc rning N w Drugs, c., from C n ral P armac u ical Affairs Council" (a : Jun 29, 1985; ff c iv : July 1, 1985).

L. BLOOD PRODUCTS AND OTHER BIOLOGICAL PRODUCTS

1. Issu

T U.S. l ga ion s a a Ja an r r s n s an impor an mark for bloo an o r biological ro uc s an r for i s r gula ion of s ro uc s is impor an . In is vi w, alks focus on wo s ara U.S. conc rns:

T numb r an kin s of s s r quir of manufac ur r, impor r, an Ja an s Na ional Ins i u of H al (JNIH) for r l as of s ro uc s, an r sul an lays caus by r un an s ing; an

T r x or of bloo ro uc s an gr o whic for ign manufac ur rs can con rol ir inv n ori s for r manufac uring.

2. Agr A roac

Ex r s from FDA an MHW me in Rockvill , Marylan , in Nov mb r 1985 o iscuss r gula ory olici s of bo coun ri s conc rning s ing an r l as of bloo ro uc s. As a r sul , Ja an s Gov rnmen agr o mak following c ang s:

To work owar armoniza ion of in rna ional bloo s an ar s an limina obsol s s. A osi iv s in is ir c ion was ak n w h n MHW ublis r vis s an ar s for bloo ro uc s in Oc ob r 1985.

To carry ou ins c ions of for ign manufac uring facili i s o rmin complianc wi goo manufac uring rac ic s (GMP) r gula ions. As for bloo ro uc s whic r quir na ional s ing, MHW will acc s a a from firms in complianc wi Ja an s GMP s an ar s an will limina n for Ja an s impor r o r a s s b for a lying for na ional s ing by JNIH. For r s n , in g n ral, un r na ional s ing rogram, o ncy, s rili y, yrog ns, an abnormal oxici y will con inu o b rforme by JNIH. (T is measur will b come ff c iv A ril 1, 1986.)

On s con issu , U.S. si r cogniz Ja an s olicy whic in rinci l ro ibi s x or of bloo ro uc s. T Ja an s Gov rnmen o s rmi r x or a ion of bloo ro uc s in same form as y - wer impor an whic o no viola ir x or olicy, as in cas of bloo ro uc s in n for r manufac ur .

M. VITAMINS -

1. Issue

T e ese istoric lly ve used t ree criteri for regul ti g vit mi s: t e s e or form of t e roduct, (2) w het er dos ge is s ecified, d ( ) w het er t e ma uf cturer makes e lt cl im. Accordi g to MHW, if y of t ese criteri re likely to rovide t e ver ge erso wit t e u derst di g t t e time of s le t t t e subst ce s medici l ur ose, t e it is cl ssified s drug. T e criteri me tio ed bove re su orted by t e ese Su reme Court.

Wit i t e MOSS discussio s o t is issue, t e U.S. side first requested t t MHW cl rify its criteri for regul ti g vit mi s. U o recei t of t e cl rific tio , t e U.S. side furt er requested t t MHW elimi te s e d dos ge require3e ts to ermit t e s le of vit mi s s food su leme ts. Simil r roducts t t re sold s food su leme ts i t e U ited St tes re bei g regul ted s drugs i . T e U.S. side s id t t t ere re two difficulties i vi g roduct regul ted s rmaceutic l s o osed to food. First, le gt y rov l rocess exists for rmaceutic l roducts. Seco d, vit mi s regul ted s rmaceutic ls ve limited distributio system.

T e ese side s id t t i t eir view, t e regul tio of vit mi s must be decided o t e b sis of t e istoric l b ckgrou d d tio l recog itio of drugs i e c cou try. T erefore, it is impossible to c ge t e rese t ese criteri . I Euro e, e c cou try s its ow n system for regul ti g vit mi s. T e ese side s id t t t e U.S. regul tio is ot t e best bec use of roblems of overuse.

MHW ex l i ed to t e U.S. side its criteri used to regul te vit mi s. MHW lso ex l i ed t t t e rocedure to get remarket rov l of vit mi s s drugs is ge er lly simple d t t vit mi s regul ted eve s drugs re widely v il ble i rmacies d drugstores wit out rescri tio s i .

I dditio to t e regul tory co cer , t e U.S.- egoti ti g te m t ckled rel ted t riff issue. Vit mi re r tio s regul ted s drugs re subject to 4.9 erce t t riff r te. Vit mi re r tio s regul ted s foods, owever, re cl ssified s "miscell eous edible re r tio s d f ce 25-28 erce t t riff. T e ig t riff effectively makes foreig - roduced vit mi re r tio s u competitive i t e ese market. T e U.S. side st ted t t t e most ro ri te resolutio would be to elimi te t e regul tio of vit mi s s rmaceutic ls, but resolutio of t e regul tory issue, wit out resolutio of t e rel ted t riff issue, would cre te ot er roblem for foreig ma uf cturers w ho reviously imported roducts s drugs d id o ly 4.9 erce t t riff, d t e fou d t emselves yi g 25-28 erce t t riff to import t eir roducts s food.

