Risk Assessment for Patients who have commenced Rabies PET in Another Country

1. Background

About 80% of patients requiring rabies PET in Ireland, will have already been assessed and commenced on treatment in the country of exposure, and will present to Irish healthcare requesting completion of their course of rabies PET, as advised by medical authorities in the country of exposure.

Each patient who has been commenced on rabies PET in the country of exposure should be risk assessed, on presentation in Ireland, to verify that:

- **They have received an approved vaccine**: It is important to confirm that the vaccine upon which they have been commenced is compatible with those in use in Ireland and the UK (see Section 3 - Post exposure vaccination regimes -below). The details of the vaccine should be checked, to determine if there is any question regarding the quality of the vaccine. Rarely, counterfeit rabies vaccines – which may have little or no capacity to generate an effective immune response - may be used to vaccinate exposed individuals. These are most likely to be encountered in low- and middle-income countries. The existence of such vaccines is one of the reasons why it is crucial to confirm authenticity of the vaccine used.
- **They were treated using an approved regime**: (see Section 3 - Post exposure vaccination regimes).
- **They are being treated in line with Irish guidelines**: it is important to check the frequency of the vaccination schedule they have been commenced is consistent with national guidance in Ireland. For example, an immunosuppressed individual may have been told they require a series of four vaccine doses in total, whereas in Ireland, they may require a total of five vaccine doses in total.

HRIG: If the person has sustained a Category 3 exposure, they may (in line with WHO guidelines) have received HRIG concomitantly with their first dose of vaccine in the country of exposure. However, if they have not been given HRIG, and more than seven days has elapsed since they received their first dose of rabies vaccine in the country of exposure, then HRIG should not be given in Ireland – even if initially indicated – as this may blunt the natural active immune response. In addition, by day 7, the body will have begun to mount its own immune response.

Individuals who have suffered an RPE in another country and have received PET should have their treatment recorded by the overseas authorities on the WHO's International Certificate of Vaccination (ICVP / "yellow card"). This is commonly not issued. The vaccinating hospital in the country of exposure should - at a minimum - provide the person with a discharge note and some details of biologics administered.

If indicated, **HRIG can be given for a period of up to one year following rabies exposure**. **There is no upper limit to the interval between clinically significant exposure and administration of vaccine,** as documented cases have arisen as long as 8 years post exposure and possibly longer.

2. Risk Assessment

This Risk Assessment should be carried out by the treating clinician. PET commenced in another country of exposure should, once the person has returned to Ireland, be continued in line with Irish national guidance.

1. Obtain (where possible) the following details from the patient:
    - The results of the risk assessment given to the person in the country of exposure (*have authorities in the country of exposure assessed and treated the patient in line with WHO recommendations?*)
    - Documentary evidence of vaccination history:
        - Vaccine type (see footnote for acceptable type of rabies vaccine)[1]
        - Intended schedule in country of exposure (*Is it WHO recommended and similar to Irish guidance; days 0, 3, 7 and 14 with HRIG on day 0 for high-risk exposures*?)
        - Date of first and any subsequent doses already administered
        - Seroconversion[2] (*if checked*).
    - Documentary evidence of HRIG/ERIG[3] History:
        - Given (*Yes/No*)
        - Amount, if known
        - If local infiltration was required (*Yes/No*)
    - The patient may possess documentation on vaccine batch numbers – record these.

2. However, if it cannot be verifiably established that:
    1. A validly approved course of PET has been commenced, with
    2. A compatible vaccine (see Appendix 1),

then the person must be considered unvaccinated and should undergo assessment using the standard national rabies risk assessment and commenced of an appropriate course of vaccine (and HRIG if indicated).

3. **Delays and Gaps in Vaccine Doses**

    If there has been a **short gap** between vaccine doses, this is not a reason to restart the course.

    - The most important dose is the first dose, and it should have been commenced as soon as possible following exposure.

[1] Modern cell-culture or embryonated egg-based inactivated rabies vaccines such as **HDCV**, **PCECV** and **PVRV** are considered by the WHO as safe and acceptable. Nerve tissue-derived vaccines such as mouse-derives SMBV **must not be used**.
[2] Testing for seroconversion following rabies vaccination is only undertaken in very specific circumstances.
[3] ERIG, or Equine Rabies Immunoglobulin, is a rabies treatment derived from horses and used in some countries for post-exposure prophylaxis, particularly in developing nations where HRIG might be scarce or expensive. WHO considers modern ERIG to be as efficacious and safe as HRIG, and an acceptable alternative to HRIG in resource-limited settings.

- Short delays (1–2 days), can be managed by continuing the course without restarting, administering the missed dose as soon as possible, and adjusting the subsequent intervals in accordance with the delay (i.e. if day 3 was delayed until day, 5 delay each subsequent scheduled dose by 2 days.)
- Delays up to a week need not mean restarting the still no need to restart the course, resume doses as soon as possible. Longer delays can be permitted later in the vaccination course, but not with earlier doses.
- However, restarting the course becomes necessary, if the person has a significant break early in the course (more than one week), particularly if there is no documentation of previous doses.

3. Post exposure vaccination regimes

1) Modified Essen Regime

Four doses of IM vaccine given on days 0, 3, 7 and 14-28.

This is the regime used in Ireland and the UK. It is used in much of Western and Northern Europe, North America, Australia, parts of the Middle East, and some urban centres in Asia. It is used in low rabies incidence countries since there are not the supply constraints that exist in other, higher incidence countries and is simpler to administer than other regimes. If the patient has been commenced on the modified Essen Regime in another country, this can be completed per Irish guidance.

2) Zagreb Regime

Four doses of IM vaccine given on days 0 (two doses, one in each deltoid), 7 and 21.

This is used in some Central and Eastern European countries and increasingly in Asia. It is used as the initial double dose induces a strong early antibody response; it is considered very effective for more high-risk exposures. **WHO considered the Zagreb and modified Essen Regimes to be equally efficacious**.

3) Intradermal Regimes

ID regimes are used in rabies-endemic, resource-limited regions (such as south and southeast Asia and in Africa) because they are dose-sparing and cost-effective. **These regimes are approved by WHO**. ID regimes are used because they require considerably less vaccine and are cost saving:

- Standard regime: 0.1ml ID over both deltoids on days 0, 3, 7 (6 doses)
- Thai Red Cross regime (older): 0.1ml ID in 2 sites on days 0, 3, 7, 28 (8 doses)

4) Continuing vaccination in Ireland if started on a regime other than modified Essen

Zagreb: If a patient presents having begun PET using the Zagreb regime, consider **each dose** as being equivalent to that on the modified Essen Regime. For example:

- If the patient presents having been vaccinated per Zagreb on day 0 (two doses) then they require follow up doses under the modified Essen regime on days 7 and 14-28.

Intradermal: If a patient presents having begun PET using an ID regime, then consider **each day's dose** as being equivalent to that on the modified Essen Regime. For example:

- If the patient presents having been vaccinated per an ID regime on day 0 (two doses) then they require follow up doses under the modified Essen regime on days 3, 7 and 14-28.

If the patient has been treated with a regime other than these, seek advice from Public Health, as such regimes may not meet WHO specifications.