2. Agreed A ro c

. FDA d MHW ex erts discussed regul tory issues i November 1985 i Rockville, M aryl d. I t ese discussio s, bot sides recog ized t t sig ific t differe ces exist i e c cou try's tio l ro c tow ard t e regul tio of vit mi s. As result, t e U ited St tes d ve greed to furt er meeti gs to ex lore d co sider ossible lter tives. Bot sides lso greed t t t e romisi g solutio to ex lore would be o e i volvi g regul tio of vit mi re r tio s s over-t e cou ter drugs, wit remarket rov ls to be made s f st s ossible. Amo g ot er dv t ges, t is ro c would remove t e ssoci ted t riff roblem, s suc re r tio s would co ti ue to be subject to t e 4.9 erce t t riff for drugs.

b. Wit reg rd to t e t riff issue, t t e e d of t e December t lks t e U.S. side rese ted list of vit mi roducts w hic rese tly re regul ted s foods. T e ese side greed to ex mi e t e matter s soo s ossible b sed u o t e materi ls rovided by t e U ited St tes.

c. T e two sides d difficulty i greei g o t e time sc edule for ll of t e issues, i cludi g t t described i r gr (b) bove. T e roblem w as t t t e issues d received t eir first i te sive discussio t t e ex erts' level i November 1985, d d ot yet bee discussed i y sig ific t det il t t e le ry, olitic l level of t e MOSS egoti tio .

T e two sides greed to old co ti ued t lks i t e ex erts' grou before t e first follow-u meeti g t t e le ry level is eld i 1986. T e e tire roblem of vit mi s will receive full vetti g i t e first le ry follow-u meeti g t t e olitic l level i 1986, t w hic time sc edules will be discussed d effort will be made to resolve t e roblem. 3

N. STABI IT AN ST I IT T STING

1. Issue

a. Accelerated Condition

In June 198 , MHW issued improved regulations for pharmaceutical products stored at room temperature which allowed the manufacturer to submit a new drug application accompanied by one-year interim stability data at room temperature and six-month accelerated stability data. For products which are not expected to be stable at room temperature, however (for example, products which require refrigeration), Japan had not defined acceptable accelerated test criteria. For such products, Japan required that the manufacturer wait until the full data of the long-term stability study under proposed conditions be available before submitting the new drug application. This meant that submission of the new drug application for such products had to be delayed until the real-time stability data had been generated.

b. Sterility Testing

Prior to the MOSS discussions, MHW regulations required that when an importer in Japan wanted to import an injectable product, the importer in Japan had to (1) have facilities to conduct sterility tests and animal tests, and (2) conduct them as acceptance tests. The regulation prohibited the foreign manufacturer or a third party in Japan from conducting these tests. The U.S. side said that when the importer did not have the facilities to conduct such tests, this requirement necessitated additional facilities investment which was both costly and time consuming.

c. Matrix Testing

The U.S. side raised the concern that in Japan real-time stability data had to be generated for all sizes and concentrations of drugs (including in-vitro diagnostics). In other words, the U.S. side believed that if a manufacturer produced a product with five concentrations and packaged it in five containers of different sizes, he had to generate real-time stability data for all concentrations at all sizes.

2. Agreed Approach

a. Accelerated Condition

 xpert-level meetings took place at F in November 1985. As a result of those meetings, the Japanese side agreed that regardless of whether or not the product is stable at room temperature, a new drug application can be submitted if it is accompanied by one-year real-time stability data, accelerated stability test data, and severe test data, as defined in MHW's notifications (No. 06, March 31, 1980, and No. 718, May 30, 1980). The method for conducting the accelerated study on the products which are not expected to be stable at room temperature can be decided by the manufacturer and will be evaluated by MHW on a case-by-case basis.

The applicant will be required to continue the real-time stability test to completion after the new drug application is submitted. All real-time data must be submitted to MHW and will be reflected in the approval.

This measure will be effective April 1, 1986.

b. Sterility Testing

Both sides agreed that sterility tests (and animal tests) for pharmaceuticals and medical devices can be contracted out to certain Japanese labs certified to conduct such tests. The importer, however, remains responsible for quality control of the products. This measure will be effective April 1, 1986.

c. Matrix Testing

As the result of the experts meetings, the Japanese side clarified for the United States that as of June 8, 198 , long-term stability tests are not required for all different concentrations and volumes of a drug. ong-term stability, severe, and accelerated tests are only required for one product considered to be most sensitive under the storage conditions, and only simple accelerated tests or relative comparison tests are required for all other 4

concentration an o ume a hown in the examp e be ow. The MHW proce ure wi permit ome f exibi ity in app ying the e tabi ity te ting tan ar when rea onab e groun exi t.

Vo ume

10ml 0ml 50ml

Concentration

5% (a)(b)(c) ( ) ( )

10% (c) ( ) ( )

0% (c) ( ) ( )

(a) Long-term tabi ity te t (b) Se ere te t

(c) Acce erate te t ( ) Re ati e compari on te t

I I I . TECHNICAL EXPERTS GROUP

During the cour e of the MOSS ta k , both i e agree that e era factua que tion rai e uring the i cu ion require the attention of technica expert . Con equent y, a technica expert ' group wa e tab i he to i cu the e etai e matter un er the in truction of the Japane e an U.S. e egation ea er . The e i cu ion pro e fruitfu an actua y e to the re o ution of certain i ue through c o e cientific con u tation at the technica e e , without requiring negotiation at the p enary e e . A a re u t, the two i e agree to continue the expert ' group' exi tence a a forum for imi ar i cu ion in the future. The group wi meet on an a hoc ba i a i ue ari e.

IV. FOLLOW-UP

A hown in the etai e e cription in Chapter II of the i ue i cu e in the e MOSS ta k an the agree approache to o ution , the ubject matter of the i cu ion wa high y comp ex. Agree o ution cou not in a ca e be ea i y re uce to imp e, comprehen i e tatement .

The thru t an intention of both i e in the ta k , howe er, wa to pro uce agreement that wou imp ify a mini trati e proce ure , e iminate a mini trati e e ay , increa e tran parency, further faci itate acce to Japan' market for me ica equipment an pharmaceutica , an thu trengthen the free tra e y tem with pecia reference to thi in u try ector. Gi en the e hare objecti e , both i e recognize that further i cu ion wi be require , a imp ementation continue , to i cu any comp ication that ari e an to han e re ate i ue that nee to be rai e an re o e . In ee , e era of the "agree approache " etai e in Chapter II make pecia reference to the negotiator ' commitment to fin practica o ution to rea bu ine prob ems, an to the anticipation that further i cu ion in a fo ow-up proce may we be nee e to obtain uch o ution .

To faci itate thi nee for ongoing i cu ion , therefore, both i e agree to che u e regu ar fo ow-up meeting , approximate y e ery ix month uring 1986 an on che u e to be eci e in ater year a nece ary, at ite to be eci e . The e fo ow-up i cu ion wi be at the p enary e e . The meeting wi re iew the imp ementation of the agree o ution ; re iew foreign firms' experience with the new ru e an proce ure that ha e been agree upon; an re o e any re ate i ue that may ari e a experience accumu ate .

V. GLOSSARY

Japane e Terms

Chuikyo -- The Socia In urance Me ica Affair Counci . A i ory bo y to MHW which e iberate the tota amount of reimbur ement an the genera ru e for reimbur ement price . The Chuikyo i ma e up of repre entati e of payer an payee of in urance reimbur ement, an of the pub ic intere t. 2

CPAC -- Cent P ceutic Aff i s Counci . Adviso y body to MHW w hic investig tes f o[m] scientific oint of view whet e it is pp op i te to pp ove nuf ctu ing o i[mp]o t of new p ceutic s o [me]dic devices

J Y -- J p nese fisc ye .

MHW -- Minist y of He t nd We f e.

NHI -- N tion He t Insu nce syste

PAL -- P ceutic Aff i s L w.

qu si-d ugs -- P oducts wit [mi] d effects on t e u n body, suc s [mo]ut w as es, b by powde s, etc.

ei bu se[me]nt p ice -- P ices given to p ceutic s, [me]dic tec no ogies, etc., by MHW fo ei[mb]u se[me]nt unde t e N tion He t Insu nce syste[m].

U.S. Te

DA -- ood nd D rug Ad[mi]nist tion.

ti[me] c ock -- Pe iod du ing w hic e t egu to y offici s ev u te [me]dic p oducts to dete [mi]ne s fety nd effic cy.s

Gene Te [ms]

bio ogic p oducts -- P oducts de ived f o[m] bio ogic sou ces, suc s p s , v ccines, etc.

c inic tests -- Tests pe fo [me]d on peop e to dete [mi]ne t e s fety nd effic cy of p oduct.

GMP -- Good nuf ctu ing p ctices.

IVDs -- In-vit o di gnostic e gents. P oducts used in outside-t e-body tests, suc s bbit se u[m] used fo u ine p egn ncy tests.

-too" d ugs -- Gene ic d ugs.

OTC d ugs -- Ove -t e-counte d ugs

p e-c inic -- A tests conducted p io to c inic testing, inc uding ni tests.

e
p ocedu e kit -- Co[mb]in tion of [me]dicines wit t ei de ive y syste[ms] in sing e p ck ge.

st bi ity tests -- Tests t t [me] su e ow ti[me], te[mp]e tu e, nd ot e conditions ffect t e qu ity (potency, etc.) of d ug co[mp]ounds.

st bi ity tests, cce e ted -- Tests t t si[mu] te t e conditions of e -ti[me] st bi ity tests in n cce e ted pe iod, p oducing co b e esu ts. An cce e ted st bi ity test y ep ic te in six [mo]nt s w h t e -ti st bi ity test wou d do in two ye s o e.

st bi ity tests, e -ti[me] -- St bi ity conducted unde t e ctu conditions (ti , etc.) fo w hic d t e being soug t to dete ne t e s e f- ife of p oduct.

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